ESPID19-0812
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Impact of a care bundle on hand hygiene compliance rates in 15 neonatal intensive care units in greece

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Background and Aims:

Healthcare-associated infections (HAIs) occur frequently in neonatal intensive care units (NICUs), causing significant morbidity and mortality. Hand hygiene (HH) is an important measure to prevent HAIs and avoid pathogen transmission. The aim of this study was to assess the impact of a care bundle on HH compliance rates in NICUs in Greece.

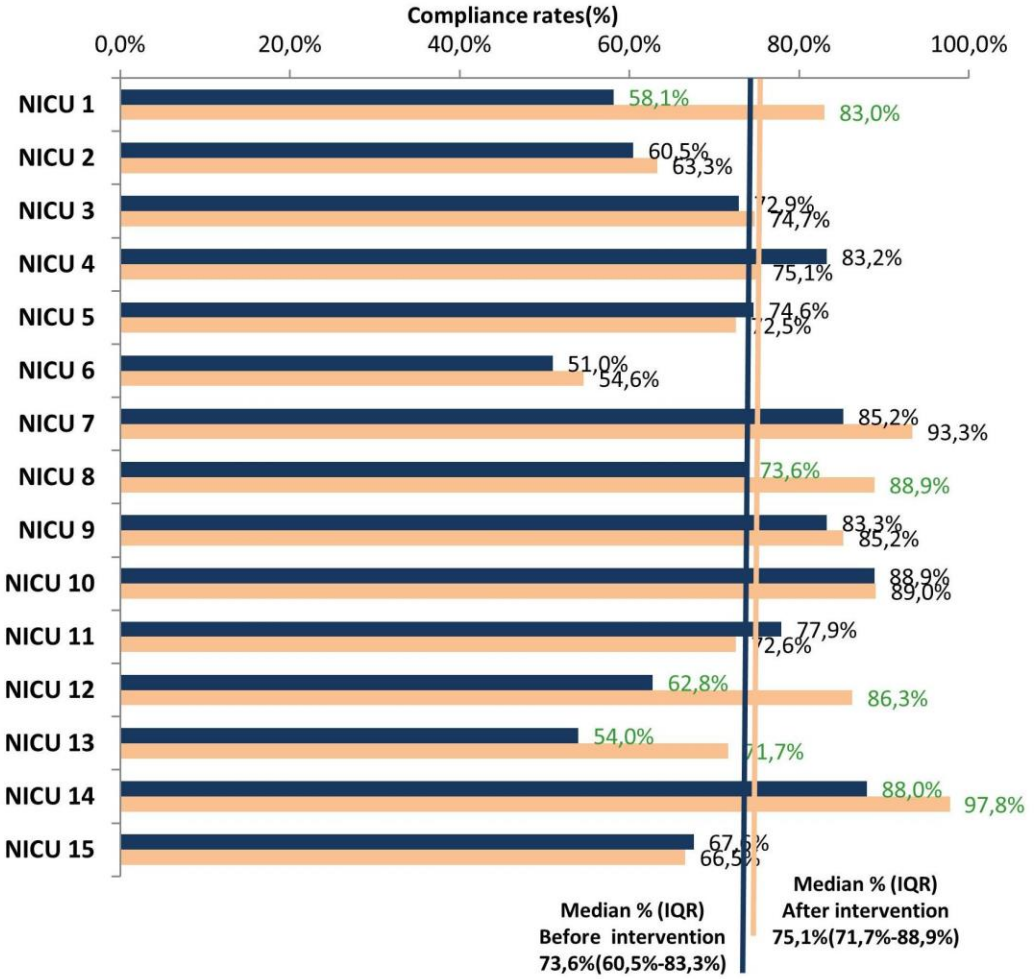
Methods:

A two phase (pre- and post-intervention) active surveillance mechanism for HH was established in 15 NICUs throughout the country. Observations were conducted from June 2016 to June 2018 using a data collection tool based on WHO guidelines. Compliance rate was defined as [(number of performed actions)/(number of opportunities)]x100. An intervention that included HH training as part of a care bundle for central line-associated bloodstream infections was implemented from March to April 2017 and consisted of on-site staff training, educational material, and reminders in the workplace such as posters,brochures and rulers representing ‘’The Five Moments of HH’’ and appropriate hand-washing technique.

Results:

A ≥10% increase in HH compliance rates was detected in five units, compared to the pre-intervention period. In no units was a decrease of ≥10% detected. The median (IQR) post-intervention HH compliance rate was 75.1%(71.7%-88.9%) while the median pre-intervention rate was 73.6%(60.5%-83.3%)(Figure 1). Stratified by type of professional, a ≥10% increase in HH compliance rates among doctors was observed in 5 NICUs and a decrease of ≥10% in only one. Similar results were found for nurses.

Figure 1: Hand Hygiene compliance rates before and after an implementation bundle in 15 NICUs



	NICU 1 N	NICU 2 N	NICU 3 N	NICU 4 N	NICU 5 N	NICU 6 N	NICU 7 N	NICU 8 N	NICU 9 N	NICU 10 N	NICU 11 N	NICU 12 N	NICU 13 N	NICU 14 N	NICU 15 N
After intervention	188	294	293	289	295	346	556	790	562	374	299	255	307	319	708
Before intervention	301	177	203	173	201	263	324	522	269	350	240	341	439	299	515

N: number of opportunities according to "My five moments for hand hygiene" of WHO
% compliance rate = (performed actions/ opportunities *100)
IQR: interquartile range
With green color depict ≥10% increase of compliance rate, while in red ≥10% decrease .

Conclusions:

The implementation of a care bundle in NICUs led to ≥10% increase in HH compliance rates in 1/3 of units indicative of difficulties in changing behavior in the workplace. Our data shows that consistent surveillance, staff training, and the use of reminders may result in significant improvement in HH compliance rates.

Systematic Review Registration:

N/A

ESPID19-0276
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Morbidity and mortality predictors in sepsis in pediatric intensive care unit (picu): an indian perspective

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Background

Sepsis and septic shock account high morbidity and mortality. This prospective study aimed to determine the incidence and bacteriological profile of sepsis in pediatric intensive care unit (PICU) with analysis of various morbidity and mortality predictors in Indian perspective.

Methods

Children admitted from January 2017 to December 2018 with clinical features of probable and proven sepsis were thoroughly investigated for any evidence of bacterial sepsis. Blood culture specimens were collected as per protocol; identification of organisms and their antibiotic susceptibility pattern detection was done. Data were analysed by student *t*-test and ANOVA test.

Results

Incidence of septicemia was 13.6%. The main etiologies in community sepsis were *S. pneumoniae* (54.2%) and *Klebseilla pneumoniae* (35.8%). *S.aureus* and *P.aeruginosa* were common nosocomial infections. Blood culture was positive in 49.2% of septicemic neonates. In cephalosporins, cefoperazone and cefotaxim both have activity against *Klebseilla* and CONS, while ceftazidime showed better results against *Klebseilla*, *E.coli*, *Pseudomonas* and unidentified gram negative bacilli. In aminoglycosides, amikacin has much better results than gentamicin ($p<0.01$). Piperacillin had better advantage over ampicillin ($p<0.01$). Vancomycin had good activity against gram positive organisms (Enterococcus, CONS and MRSA). Multivariate analysis showed that presence of underlying disease, nosocomial infection, septic shock and multiple organ failure were variables that were independently associated with mortality risk. The PRISM score; need of mechanical ventilation; C-reactive protein (CRP), serum lactate & lower platelet count on admission were associated with poor outcome with more length stay and more sequelae.

Conclusions

Patients with sepsis and multiorgan failure, especially nosocomial and higher values of PRISM, CRP and lactate, are at greater risk of poor outcome and should therefore be carefully monitored and treated.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-1182
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Risk factors for carbapenem-resistant enterobacteriaceae colonization in a paediatric portuguese population

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Background and Aims:

Carbapenem-resistant Enterobacteriaceae (CRE) infection and colonization are increasing worldwide, although data on paediatric epidemiology remains poorly described. The aim of our study is to characterize risk factors for CRE colonization and describe the natural history of paediatric decolonization.

Methods:

A matched case control study, from June to December 2018, was conducted in a tertiary Portuguese hospital. Cases were defined as CRE-colonized patients, detected by molecular methods, and were individually matched to 3 CRE-negative controls by the same age, ward and admission period. Risk factors for colonization were evaluated using bivariate logistic regression.

Results:

During the 7-months period of study, 17 CRE were identified, with one case of KPC osteomyelitis excluded. Sixteen cases of CRE colonization (8 KPC, 7 VIM and 1 OXA-48) in 15 patients were enrolled, and matched to 48 controls.
Hospitalization in the previous 3 months (OR,6.7; 95%CI 1.3-16.3; p=0.003), patient comorbidities (OR,11.7; 95%CI 2.4-57.4; p=0.003), intensive care admission (OR,4.3; 95%CI 1.3-14.3; p=0.016) and invasive devices (OR,3.9; 95%CI 1.2-12.6; p=0.002) were identified as risk factors. All colonized patients were previously treated with antibiotics, and an association with penicillins (OR,6.6; 95%CI 1.8-23.9; p=0.004) and aminoglycosides (OR,5.6; 95%CI 1.6-18.9; p=0.005) was found. Spontaneous decolonization occurred within the first 15 days, 1, 2 and 3 months in 21%, 50%, 78% and 100% of cases, respectively.

Conclusions:

Previous hospitalization, invasive procedures, antibiotic therapy and comorbidities play a role in the development of CRE colonization in children. Outpatient care encouragement, antibiotic stewardship with shorter IV courses are essential to control this spreading threat, mainly in chronic patients. All patients presented spontaneous decolonization in a 3-months period, suggesting that pediatric carriage resolution may occur more promptly than the described protracted course in adults.

Systematic Review Registration:

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ESPID19-1103
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

A picture of febrile children in a pediatric emergency department and relative antimicrobial prescribing rates

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Background and Aims:

Fever is one of the most common reasons for referring children to the Emergency Department(ED). The burden of work and the inability to carry out control visits, may lead the attending pediatricians to over-prescribe antimicrobial therapies. We therefore conducted a monocentric retrospective observational study to take a picture of the antimicrobial prescription in our pediatric ED.

Methods:

We reviewed electronic records of children (age < 18) who were conducted in the first three months of 2017 to the pediatric ED of our tertiary care hospital in Bologna, Italy. We included in the study all the children who presented or reported a body temperature >37,0°C and who were not admitted to the ward. We collected discharge diagnosis and antimicrobial prescriptions.

Results:

1588 children were enrolled. The main causes of fever were: upper respiratory tract infections(URTIs) n=530(33.3%), lower respiratory tract infections(LRTIs) n=232(14.6%), tonsillitis n=171(10.7%), acute otitis media n=155(9.7%), community acquired pneumonia n=119(7.4%), gastroenteritis n=303(19%) and urinary tract infections n=22(1,4%). Antibiotic prescription rate was 855/1588(53.8%). Amoxicillin was prescribed in 335(39.2%) cases, followed by amoxi-clavulanate (294 cases, 34,4%). The antibiotic prescription rates for URTIs and LRTIs were 201/530(38,0%) and 186/232(80,2%), respectively. Prescription of domiciliary intramuscular ceftriaxone for pneumonia was also noteworthy (65/1588 [7,6%]).

Conclusions:

More than half of the children discharged by our ED received an antimicrobial prescription, despite the fact that most of them had a diagnosis of a mild respiratory infection (URTI or LRTI) that, generally, has viral aetiology. Furthermore, there was a high rate of broad-spectrum antimicrobials prescription. Promoting guidelines application, implementing tools to discriminate viral infections and informing about local prevalence of antimicrobial-resistance are fundamental strategies needed to limit antimicrobial abuse and reduce the risk of antibiotic resistance.

Systematic Review Registration:

N/A

ESPID19-1037
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Prospective surveillance of antimicrobial use and antimicrobial resistance of pathogens in paediatric intensive care units in greece: a multicentre study

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Background and Aims:

The indiscriminate use of broad-spectrum antimicrobial agents in community, general hospitals, and paediatric intensive care units (PICUs) promotes the emergence of multidrug resistant pathogens. The objective to quantify the antibiotic use and antimicrobial resistance in PICUs in Greece.

Methods:

Prospective surveillance study (July-December 2017) conducted in four PICUs (two in children's and two in general hospitals) in Greece, using European Centre for Disease Prevention and Control (ECDC) HAI-net ICU protocol, version2.2. Included patients were 1month to 18year-old and admitted for >48 hours to PICU. Medical records were assessed daily. Antibiotic drug use data and isolated pathogens with antibiogram results were collected

Results:

Overall infection rate was 26.1 per 100patient-days. 40 organisms were isolated: Enterobacteriae spp 40%, Acinetobacter baumannii 12.5%, Pseudomonas aeruginosa 22.5%, with resistance to carbapenemes 43.8%, 80% and 33.3% respectively, Staphylococcus spp 12.5% with 60% resistance to oxacillin, and other 12.5%. Overall antimicrobial use was 2,139 days of therapy (DOT) per 1000patient-days. Most commonly prescribed agents were cephalosporines, glycopeptides, aminoglycosides, carbapenemes, colistin and tigecycline with 332, 320, 234, 234, 124, and 115 DOT per 1000patient-days respectively. Types and amounts of antibiotics differed among PICUs ($p<0.001$). PICU settings in exclusively children's institutions compared to general hospitals had lower rates of antimicrobial use (1,301 vs 2,792 DOT per 1000patient-days, $p<0.001$) and lower resistance ($p<0.001$).

Conclusions:

This is the first attempt to estimate antimicrobial use practice and the burden of pathogen resistance in PICUs in Greece. These data may be useful for implementation of antimicrobial utilization and infection control bundles.

Systematic Review Registration:

non applicable

ESPID19-1032
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Identifying targets for improvement of perioperative antimicrobial prophylaxis in a tertiary children's hospital

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Background and Aims:

Antibiotic overuse has led to the development of multidrug resistant microorganisms with an impact on patients' length of stay and hospital costs. Perioperative Antimicrobial prophylaxis(PAP) is the administration of antibiotics before an operation to help prevent surgical site infections. We sought to describe practices in a surgical department of a tertiary Children's hospital in Greece in order to identify targets for improvement of judicious antibiotic use.

Methods:

All operations performed in the ENT department of a tertiary Children's hospital were recorded prospectively between 01/08/2018-31/10/2018. Data recorded included patient demographics, type of operation and wound class, antibiotic agents administered along with time, dose and duration, as well as reasons for continuation after the surgery. Study data were collected using REDCap electronic data capture tools.

Results:

130 surgeries were recorded: 52(40%) adenoidectomy with tonsillectomy, 13(10%) adenoidectomy, tonsillectomy and myringotomy, 15(11.5%) tonsillectomy, 10(7.7%) adenoidectomy, 10(7.7%) adenoidectomy and myringotomy, 8(6.1%) myringotomy and 22(17%) were other operations.

Of 108 patients that underwent tonsillectomy,adenoidectomy, myringotomy in any combination, 57(52.7%) received no antibiotics. 47(43.5%) patients were administered 'antibiotic prophylaxis' after the end of the operation; in 34(72.3%) of these, antibiotics were initiated the day after the operation. In all cases the duration of the regimen was 7 days. In 40/47 cases antibiotics were initiated after discharge. 1(1%) patient received treatment due to the development of fever and 3(2.8%) due to pre-existing infection.**Conclusions:**

We identified injudicious antibiotic use regarding perioperative prophylaxis both in the indication(type of operation) as well as in the time of initiation and the duration of the regimen prescribed. These targets will be used to educate the design of an intervention with the aim of decreasing unnecessary antibiotic use and to improve the quality of healthcare provided.

Systematic Review Registration:

N/A

ESPID19-0982
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Antibiotic treatment in abdominal collection following acute appendicitis in children

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Background and Aims:

Abdominal collection following appendicectomy in children is an important cause of morbidity. Patients can be managed conservatively with antibiotics. Hospital guidelines recommend 24 hours of co-amoxiclav and gentamicin as first line treatment for simple appendicitis and five to ten days of antibiotics postoperatively in complicated appendicitis. The aim of this study was to describe antibiotic use in the context of appendicitis and postoperative collection.

Methods:

Data were collected retrospectively from medical records of paediatric patients undergoing appendicectomy over a 12-month period; September 2016 - August 2017 inclusive. All patients who underwent emergency appendicectomy at Evelina Children's hospital for histologically confirmed appendicitis were included in the study (n = 82). Patients were divided into two groups based on histology; simple (A) and complicated (B) appendicitis.

Results:

Overall, 63.6% of postoperative collections were managed conservatively. Intra-operative peritoneal fluid samples were sent for microbiology investigations in 52.4% of cases; 67.4% showed growth of at least one organism. The most common organisms were *Escherichia Coli*, *Streptococcus milleri* and *Pseudomonas* species. In four cases, treatment differed from recommended antibiotics following input from paediatric infectious disease specialists (figure). Patients received longer courses of antibiotics than recommended; specialist input was seldom documented for these cases.

Conclusions:

These data suggest that the recommended antibiotic treatment is adequate in managing appendicitis and postoperative collection. Where changes to treatment are required, microbiology samples remain important to guide these with input from paediatric infectious disease specialists. Extended courses of antibiotics are sporadically discussed with the specialist team and may lead to over-treatment. Changes to current practice are required to ensure antibiotic use is appropriate; including early paediatric infectious diseases specialist input in patients who may require alternative treatments.

Systematic Review Registration:

N/A

ESPID19-0916
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Perioperative antimicrobial stewardship in pediatric liver transplantation in bambino gesù children hospital: a retrospective study.

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Background

Bacterial infections are a leading cause of morbidity and mortality among solid organ transplant recipients. The aim of this retrospective study is to evaluate the results of a strict protocol of infection monitoring after pediatric liver transplantation in terms of reduction of inappropriate antimicrobial prescription in the postoperative period.

Case Presentation Summary

We analyzed 44 pediatric patients who underwent cadaveric or living donor liver transplantation from January 2017 to December 2018. All patients received antimicrobial prophylaxis for 5 days with amoxicillin/clavulanic and cephoxitine and were divided in 2 groups. Group A (January to December 2017): In 28 consecutive patients, blood and urine cultures were collected on post operative day (POD) 7 and /or in case of fever. All patients in this group underwent serum dosage of fungal antigens, hepatotropic viruses on POD 7. Empirical antimicrobial therapy was started in case of fever and/or leukocytosis and antimycotic therapy was started if serum level of fungal antigens were found above reference level. Group B (January to December 2018): in 18 consecutive patients a prospective protocol for infection monitoring was followed: blood and urine cultures were collected on POD 1 and 7 and then once a week. Blood samples for detection of hepatotropic viruses were collected on POD 4 and then every week. Further blood cultures were collected in case of fever.

Learning Points/Discussion

Based on this experience:

- In group A, out of 26 liver transplant recipients, 61,5% received empiric antimicrobial therapy without any evidence of infection.

- In group B, out of 18 patients only 44,4% started empiric antimicrobial therapy while 27,7% of patients with fever received a diagnosis of viral infection thus avoiding empiric antimicrobial therapy. A strict infectious monitoring allowed avoiding a non needed antimicrobial treatment.

ESPID19-0769
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Stool culture results from a district general hospital in crete, greece

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Background and Aims:

Acute gastroenteritis is a common cause of paediatric morbidity, especially under the age of 3 years old. Causative pathogen is identified in 45-75% of cases. Rota virus remains the most common pathogen, while bacterial gastroenteritis is less common, with Salmonella being the main representative.

The aim of the present study was to report the pathogens from stool samples among hospitalized children with acute gastroenteritis.

Methods:

This 5-year (2013-2017) retrospective study recorded pathogens from stool cultures among children 30 days to 16 years old, with acute gastroenteritis, who were hospitalized in a District General Hospital in Crete.

Results:

Acute gastroenteritis was diagnosed in 632 children (63,5% males, 53,4% infants). Causative pathogen was found in 199 from 632 stool samples, while bacteria were recorded in 69% and viruses in 31% of them. Rota virus was recorded in 58,7%, Adeno virus in 28,3% and both viruses in 13%, among cultures with viral pathogens. 84,6% of Adeno positive and 59,5% of Rota positive cultures were recorded in infants. The occurence rates of isolated bacterial pathogens were: Salmonella enterica 38,2%, Staphylococcus aureus 25,5%, Escherichia coli (EPEC) 21,6%, Clostiridium difficile 5,9%, Yersinia enterocolitica 4,9%, Shigella spp 3,9% and Campylobacter jejuni 3,9%. 65% of cultures with identified pathogen and 85% of Salmonella positive cultures were found in summer period.

Conclusions:

Salmonella enterica remains the major pathogen of bacterial gastroenteritis, especially during summer. Adeno and rota viruses are more common among infants < 1 year old.

Systematic Review Registration:

N/A.

ESPID19-0657
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Comparison of antimicrobial utilization metrics in paediatrics: days of therapy versus defined daily doses

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Background and Aims:

Antimicrobial utilization is usually expressed as the World Health Organization (WHO) Daily Defined Doses (DDD), which is the “assumed average maintenance dose per day for a drug used for its main indication in adults”. An alternative metric, such as Days of Therapy (DOT) has been proposed for use in paediatrics. However, discordance between both metrics has only been studied in adults. We aim to determine the degree to which DDD agrees with DOT in paediatrics.

Methods:

DDD and DOT data, standardized to 100 patient-days, of 10 common intravenous antibiotics were obtained from electronic medical administration records from 2015 to 2017. Comparison of both metrics were performed by linear regression.

Results:

The DDD and DOT estimates for Ciprofloxacin, Ampicillin, and Ceftriaxone were relatively similar, as there is a wide dosing range per body-weight for these antibiotics in children. However, DOT exceeded the DDD estimates for Benzylpenicillin G, Gentamicin, Amikacin, Vancomycin, Meropenem, Piperacillin-Tazobactam, and Amoxicillin-Clavulanate, The usual paediatric doses for Benzylpenicillin G and Gentamicin (2 commonly used antibiotics for neonatal pyrexia), Piperacillin-Tazobactam, and Amoxicillin-Clavulanate are markedly lower than the WHO DDD. On the other hand, DOT estimates are only 32% and 38% greater than the DDD estimates for Amikacin and Vancomycin respectively, as therapeutic drug monitoring based on patient-specific pharmacokinetic parameters is routinely performed, with paediatrics frequently requiring higher-than-usual adult doses, due to faster drug clearance. The DOT estimate is only 24% greater than the DDD estimate for Meropenem, as the WHO DDD is markedly lower than the usual doses in clinical practice.

Conclusions:

DDD estimates, standardized to 100 patient-days, frequently underestimates antimicrobial utilization in paediatrics for most antibiotics, as they do not take into account the range of doses per body-weight.

Systematic Review Registration:

N/A

ESPID19-0627
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Mrsa colonisation on the neonatal and paediatric intensive care unit: the maltese perspective

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Background and Aims:

Methicillin-resistant *Staphylococcus aureus* (MRSA) colonisation is a challenge in healthcare institutions worldwide. Colonisation may progress to infection, leading to significant morbidity, and children needing intensive care are at a particular risk. In this retrospective study, we determined the rates of MRSA colonisation and infection from 2012 to 2015, on the only neonatal and paediatric intensive care unit (NPICU) in Malta.

Methods:

All MRSA isolates from sterile and non-sterile sites in children admitted to NPICU between 2012 and 2015 were collected. The rates of MRSA colonisation on admission, MRSA colonisation acquired during hospitalisation, and MRSA non-invasive and invasive infections were calculated. The Chi squared test was used to assess differences between the study years. Mean local rates were compared to rates of MRSA colonisation reported in units in North America, Asia, and Europe between 2001 and 2010.

Results:

The mean rate of colonisation on admission was 3.71% (95% CI 2.17%-5.25%), which is higher than the pooled prevalence rate of MRSA colonisation on admission of 1.9% ($p=0.04$) in other units within Europe. The mean rate of acquired colonisation was 14.60% (95% CI 6.16%-23.04%), also higher than the pooled acquisition rate of MRSA colonisation of 4.1% ($p<0.001$) in units within Europe and the US. There were no cases of invasive MRSA infection, whilst the mean rate of non-invasive infection was 0.77% (95% CI 0.54%-1.01%).

Conclusions:

More efforts need to be taken to adhere to infection control measures in order to decrease the rate of acquisition of MRSA colonisation on the Maltese NPICU. Newer molecular diagnostic techniques, more efficient decolonisation regimes, and local epidemiology must be researched. A local guideline specifically targeted for MRSA colonisation and infection in the NPICU may need to be set up.

Systematic Review Registration:

NA

ESPID19-0514
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Cognitive function in children with hiv

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Background

It is well established from studies in adults that HIV is associated with reduced cognitive function however the pathophysiology of this process is poorly understood. Cognitive assessments of HIV positive children are carried out when a concern has been raised by school, parents or clinicians in services where there is access to a Clinical Psychologist. Such data may be useful in establishing the onset and trajectory of impairments and thus contribute to our understanding of its cause, prognosis and management.

Case Presentation Summary

Over a 5 year period, data were collected from all HIV positive children referred for cognitive assessment as part of their clinical management. A total of 25 children were assessed, with an age range of 6 to 16 years old. Assessments were carried out by a specialised Paediatric Clinical Psychologist using the Wechsler Intelligence Scale for Children (WISC) and the Wechsler Individual Achievement Test (WIAT). As expected, the group scored poorly in comparison to the standardised population norms. Older children showed more marked deviation from the population mean than the younger ones in the cohort. Interestingly, academic achievement in literacy appeared to be a strength for many, with some scoring well above the standardised average despite otherwise showing significant cognitive delay.

Learning Points/Discussion

Formal observational studies involving larger numbers of children are required to describe the impact of HIV on the cognitive performance of children. Such studies should also attempt to describe biological and social factors which may be linked to this progression. Through better understanding of the nature and prognosis of HIV-associated cognitive impairment in children, clinicians might better council families following cognitive assessment and enable meaningful support to be put in place earlier in children's schooling.

ESPID19-0501
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

The perceptions of healthcare workers from english hospitals on the use of rapid point-of-care tests for the clinical management of febrile children: a qualitative study

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Background and Aims:

Distinguishing between self-limiting viral illness and bacterial infection is difficult in children. Consequently, antibiotics are overprescribed. The WHO recommends introducing rapid point-of-care tests (POCTs) to improve antibiotic stewardship. The impact of POCTs depends partially on their adoption by clinicians. We aimed to explore the perception of healthcare workers regarding the use of POCTs in children to identify factors that influence their adoption.

Methods:

Using purposive sampling, 35 paediatricians and nurses with ranging clinical experience were recruited from two hospitals in England (London and Newcastle) to participate in in-depth one-to-one interviews. The interviews were audio-recorded, lasting between 45 to 60 minutes each, and transcribed by the interviewers. A thematic analysis approach was used to iteratively identify themes that are important to healthcare workers.

Results:

Participants felt that point-of-care testing could improve the management of febrile children by decreasing diagnostic uncertainty, speeding-up the medical decision-making process, and enhancing their ability to identify children who require antibiotics. However, they perceived that most current diagnostics, particularly POCTs, were not accurate enough to fulfil these purposes. This made them prioritise their clinical judgement over diagnostic tests. Moreover, participants feared that the scaling-up of POCTs may lead to their overuse because they are easy to use. Finally, the provision of training, the inclusion of POCTs in guidelines and allowing nurses to use POCTs were recommended to facilitate their implementation.

Conclusions:

Clinicians perceived potential benefits of introducing POCTs in the management of febrile children. However, they felt that making the shift from reliance on clinical judgement to reliance on POCTs requires a substantial improvement of POCTs accuracy. In addition, clinicians required training and guidance, and suggested that allowing nurses to use POCTs may facilitate their adoption in clinical practice.

Systematic Review Registration:

NA

ESPID19-0494
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Antimicrobial stewardship program in a pediatric intensive care unit

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Background and Aims:

Background
The majority of patients in the pediatric intensive care unit (PICU) are critically ill; thus, antibiotic stewardship poses a special challenge in such patients, physicians must balance concerns about antimicrobial resistance with the use of broad-spectrum antimicrobial agents. In our hospital intensive care unit, we started an antimicrobial stewardship program (ASP) with infection consultation in April 2016 and published an original guide to perioperative prophylactic antibiotics in June 2017.
Objective
To evaluate antimicrobial utilization and prescription practices in a PICU after implementation of an ASP and perioperative antibiotic guide.

Methods:

Design: Retrospective chart review before and after intervention
Setting: PICU and cardiac intensive care unit(CICU) in a tertiary children's hospital
Methods: Outcome measures are listed below
1 An interrupted time-series analysis was used to evaluate change in consumption of carbapenems, as measured by days of therapy (DOT) per 1000 patient-days (PD) (DOT/1000 patient-days) for each unit. We also evaluated the length of ICU stay, all-cause ICU mortality, and hospital mortality.
2 The time period before and after implementing the prolongation of perioperative prophylactic antibiotics measured by the number of perioperative antibiotics administrations.

Results:

Result
1 At 2017, DOT of carbapenem achieved a 90% decrease compared to 2014 (PICU DOT;115.8→10.2 /1000 PD, CICU DOT;36.7→3.3/1000PD)
There were no statistically significant differences in the length of stay in each unit and hospital; mortality rate was also not significantly different
2 The number of perioperative prophylactic antibiotics decreased for each surgery after the implementation of ASP (pediatric surgery: 5→4times, pediatric cardiac surgery: 9→6 times)

Conclusions:

Conclusion
Our ASP intervention reduced the use of broad-spectrum antimicrobials with no change in length of stay and mortality rate. The use of perioperative antibiotics was also reduced through the announcement of the guide.

Systematic Review Registration:

ESPID19-0464
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Differential diagnosis of children influenza and other acute viral upper respiratory tract infections

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Background

To evaluate clinical manifestations and laboratory parameters between children with influenza and other acute viral upper respiratory infections (OURI).

Methods

A retrospective study was performed during 2017/2018 influenza season. In total 438 children with suspected influenza were enrolled, among them 225 (51.4%) boys and 213 (48.6%) girls. Influenza was confirmed by rapid antigen test in 352 (80.4%) and OURI was diagnosed in 86 (19.6%) patients.

Results

Influenza was more often in 6-12 years of age group (38.6% of all influenza patients). OURI was more common in children under 2 years of age (43%).

Main clinical symptoms in influenza patients as compared to OURI were as follows: fever (100% *vs* 97.7%, p=0.04), cough 56.8% vs 39.5%, p=0.004), sore throat (15.6% *vs* 7.0%, p=0.38), hyperaemia of throat (87.8% *vs* 73.3%, p=0.001) skin rash (17.4% *vs* 9.9%, p=0.05). Complications developed in 21.9% patients of influenza group and 12.8% - in OURI.

There were some differences in the blood count in children above 2 years of age. Neutropenia was more common in children with influenza (20.2% *vs* 15.5%, p=0.02), neutrophilia and monocytosis in OURI group (22.6% *vs* 8.9%, p=0.02 and 41.7% vs 23.9%, p=0.003, respectively). There was no significant difference in C-reactive protein.

Conclusions

The incidence of influenza is increasing in children under 12 years of age and the incidence of OURI decreases with increasing age of children. There were no significant differences in clinical manifestation of influenza *vs* OURI, however rash was more often among OURI patients. Neutrophilia and monocytosis were more common in children with OURI, neutropenia – with influenza.

Clinical Trial Registration (Please input N/A if not registered)

Vilnius Regional Biomedical Reseach Ethics Commitee permission to conduct a biomedical research
2018-04-03 Nr. 158200-18/4-1025-525

ESPID19-0409
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Controlling endemic multidrug-resistant acinetobacter baumannii in a pediatric intensive care unit

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Background and Aims:

Acinetobacter baumannii and its antimicrobial resistance are serious emerging problem that cause high morbidity and mortality in critically ill patients. In our pediatric intensive care unit with 13 beds, an endemic situation with a single specific strain of multidrug-resistant *Acinetobacter baumannii* (MDRAB) occurred, and we investigated the effectiveness of comprehensive intensified infection control measures for controlling endemic MDRAB.

Methods:

The study period was divided into three periods, from the month of introduction of the single strain of MDRAB to the implementation of the intervention (Period 1; Jun 2017 to Feb 2018), from the implementation until the end of the MDRAB spread (Period 2; Mar to Aug 2018), and a follow-up period (Sep to Dec 2018). A comprehensive intensified infection control strategy was implemented to prevent the new colonization of MDRAB by a multidisciplinary team. All patients, as well as MDRAB colonized patients, were isolated with contact precaution. And the strategy focused on environmental cleaning, disinfection enforcement, hand hygiene promotion through PICU staff education, and active surveillance.

Results:

The incidence density rate of MDRAB, defined as the number of new colonizations or infections per 1,000 patient-days, decreased from 9.10 ± 6.46 (median, 10.56; range, 0 to 18.09) to 5.76 ± 4.00 (median, 4.48; range, 0 to 11.68) after the interventions were implemented. No MDRAB colonization or infection occurred during the 4-month follow-up period.

Conclusions:

Comprehensive infection control measures effectively controlled endemic MDRAB in our PICU. Universal contact precaution and environmental disinfection were crucial in controlling the horizontal spread of MDRAB.

Systematic Review Registration:

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ESPID19-0380
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Antibiotic therapy on the pediatric envin-helics registry

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Background and Aims:

To compare the evolution of antibiotics used for healthcare-associated infections (HAI) in Paediatric Intensive Care Units (PICU) from the Spanish registry Paediatric-ENVIN-HELICS.

Methods:

Multicentre, prospective and observational study. HAI diagnosed in 24 Spanish PICU, from April to June of 2013–2017, were included. The ENVIN diagnostic criteria adapted to paediatrics were used, based on CDC recommendations. SPSS®21 programme was used.

Results:

The number of patients included were 8717. Eight PICU (32%) had Antimicrobial Stewardship Program in 2017 compared with 0 in 2013 (p=0.000). Rate of antibiotics use decreased (4%, p=0.0179).

There was an increase use of meropenem of 1.64% for HAI previous PICU admission (not significant), while the use of piperacillin-tazobactam decreased (4.97%, p=0.0123). However, meropenem indication for HAI in PICU dropped (4.62%, p=0.05).

During 2017, antibiotic stewardship was 13.93% higher (p=0.0048). The early suspension antibiotic rate increased (6.78%, not statistically significant). Antibiotic modification due to adverse event decreased (1.19%, p=0,0021).

Conclusions:

The rate of antibiotics use was high, but results showed a decreasing trend during 2017. The implementation of ASP in PICU probably has led to a better use of carbapenems, and to an increase of antibiotic de-escalation and early suspension rate. Modifications of the antibiotic regime due to adverse event have decreased.

Systematic Review Registration:

N/A

ESPID19-0161
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Day of therapy and ratio of the consumption of broad- to narrow-spectrum antibiotics for quality indicator of antimicrobial stewardship program in pediatric ward

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Background and Aims:

Antimicrobial stewardship program (ASP) is important to prevent antimicrobial resistance. Day of Therapy (DOT) is commonly used in pediatrics. Some studies analyzed the ratio of consumption of broad- to narrow-spectrum (B/N ratio) of oral antibiotics for a quality indicator of ASP. However, they are influenced by characters of each facilities. The purpose of this study is to evaluate the effect of index using DOT and B/N ratio as indicators for comparing the progress of ASP of each hospital.

Methods:

We investigated the usage of antibiotics and diagnosis on admission with medical records from 2012 to 2017 in pediatric wards at related facilities of Juntendo University, retrospectively. We calculated the DOT, modified DOT (DOT/ratio of infectious disease) and B/N ratio (Narrow: Ampicillin and Cefazolin, Broad: except for Narrow) every two years.

Results:

At Facility A, DOT (2012-13, 2014-15, 2016-17) = (321, 333, 303) remained flat, modified DOT (689, 782, 720) and B/N ratio (0.53, 2.23, 4.30) increased. At Facility B, DOT (224, 174, 186), modified DOT (721, 628, 598) and B/N ratio (1.37, 0.98, 0.76) decreased. At Facility C, DOT (330, 275, 234) and modified DOT (531, 503, 446) decreased, and B/N ratio (0.34, 0.44, 0.45) remained in a low value.

Conclusions:

The trend of Facility A indicated that additional survey could be necessary for the ASP. In Faciliy, B and C, modified DOT and B/N ratio were both low and further decreased, those showed conducting appreciate use of antibiotics. DOT is affected by the proportion of infectious diseases in each facility. Our results suggested that this modified DOT and B/N ratio might be more accurately for ASP. This index may be more efficiently for active intervention of ASP, more efficiently.

Systematic Review Registration:

ESPID19-0100
E-Poster Viewing - May 7-10 - E-Poster Hours

Antibiotic stewardship and infection control

Difference in influenza vaccination rates among healthcare workers; a single-center study in korea

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Background and Aims:

Influenza virus, like in the community, is a highly communicable respiratory virus in the healthcare environment and vaccination is a major preventive strategy. Many health organizations have recommended flu vaccination of healthcare workers (HCWs), but vaccination rates vary from center to center. In order to increase the immunization rate among HCWs, it is necessary to investigate the characteristics of HCWs. We investigated factors affecting the flu vaccination rate of HCWs, including occupational characteristics.

Methods:

This study was conducted on all HCWs working at National Cancer Center, South Korea. Prior to the 2017-18 influenza season, flu vaccinations were provided to all HCWs, and retrospective analysis of vaccination rates by occupation/sex/age was performed.

Results:

In the 2017-18 season, 2,994 out of 3,181 HCWs (94.1%) were eligible for enrollment and the overall flu vaccination rate was 79.7%. Nurse group showed the highest vaccination rate of 97.8%, followed by health technician group (87.9%), doctor group (84.9%), other occupation group (71.2%) and the volunteer group (70.9%). According to the detailed occupational groups, vaccination rate of the surgeon group was 77.3%, which was significantly lower than that of non-surgeon doctor group (88.0%)(P= 0.035). In particular, the vaccination rate in doctors was the highest in the 20s (93.9%) and the lowest in the 50s to 60s and older (73.1%)(P= 0.013). Among the other occupation group, the vaccination rate (Other A, 81.7%) of transporters, security personnel, and cleaning personnel who had frequent contact with patients was significantly higher than those (Other B, 66.0%) of less-patient-contact occupations, such as researchers or office workers (P< 0.001).

Conclusions:

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Systematic Review Registration:

Flu vaccination rates among healthcare workers are different by occupation and age, and multifaceted efforts are needed to increase the vaccination rate.

ESPID19-1127
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Clinical evaluation and susceptibility profile of pediatric carbapenem-resistant enterobacteriaceae bloodstream infections at a teaching hospital in são paulo, brazil.

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Background and Aims:

Carbapenem-resistant enterobacterial infections in pediatric patients are already a reality worldwide and cause great concern. The aim of this study is to determine the antimicrobial susceptibility profile of polymyxin, tigecycline, meropenem and amikacin in carbapenem-resistant Enterobacteriaceae strains isolated from blood cultures of pediatric patients, and correlate the clinical outcome according to the treatment performed.

Methods:

We conducted a retrospective study of the pediatric cases of carbapenem-resistant Enterobacteriaceae bloodstream infections, from January 2012 to May 2018. The susceptibility assessment was performed by epsilometry or microdilution methods. Molecular analysis was performed by PCR (BD MAX System ®) with search of the blaKPC, blaOXA48, blaNDM and mcr-1 genes. Clinical data were collected from medical records.

Results:

During the studied period were detected 39 episodes of bacteremia by carbapenem-resistant Enterobacteriaceae. The episodes were classified as primary bloodstream infections in 74.4%. Previous antimicrobial use occurred in 92.3%, with meropenem the most used antimicrobial (72.2%). Combined therapy was used in 84.4% of the cases. The mean duration of the treatment was 19 days and the lethality rate was 48,7%. The presence of the blaKPC gene was detected in all isolates, and in no case the gene mcr1 was detected. We observed high rates of antimicrobial resistance: amikacin - MIC50 = 12 and MIC90 = 24; meropenem - MIC50 = > 32 and MIC90 = > 32; polymyxin - MIC50 = 16 and MIC90 = 64 and tigecycline - MIC50 = 2 and MIC90 = 3.

Conclusions:

We conclude that carbapenem-resistant Enterobacteriacea infections have a high impact on pediatric patients and are difficult to manage due to the scarce therapeutic options. Therefore, prevention and control measures remain the best strategy.

Systematic Review Registration:

Bloodstream infection
Pediatrics
Carbapenem-resistant Enterobacteriacea

ESPID19-1120
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Seven-year surveillance of pediatric group a streptococcal isolates in central greece

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Background and Aims:

A greatly variable incidence in macrolide resistance of Group A *Streptococcus pyogenes* (GAS) has been reported world-wide. The aim of this study was the molecular characterization of GAS isolates regarding macrolide resistance and relevant *emm* types in Central Greece.

Methods:

During, 2011-2017 GAS isolates were collected from consecutive children with pharyngeal and non-pharyngeal infections, who were either examined at the outpatient clinics or admitted to the pediatric wards of the University General Hospital of Larissa. Isolates were studied for antimicrobial susceptibility, macrolide resistance determinants and *emm* typing.

Results:

GAS was recovered from 606 children aged 0.8 to 15.5 years (median age: 6.5 years, IQR: 4.5-9.0 years). Overall, 15.4% (93/606) of GAS isolates were resistant to macrolides. Along the study period we noted a tendency towards significantly decreased rate of resistance (*p* value for trend=0.0024), with the lowest rates occurring in 2014 (13.1%), 2016 (5.5%), and 2017 (8.0%). No difference was observed in macrolide resistance between pharyngeal and non-pharyngeal isolates (*p*=1.00). 519 isolates were further analyzed and the most prevalent *emm* types were: 1 (17.7%), 89 (13.7%), 4 (12.5%), 12 (11.6%) and 28 (11.2%). The two predominant *emm* clusters were E4 (*emm*: 89, 28, 77, 2, 8) and A-C3 (*emm*1) with 167 (32.2%) and 92 (17.7%) isolates, respectively. A statistically significant association was found between macrolide resistance and emm28 and emm77. Among 85 macrolide-resistant isolates, *erm*(B) and *erm*(TR), either alone or in combination with *mef*, were detected in 48 (56.5%) and 31 (36.5%), respectively, whereas *mef* as the sole determinant in 6 (7.1%).

Conclusions:

In Central Greece during the recent 7-year period (2011-2017), 15.4% of GAS isolates were resistant to macrolides. A limited number of *emm* types dominated among macrolide-susceptible and macrolide-resistant isolates.

Systematic Review Registration:

N/A

ESPID19-1116
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Gram-negative bacterial infections in children

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Background and Aims:

Bloodstream infection is the most significant health-related infection in pediatric patients, with gram-negative bacteria being the most prevalent etiological agents. We aimed to revise bloodstream infection due to gram-negative bacteria (GNB) and bacterial resistance in children in a tertiary-level Brazilian university hospital.

Methods:

Retrospective and observational study including pediatric patients. All bloodstream infection caused by GNB from January 1st, 2013, to December 31th, 2016 were included. Duplicate samples and polymicrobial culture were excluded.

Results:

331 strains were identified among 320 patients. 54.7% were male, and the median age was 7 months. 84.8% of bloodstream infections were classified as healthcare-related. 60.2% of the infections occurred in intensive care units and 19.9% in the neonatal unit. Antibiotic resistance profiles are shown in Table 1.

Pathogen	Total (%)	MDR (%)	XDR (%)	PDR (%)	ESBL (%)	Resistance to carbapenems (%)
Klebsiella sp	125 (37,7)	75 (60)	32 (25,6)	5 (4)	72 (57,6)	39 (31,2)
Acinetobacter sp	48 (14,5)	19 (39,5)	12 (25)	3 (6,2)	NA	19 (39,5)
Pseudomonas sp	43 (12,9)	12 (27,9)	7 (16,2)	1 (2,3)	5 (11,6)	13 (30,2)
Escherichia coli	40 (12)	8 (20)	0	0	3 (7,5)	0
Enterobacter sp	30 (9)	12 (40)	0	0	NA	1 (3,3)
Serratia sp	13 (3,9)	5 (38,4)	1 (7,6)	0	NA	2 (15,3)
Burkholderia cepacia	4 (1,2)	1 (25)	1 (25)	0	NA	3 (75)
Citrobacter sp	4 (1,2)	1 (25)	0	0	NA	0
Outher agents	24 (7,2)	4 (16,6)	2 (8,3)	0	NA	2 (8,3)
Total	331	137 (41,3)	55 (16,6)	9 (2,7)	80 (24,1)	79 (23,8)

Conclusions:

We provide data for empirical antibacterial therapy and for antimicrobial stewardship programs to be implemented

Systematic Review Registration:

Antimicrobial stewardship programs; Gram-negative bacteria; Bloodstream infection; bacterial resistance

ESPID19-0738
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Staphylococcus aureus antimicrobial resistance patterns among children with skin and skin structure infections in crete, greece over a five–year period (2014-2018)

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Background and Aims:

Staphylococcus aureus, a Gram positive coccus, represents the most common pathogen causing skin and soft tissue infections in children. Infections caused by antimicrobial-resistant S. aureus, especially methicillin-resistant *S. aureus* (MRSA) strains, often occur in “epidemic waves”. The aim of the present study was to report S. aureus antimicrobial resistance patterns among children with skin and skin structure infections in Crete.

Methods:

This 5-year retrospective observational study evaluated trends in *Staphylococcus aureus* antimicrobial susceptibility in the department of paediatrics in a general district hospital in children 30 days to 16 years old between 2014 and 2018.

Results:

A total of 235 clinical isolates were tested for susceptibility by the MicroScan WalkAway system. 58% of the isolates were from inpatients whereas the majority of S. aureus infections were reported during summer and autumn months (68%). Antimicrobial resistance of S. aureus was most common to penicillin (73%), ampicillin (73%), mupirocin (34%) and tobramycin (25%). More than 88% of microorganisms were susceptible to amoxicillin/clavulanic acid while 4% of S. aureus strains were methicillin resistant. A significant decrease in MRSA rate was observed, compared to previous studies in the study area.

Conclusions:

The prevalence of MRSA strains has significantly decreased in the study area. Resistance rates to mupirocin and tobramycin make these agents inappropriate for empirical treatment of skin infections, whereas, amoxicillin/clavulanic acid still seems to be effective for empirical treatment of non-invasive S. aureus infections in children in our region.

Systematic Review Registration:

n/a

ESPID19-0500
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Decrease in vancomycin resistance and prevalence of hgisa in mrsa and mssa isolates from a german university children‘s hospital

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Background and Aims:

Resistance of *Staphylococcus aureus* to glycopeptides such as vancomycin is an emerging problem. Both methicillin-sensitive (MSSA) and methicillin-resistent *Staphylococcus aureus* (MRSA) have been isolated that show reduced susceptibility to vancomycin. This includes an general increase over time within the susceptible range, ("vancomycin minimum inhibitory concentration (MIC) creep") and the presence of a subset of the bacterial population that expresses resistance (heterogeneous glycopectide-intermediate s.aureus hGISA). Reported data from pediatric subjects is conflicting, suggesting the importance of regional surveys.

Methods:

We performed a retrospective analysis at a German university children’s hospital. Isolates from 2002-2017 were selected which were either newly identified MRSA or samples from invasive MSSA or MRSA infections such as bacteraemia. Multiple samples from individual patients were excluded. Vancomycin and oxacillin MICs as well as GISA/hGISA were measured using MIC test strips and resistance was evaluated over time.

Results:

In total, 540 strains were tested, 200 from the early (2002-2009) and 340 from the later period (2010-2017). All samples were vancomycin sensitive, but MIC was higher for the earlier samples compared to the later ones (1.11 vs 0.99; $p<0.001$). In total, 2% showed intermediate glycopeptide sensitivity and 13% were hGISA. Again, the vancomycin resistance decreased over time with 3 vs 1% GISA and 25 vs 6% hGISA ($p<0.001$). Vancomycin MICs did not differ between MSSA and MRSA samples ($p=0.80$).

Conclusions:

The data from our institution clearly shows a decrease in both vancomycin MICs and presence of hGISA in MSSA and MRSA samples. Accordingly, Vancomycin remains the primary treatment option for suspected severe infections with gram positive cocci and proven infection with MRSA. Our data underline the importance to monitor local susceptibilities which can differ from global trends.

Systematic Review Registration:

N/A

ESPID19-0274
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Epidemiology, clinical spectrum and bacteriological profile of neonatal bacterial sepsis with their antibiotic susceptibility pattern

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Background

Neonatal sepsis is one of the major causes of morbidity and mortality in the newborns. This prospective study aimed to determine the incidence, the bacteriological profile of neonatal septicemia and their antibacterial susceptibility pattern in the tertiary care neonatal center.

Methods

Neonates admitted from January 2017 to December 2018 with clinical features of sepsis were thoroughly investigated for any evidence of bacterial sepsis. Blood culture specimens were collected; identification of organisms and their antibiotic susceptibility pattern detection was done. Data were analysed by student *t*-test and ANOVA test.

Results

Incidence of neonatal septicemia was 18.2%. Prematurity (56.15%), low birth weight (60.94%) and prolonged rupture of membranes (28.3%) were major predisposing factors for neonatal sepsis. Gram negative organisms were more common (77.4%) than gram positive ones (22.6%). *Klebseilla pneumoniae* was the commonest pathogens (59.2%) recovered; mostly presented with early onset sepsis. Amongst the gram positive organisms, *Enterococci* (18.6%) and coagulase negative *Staphylococcus* (CONS) (12.1%) were recovered commonly. Blood culture was positive in 59.2% of septicemic neonates. In cephalosporins, cefoperazone and cefotaxim both have activity against *Klebseilla* and CONS, while ceftazidime showed better results against *Klebseilla*, *E.coli*, *Pseudomonas* and unidentified gram negative bacilli. In aminoglycosides, amikacin has much better results than gentamicin ($p<0.01$). Piperacillin had better advantage over ampicillin ($p<0.01$). All organisms except *E.coli* showed sensitivity to cefotaxime, while only one organism (*S.faecalis*) is sensitive to ceftriaxone. Vancomycin had good activity against gram positive organisms (Enterococcus, CONS and MRSA). Neonatal mortality rate was 11.4%.

Conclusions

This study showed gram negative organisms as commonest cause of sepsis and their alarming antibacterial sensitivity pattern that routinely used antibiotics like ampicillin and ceftriaxone showed poor activity against most of the organisms.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0610
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Further decline of methicillin-resistant staphylococcus aureus isolates in central greece during 2018

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Background and Aims:

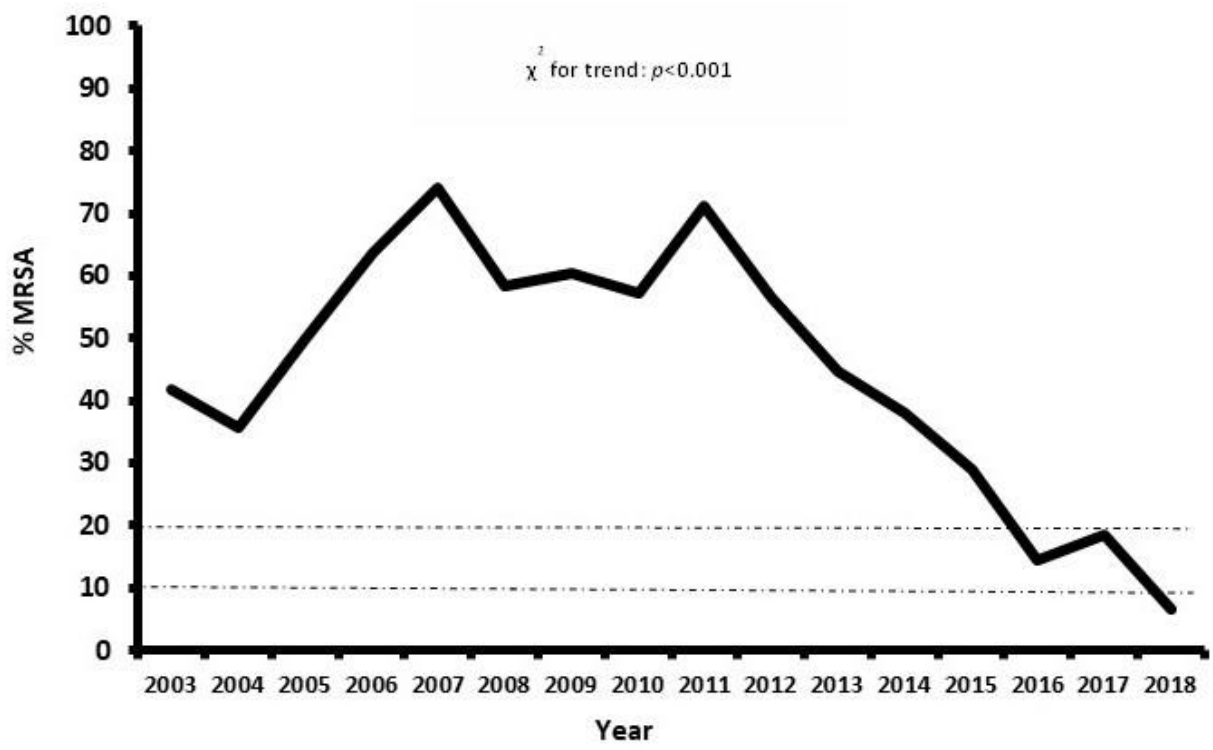
In Central Greece during 2003-2009, more than half of community-associated (CA) staphylococcal infections among children were caused by a methicillin-resistant *S. aureus* (MRSA) isolate. However, during the last years there has been a significant decline in CA-MRSA rates. The present study investigated the rate in 2018.

Methods:

From January 2003 to December 2018, we recorded all children examined at the outpatient clinics or admitted to the pediatric wards of the University General Hospital of Larissa, Central Greece, with community-associated staphylococcal infections. The first part of the study (2003-2009) was retrospective, whereas the second one (2010-2018) prospective. Samples included were pus, blood, tissue in case of surgical intervention, synovial or pleural fluid. Cases in which *S. aureus* isolate was recovered from a nasal or ophthalmic swab were excluded from the present analysis.

Results:

Of 730 children aged 5 days to 14.6 years, 60 (8.2%) had invasive infections and 670 (91.8%) skin and soft tissue infections. The proportion of staphylococcal infections caused by a CA-MRSA isolate was 59.2% in 2003-2012, 36.6% in 2013-2015 and 13% in 2016-2018 (χ^2 for trend $p<0.001$) (Figure). Specifically the rate was: 14.5% in 2016, 18.5% in 2017 and 6.7% in 2018. The rate of clindamycin-resistant *S. aureus* isolates was 19.8% in 2003-2012, 22.3% in 2013-2015 and 17.7% in 2016-2018 (χ^2 for trend $p=0.67$). Specifically the rate was: 25.4% in 2016, 16.7% in 2017 and 11.7% in 2018.



Conclusions:

In Central Greece, in 2018, a further substantial decline in the rate of CA-MRSA isolates was noted. Continuous surveillance is required in order to assess the methicillin resistance trends of *S. aureus* in the future.

Systematic Review Registration:

N/A

ESPID19-1067
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Antibacterial treatment strategy and antimicrobial resistance for staphylococcus aureus associated skin, soft tissue, bone and joint infections in children`s clinical university hospital (ccuh) in 2017

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Background and Aims:

Staphylococcus aureus is associated with more than 70% of all skin and soft tissue infections among children. The aim of this study was to analyse Staphylococcus aureus susceptibility to most often prescribed antibiotics in CCUH in 2017.

Methods:

The retrospective single centre study enrolled all Staphylococcus aureus positive skin, soft tissue, bone and joint infection culture cases in CCUH in 2017. Following parameters were analysed –localisation of the infection, antibacterial sensitivity of Staphylococcus aureus, antibacterial treatment choice and duration of antibacterial treatment.

Results:

All together 155 cases were analysed in this study, all children were aged 1 month to 18 years. Mean age of patients was 9 years and 5 months, and there was predominance of boys 55 % (86 out of 155). Systemic antibacterial treatment was used in 88 % of cases. The most often used antibiotics in inpatient settings was Oxacillin 45 % and Cefuroxime 21 %, but in outpatient settings antibacterial treatment was continued in 56 % (87 out of 155) of cases, the most common antibiotic prescribed in outpatient settings was Cefuroxime – 59 %. Staphylococcus aureus antibacterial resistance was checked to Amikacin, Gentamicin, Tetracycline, Ciprofloxacin, Clindamycin, Erythromycin and Penicillin, but only resistance to Penicillin was found in 71 % cases; prevalence of MRSA was 0.64 % (1 out of 155).

Conclusions:

1. In 88% of cases with Staphylococcus aureus associated skin, soft tissue, bone and joint infections systemic antibacterial treatment was prescribed.
2. The prevalence of MRSA at CCUH was very low compared to European average rate, which must be considered prescribing antibacterial treatment and preference to narrow spectrum antibiotics should be given.

Systematic Review Registration:

N/A.

ESPID19-1058
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Pathogens and antibiotic resistance patterns in pediatric bacterial conjunctivitis in western greece.

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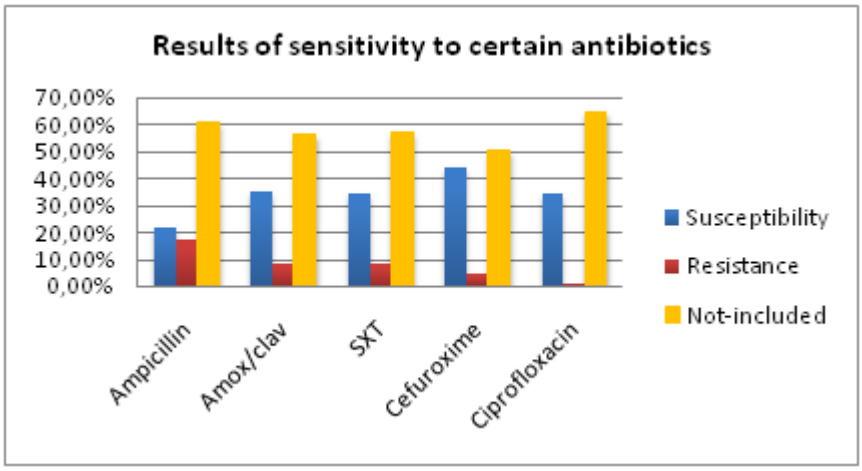
Background

Acute bacterial conjunctivitis is a common, highly contagious infection in children which presents with mucopurulent (unilateral or bilateral) discharge with normal visual acuity. Treatment is generally empirical by broad spectrum topical antibiotics. In the current study microbiologic and antibiotic resistance patterns are investigated in children under 14 years old in Western Greece.

Case Presentation Summary

A total of 191 specimens from the lower conjunctiva fornix were isolated from presumed acute bacterial conjunctivitis cases in General Pediatric Hospital of Patras, Western Greece over the period February 2013- January 2018 and outcomes were retrospectively analyzed, in order to identify the pathogenic bacteria and their corresponding antibiotic susceptibility patterns. Patients were divided in three groups: Group A included neonates ; Group B infants and toddlers up to 2 years old and Group C included children up to 14 years old. Seventy-eight out of 191 cultures (40.8%) were negative. From the remaining 113 positive cultures in 107 (94.7%) a single pathogen was identified, whereas in 5.3% two pathogens were isolated. Patients in group A were mainly infected by *Staphylococci spp. (70.5%), in* group B by *Haemophili spp* (38.1%) and *Staphylococci spp* (30.1%) whereas 45.5% of specimens in group C revealed *Staphylococci spp.* Antibiotics with the highest resistance rates were ampicillin (17.65%), amoxicillin/clavulanate (8.4%) and SXT (8.4%), reporting an overall high susceptibility (Figure 1.).



Learning Points/Discussion

Predominant pathogens of acute bacterial conjunctivitis remained *Haemophili spp., Staphylococci spp*. and *Streptococci spp*. Considerable variation of their concomitant frequencies was observed between neonates and children. Antibiotic resistance rates in Western Greece were low. Continuous surveillance, focused in distinct geographic areas, is encouraged to guide empirical treatment.

ESPID19-1056
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Antimicrobial resistance and antibacterial treatment of acute hematogenous osteomyelitis (aho) in children's clinical university hospital (ccuh) 2014 - 2017

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Background and Aims:

Acute hematogenous osteomyelitis (AHO) can lead to severe complications, for example, bone and joint destruction, sepsis and even death. The aim of this study was to analyse most often used antibacterial therapy in the case of AHO in CCUH and microorganism resistance.

Methods:

The retrospective single centre study enrolled all AHO cases in CCUH in the time period from 2014 to 2017. Following parameters were analysed – antibacterial sensitivity of isolated microorganism, antibacterial treatment choice and duration of antibacterial treatment.

Results:

All together 94 cases were analysed in this study, all children were aged 1 month to 18 years. The most often applied antibiotic in the case of AHO was Oxacillin and was received by 84 out of 94 patients (89 %). 42% from all patients received a combination of two or even more antibiotics. The most frequently used combination was Oxacillin with Clindamycin, which was applied in 24 out of 94 cases. 75% (71 out of 94) of patients received intravenous antibacterial treatment during their stay in hospital, and the conversion to oral antibiotics was not carried out. The predominant causative agent in this study was MSSA, which was isolated in 40% of the obtained blood cultures and in 79% (n=57) of the surgery materials. The prevalence of MRSA in our study group was 1.4% (n=1), but no PVL testing is available in CCUH.

Conclusions:

1. More frequent evaluation for possible conversion to oral treatment should be done in CCUH to decrease the rate of complications associated with intravenous access, and to improve comfort for the patients.
2. In earlier reports a high prevalence of PVL positivity in *S.aureus* infections at CCUH is shown, and PVL status should be checked in *S.aureus* AHO cases.

Systematic Review Registration:

N/A.

ESPID19-1027
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Antimicrobial resistance pattern of streptococcus pneumoniae

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Background

Streptoccocus pneumoniae (SP) can colonize the upper respiratory tract with impact of morbidity.Streptococcus pneumoniae is a common cause of acute respiratory tract infections in children. Conjunctivitis with SP became more frequent in the last two years.
Local antibiotherapy guidelines should be used in current practice for treatment at outpatient children.
To investigate antibioresistance pattern of Streptoccocus pneumoniae isolates to carriers and noncarriers associated with acute infectious diseases (upper respiratory infection, otitis and conjunctivitis).

Methods

We considerred children aged between 3 months and 10 years, with confirmed SP infection. Less patients were immunized against Streptoccocus pneumoniae.
Patients were treated in outpatient departments of pediatrics, ophthalmology, otorhinolaryngology and infectious diseases in „Dr.V.Babes" Center, Bucharest, Jan-Dec 2017-2018. Streptococcus pneumoniae (SP) strains were isolated from throat, nasal and conjunctival swabs.
Some patients performed pulmonary radiological examination and blood tests.
The antibiotic susceptibility profiles were analyzed for Streptococcus pneumoniae using both Kirby Bauer test procedure and E test, for macrolides and betalactam antibiotics, fluoroquinolones, glycopeptides (CLSI 2017/2018).

Results

Streptococcus pneumoniae was isolated from nasal(209), throat(13) and conjunctival(13) swabs. All strains were non-meningeal cases.
Streptococcus pneumoniae from nasopharyngeal samples was resistant to erythromycin 60% (126 isolate) and sulfamethoxazole-trimethoprim (SMX-TMP) was 48% (101 isolate).
Penicillin resistance in S. pneumoniae of non-meningeal infections is still low. All isolates were susceptible to fluoroquinolones and vancomicin.

Conclusions

1. Resistance to erythromycin has increased considerably in two years because empirical treatment with macrolide is frequently in these patients.
2. Penicillin can be used for patients with susceptible strains because penicillin-resistance of non-meningeal infections was very low.
3. High carriage rates of SP in the community increased incidence of clinical infection.

Systematic Review Registration (Please input N/A if not registered)

ESPID19-1011
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Antibiotic susceptibility patterns of uropathogens among children with community-acquired urinary tract infection in a tertiary referral hospital in spain

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Background and Aims:

Urinary tract infection (UTI) is one of the most common pediatric bacterial infections. The aim of this study was to investigate the bacterial pathogens involved in community-acquired UTI in a tertiary referral Spanish hospital over one-year period (2016), and their antibiotic susceptibility patterns in order to select the appropriate empiric treatment.

Methods:

A total of 642 episodes of UTIs were identified. Applying exclusion criteria (asymptomatic bacteriuria; urine culture contamination; bag urine specimens or those whose urine collection method was not specified or unknown; repeated urine cultures from the same patient, lacking or deficient clinical information and nosocomial or health -care associated infection), a final sample of 192 UTIs were analyzed. Antimicrobial susceptibility testing was performed using EUCAST guidelines.

Results:

Median age of children (women 74.5%) was 39 months. Urinary tract malformations were present in 45 cases (23%): 19 hydronephrosis, 22 vesicoureteral reflux. Three bacteria accounted for 90% of isolates: *Escherichia coli* (76.5%), *Proteus mirabilis* (10%) and *Klebsiella pneumoniae* (5%). Sixty percent of isolates were ampicillin-resistant; 22,4% were resistant to amoxicillin/clavulanic (A/C); 25% to trimethoprim/sulfamethoxazole; 12% to nitrofurantoin; 5.2% to fosfomycin; 3.9% to gentamicin; 3,4% to cefuroxime and 2,4% to cefotaxime.

Conclusions:

Antimicrobial resistance of uropathogens to commonly prescribed antibiotics is high. Our results suggest that the use of cotrimoxazole and A/C as empiric therapy for UTIs in our health area should be avoided. Fosfomycin for lower UTIs and second or third generation oral cephalosporins for pyelonephritis are appropriate antibiotics for outpatient therapy. Parenteral aminoglycosides and third generation cephalosporins are the treatment of choice for complicated UTI requiring hospitalization.

Systematic Review Registration:

N/A

ESPID19-0998
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Antibacterial resistance pattern of pathogens in paediatric haematology-oncology department – are broad-spectrum antibiotics always justified?

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Background and Aims:

Broad-spectrum antibiotics are commonly used in empiric therapy in haematology-oncology units regardless of antibiotic resistance pattern. In terms of antibiotic susceptibility Estonia belongs to countries with low level resistance. In paediatric haematology-oncology department of Tartu University Hospital (TUH) it is common practice to start empiric antibiotic treatment for febrile neutropenia (FN) with cefepime, irrespective of patients' risks. We aimed to evaluate the antibacterial susceptibility of pathogens in haematology-oncology patients.

Methods:

We conducted a retrospective review of hospital charts of all 0-19-year-old patients' histories who had a culture taken from a sterile site in the haematology-oncology department of TUH from 1/1/2014 to 31/12/2017. Coagulase-negative staphylococci (CoNS) were included if a patient was treated adequately for that infection >5 days. FN was defined as an absolute neutrophil count ≤0,5×10(9)/l with body temperature >38°C or symptoms indicating infection.

Results:

Altogether 361 cultures from sterile sites were taken from 55 subjects; 171 (47%) from patients with FN. Culture positivity rate was 13,8% and 18,1%, respectively. The main pathogens are presented in Table 1. Excluding CoNS, Gram-negatives predominated (67%). Only 11% of the latter were resistant to ciprofloxacin. ESBL-positivity was detected in 15% of *Enterobacteriaceae*. All isolated *Staphylococcus aureus* were susceptible to oxacillin and clindamycin. None of the patients died of infection.

Table 1. Patients' demographic characteristics and percentage of susceptible strains

Patients' demographic characteristics					
Age at first culture (median, IQR)	6,5 (3,3-13,9)				
Male (n, %)	22 (40)				
Percentage of susceptible strains					
	Enterobacteriaceae n=13	*Pseudomonas aeruginosa* n=5	*S. aureus* n=4	CoNS n=20	*Enterococcus faecium* n=2
Ampicillin-sulbactam	NA	NA	NR	NR	50
Oxacillin	NA	NA	100	10	NA
Clindamycin	NA	NA	100	60	NA
Ceftazidime	NR	100	NA	NA	NA
Cefotaxime	85	NR	NA	NA	NA
Cefepime	77	100	NA	NA	NA
Gentamicin	85	NR	NR	70	50
Ciprofloxacin	85	100	NR	65	NA
Ertapenem	100	NR	NR	NR	NA
Meropenem	NR	100	NR	NR	NA
Vancomycin	NA	NA	100	100	100

Conclusions:

In our study the majority of causative pathogens' antibiotic resistance level was low. Therefore, in a number of FN patients we could commence treatment with a more narrow-spectrum antibiotic regimen (e.g. clindamycin in combination with ciprofloxacin). In order to identify those patients we should consider implementing risk-based strategy for the choice of empiric antibacterial treatment. The high incidence of CoNS-infections might implicate the need to review our clinical practice.

Systematic Review Registration:

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ESPID19-0726
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Emergence of carbapenem hydrolyzing oxacillinases in acinetobacter baumannii in children from croatia

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Background and Aims:

Carbapenem resistance in *A. baumannii* can be mediated by carbapenemases of class A, class B metallo-β-lactamases (MBLs) and class D carbapenem-hydrolyzing oxacillinases (CHDL).

The aim of the study was to investigate the antimicrobial susceptibility and carbapenemases class of resistant *A.baumannii* isolates from Children's Hospital Zagreb, Croatia.

Methods:

A. baumannii strains (12) collected between August 2016 and March 2018 were analyzed. Antibiotic susceptibility was determined by broth microdilution method. Carbapenemases were screened by modified Hodge and CIM test. The presence of MBLs was explored by combined disk test with EDTA. The genes encoding carbapenemases of class A,B and D were saught by PCR. The occurrence of the IS*Aba1* upstream of the *bla*$_{\text{OXA-51-like}}$ or *bla*$_{\text{OXA-23-like}}$ was determined by PCR mapping. Epidemiological typing was performed by determination of sequence groups. Genotyping were performed by sequence group determination, rep-PCR and MLST.

Results:

All isolates were resistant to piperacillin/tazobactam, ceftazidime, cefotaxime, ceftriaxone, cefepime, imipenem, meropenem, gentamicin and ciprofloxacin. Moderate resistance rates were observed for ampicillin/sulbactam (67%) and tigecycline (42%). The isolates were uniformly susceptible to colistin. PCR revealed OXA-24-like CHDL in nine and OXA-23-like CHDL in three isolates. *bla*$_{\text{OXA-51}}$ genes were preceeded by IS*Aba1*. PCR for the common MBLs in Acinetobacter was negative.

All isolates belonged to SG 1 corresponding to ICL II. Rep-PCR identified four major clones.

Conclusions:

The study found OXA-24-like beta-lactamase to be the dominant CHDL among children's *A. baumannii* isolates. The predominant spread of OXA-24 is in contrast with recent global dissemination of OXA-23 reported all over the world. In contrast to the previous studies in which emergency of OXA-24 positive isolates was monoclonal we found high genetic diversity of the isolates.

Systematic Review Registration:

N/A

ESPID19-0718
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Dual therapy among hiv-infected children and adolescents within the spanish national cohort of hiv-infected children (corispe)

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Background and Aims:

The advent of potent and well-tolerated drugs has allowed reducing HIV treatment to dual antiretroviral therapy (DAT), combining two different antiretroviral classes. We aimed to describe the use of DAT as a switching strategy in children and adolescents within the Spanish National Cohort of HIV-infected children (CoRISpe).

Methods:

A retrospective review of virologically suppressed <18-year-old HIV-infected patients who received DAT within CoRISpe was conducted between January 2010 and August 2018. Patients were followed-up during the first 24 months to assess virologic and immunological responses. Virologic suppression was defined as a viral load ≤50 copies/mL. Virologic failure was defined as 2 consecutive viral loads >50 copies/mL.

Results:

Twenty-seven DAT were included (table 1), combining PI+II in 15 (55.6%), 8 (29.6%) PI+NRTI and 4 (14.8%) PI+NNRTI, with a median of follow-up on DAT of 23.7 months (IQR: 13-24 months). Five patients received 2 different DAT. The most common combination was DRV+DTG (6 cases), followed by DRV+RAL (4 cases) and DRV+EVG (4 cases). Seven DAT were further modified (at 10 days, 3, 8, 13, 16, 17 and 24 months); 2 due to adverse effects (psychiatric and hypersensitivity with DRV/r+EVG and DRV/r+ ETR, respectively). Virologic suppression during follow-up was: at 6 months 16/17 (94.1%); 12

months 17/18 (94.4%); 18 months 16/18 (88.9%); and 24 months 11/15 (73.3%). No DAT showed virologic failure, and CD4 counts remained stable.

Table 1. Basal characteristics (n=27), median (IQR) or n (%)

Age started ART (median)	13.9 years	IQR: 10.5-16.9 years
Male gender	12	44.4%
Transmission		
Vertical	25	92.6%
Unknown	2	7.4%
Clinical stage (CDC)		
A	11	40.7%
B	6	22.2%
C	10	37%
Number of previous ART (median)	4	IQR: 3-5
High-level resistance mutations		
≥1 ART classes	11/23	47.8%
≥2 ART classes	9/23	39.1%
≥3 ART classes	2/23	8.7%
CD4 (median)	708/mm3	IQR: 420-1138/mm3

Conclusions:

DAT was effective among virologically suppressed pediatric patients. Further studies and a longer follow-up are needed to evaluate the use of these combinations among children.

Systematic Review Registration:

ESPID19-0698
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Colonisation of term and preterm neotaes and breast milk with esbl-positive enterobacteriaceae in the first month of life

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Background

Enterobacteriaceae spp. expressing extended-spectrum β-lactamase (ESBL) are frequent in hospitals, but can also spread in community. We aimed to identify their prevalence and risk factors by evaluating ESBL-positive *Enterobacteriaceae* colonisation of skin and gut of mother's own breast milk (MOBM) fed neonates and mother's own breast milk.

Methods

Stool and skin swabs from 49 hospitalized preterm and 20 healthy term neonates (mean gestational age 39.6±0.8 and 28.3±3.4 weeks, respectively) and their MOBM collected weekly during the first month of life were cultured onto MacConkey agar. Isolates were identified using MALDI-TOF. The presence of ESBL was detected by Chromatic^{TM} ESBL media and cefpodoxime disks (10µg) in one strain of each different species isolated in different time points from each participant. Genetic relatedness of ESBL was determined by PFGE.

Results

Altogether 158 *vs* 59 enterobacterial isolates were identified from preterm and term neonates; 124 *vs* 53 from faeces; 17 *vs* 5 skin, 17 *vs* 1 MOBM, respectively. There were 66 *Escherichia coli,* 55 *Enterobacter cloacae* and 55 *Klebsiella oxytoca* strains. Of these 7.6%, 7.3% and 0%, respectively, were ESBL-positive. Carriage of ESBL-positive *Enterobacteriacae* was 6/49 (12%) in preterm (6.1%, 10.4%, 8.1% and 4.9% colonised in the 1st, 2nd, 3rd and 4th week, respectively), but none in term neonates. Similar PFGE genotype in different locations was found in two neonates: *E. asburiae* in faeces in 2nd week and in MOBM in 3rd week; *E. cloacae* in faeces and on skin, both in 2nd week. Smaller gestational age and

use of cefotaxime were increased the odds of colonisation with ESBL-positive *Enterobacteriacae* (Table).

Table. Univariate logistic regression of factors influencing colonization with ESBL-positive *Enterobacteriaceae* (statistically significant odds ratios are presented in bold)

	Colonized with ESBL (n=6)	Not colonized with ESBL (n=43)	Odds ratio	95% confidence interval
Gestational age (mean ±SD)	25.17 ±1.17	28.77 ±3.39	**0.6**	**0.37-0.95**
Caesarean section (%)	16.7	60.5	0.13	0.01-1.22
Birth weight (mean ±SD)	879.33 ±203.31	1382.58 ±677.37	1	0.99-1
Broad spectrum antibiotics (%)	83.3	39.5	7.65	0.82-71.29
Narrow spectrum antibiotics	100	97.7	0.49	0.005-45.8
Cefotaxime (%)	66.7	13.95	**12.33**	**1.84-82.79**

Broad spectrum antibiotics: meropenem, piperacillin-tazobactam, cefotaxime, cefepime; narrow spectrum antibiotics: penicillin, ampicillin, gentamicin, cefuroxime, cefazolin, cefoxitin.

Conclusions

ESBL-positive *Enterobacteriacae* colonise hospitalized preterm neonates, but not term neonates or MOBM, regardless of duration of pregnancy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0619
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Attainment of target levels with the currently used triazole dosing regimens in paediatric patients: a systematic review

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Background and Objective

Triazole antifungals are commonly used in clinical practice for the prevention and treatment of invasive fungal infections (IFI) in neonates and children. Although there is a reasonable amount of pharmacokinetic data, yet target concentrations and validation of these are lacking in paediatric patients. We reviewed the literature and assessed whether the current dosing regimens achieve predefined exposures as measured by therapeutic drug monitoring (TDM).

Methods

We undertook a systematic review using keyword searches of Medline and Embase databases (2000-2018) and results were reviewed by two independent investigators. Inclusion criteria: patients aged 0 – 18 yrs; treatment or prophylaxis with triazole antifungal; triazole plasma levels. Exclusion criteria: patients aged >18 yrs; drug monitoring in compartments other than plasma; no information about plasma levels. Reviews, case reports and case series < 5 patients were not included. Dosing was judged adequate if plasma levels were within the therapeutic ranges as recommended in international guidelines.

Learning Points Discussion

Data were available from 54 studies and 2058 children: voriconazole (n=28), fluconazole (n=6), posaconazole (n=12) and itraconazole (n=8). Majority of the studies included patients with underlying haematological malignancies. Given the wide range of dosing regimens, different formulations and varied patient populations, variable trough concentrations was observed when using a given dose based on body weight or body surface area. In general, a poor attainment of target levels was obtained in the majority of the children.

Dosing regimens for the triazole antifungals need to be optimized to result in sufficient exposure. PK modelling tools should be considered to optimize paediatric dosing algorithms. In the meantime, caution is warranted when prescribing triazoles in clinical practice and TDM monitoring is needed.

ESPID19-0468
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Efficacy of voriconazole therapeutic drug monitoring in children

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Background and Aims:

Invasive fungal infection is a life-threating infection. Voriconazole is a first line drug against invasive aspergillus infection. Considering the clearance, the dose for children is determined that 8mg/kg/dose twice on first day and the after 7mg/kg/dose twice per day. Voriconazole is also reported some side effects such as hepatotoxicity and visual disturbance. So therapeutic drug monitoring (TDM) is recommended. But there are only few reports about TDM of voriconazole in children.

Methods:

We investigated the serum concentration of voriconazole, gender, basal disease, side effect and efficacy from 7 children cases treated with voriconazole against fungal infection in Kurume University Hospital from electric medical records between April 1st 2014 and March 31st 2017.

Results:

There were 4 male cases. All cases had basal diseases. Four cases had blood malignancy disease. And there were each one case of Kawasaki disease, chronic granulomatous disease and very low birth weight infant. Four cases of first voriconazole serum concentration were under 1.0μg/ml and one case of that were over 5.0μg/ml. Otherwise increased the dose of voriconazole, 3 cases of voriconazole serum concentration were continued under 1.0μg/ml and finally they needed 10mg/kg/dose to reach the serum concentration over 1.0μg/ml. Three cases were admitted some side effect that two cases had visual disturbance and one case had hepatotoxicity.

Conclusions:

For treatment of invasive fungal infection in children with voriconazole, TDM is needed continually for safety and efficacy.

Systematic Review Registration:

N/A

ESPID19-0371
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Extensively drug-resistant salmonella enterica serovar typhi in a 7 year old girl returning from pakistan to scotland

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Background

Salmonella Typhi is increasingly resistant to antibiotics. Strains resistant to ampicillin, chloramphenicol and co-trimoxazole were reported in the 1980s, followed by resistance to fluoroquinolones in the 2000s. Recently, an extensively drug-resistant (XDR) strain of *S.* Typhi also resistant to cephalosporins has been reported from the Sindh district of Pakistan. This outbreak has been attributed to the contamination of drinking water from sewerage and children <15 years are particularly at risk.

Case Presentation Summary

A 7 year old girl presented to hospital in central Scotland with a five day history of fever, headache, abdominal pain and vomiting. She had returned from a two-month trip visiting family in Karachi, Pakistan two weeks previously. On examination she was febrile without a tachycardia and had epigastric tenderness. Typhoid was suspected and she was commenced on ceftriaxone. *S.* Typhi was isolated from blood and stool samples. Antimicrobial sensitivity testing confirmed resistance to ampicillin, chloramphenicol, trimethoprim, co-trimoxazole, ciprofloxacin and cefotaxime. It was susceptible to meropenem, gentamicin and azithromycin. Extended spectrum beta lactamase (ESBL) test was positive. Antibiotics were changed and the patient received 10 days meropenem and 10 days oral azithromycin with complete recovery.

Further investigation of the *S.* Typhi isolate using whole-genome sequencing revealed that it was of the globally dominant H58 haplotype. The isolate carried the CTX-M-15 gene (cephalosporin resistance) together with the qnrS1 gene and gyrA[83:S-F] mutation (fluoroquinolone resistance) which have been described in the XDR variant of H58 haplotype.

Learning Points/Discussion

To our knowledge this is the first report of XDR *S.* Typhi in Scotland. A high index of suspicion of XDR *S.* Typhi in returning travellers is essential for selecting appropriate empirical antibiotics. It also highlights the importance of pre-travel immunisation against typhoid, particularly for children.

ESPID19-0257
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Risk factors for extended-spectrum β-lactamase-producing enterobacteriaceae among children with urinary tract infections

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Background

Urinary tract infections (UTIs) are the most common infection caused by Extended spectrum beta-lactamase-producing Enterobacteriaceae (ESBLE) in children. ESBLE are resistant to most beta-lactams and often co-resistant to other classes of antibiotics, which limits therapeutic options and leads to delays in appropriate treatment. This study aimed to assess the risk factors for UTIs due to ESBLE in children.

Methods

Children with Enterobacteriaceae UTIs were enrolled at Tokyo Metropolitan Children's Medical Center between March 2010 and March 2016. Multivariate logistic regression was used to identify independent risk factors for ESBLE UTI.

Results

Among 479 cases of Enterobacteriaceae UTIs, 96 (20.0%) cases had ESBL producing isolates. Most ESBLE UTIs were due to Escherichia coli (95.8%). In univariate logistic regression, over a 1-year of age ($p<0.001$), hospitalization within 1 month of UTI ($p<0.001$), urological procedures within 1 month ($p<0.001$), antibiotic prophylaxis ($p<0.001$), colonization with ESBLE within 12 months ($p<0.001$), and prior antibiotics used within 3 months ($p<0.001$) were associated with ESBLE UTI. After adjustments in the multivariate model, independent risk factors for ESBLE UTI included colonization with ESBLE within 12 months (adjusted odds ratio [AOR], 47.6; 95% confidence interval [CI], 16.6–137.0; $p<0.001$), multiple courses of antibiotics used within 3 months (AOR, 9.1; 95% CI, 2.6–31.3; $p<0.001$), and urological procedures within 1 month (AOR, 3.9; 95% CI, 1.4–10.8; $p=0.009$).

Conclusions

Children may be likely to acquire a UTI caused by ESBLE when they meet the following conditions: colonization with ESBLE within 12 months, multiple courses of antibiotics used within 3 months, and urological procedures within 1 month.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0199
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Clavulanate stability in widely used child-appropriate formulations is unlikely to be adequate for use in treating young children in asia

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Background

Amoxicillin-clavulanate (AMC) is among the most frequently used antibiotic for paediatric infections globally. AMC child-appropriate formulations are largely limited to dry powder suspensions, which have to be stored refrigerated once reconstituted due to stability limitations of clavulanate.

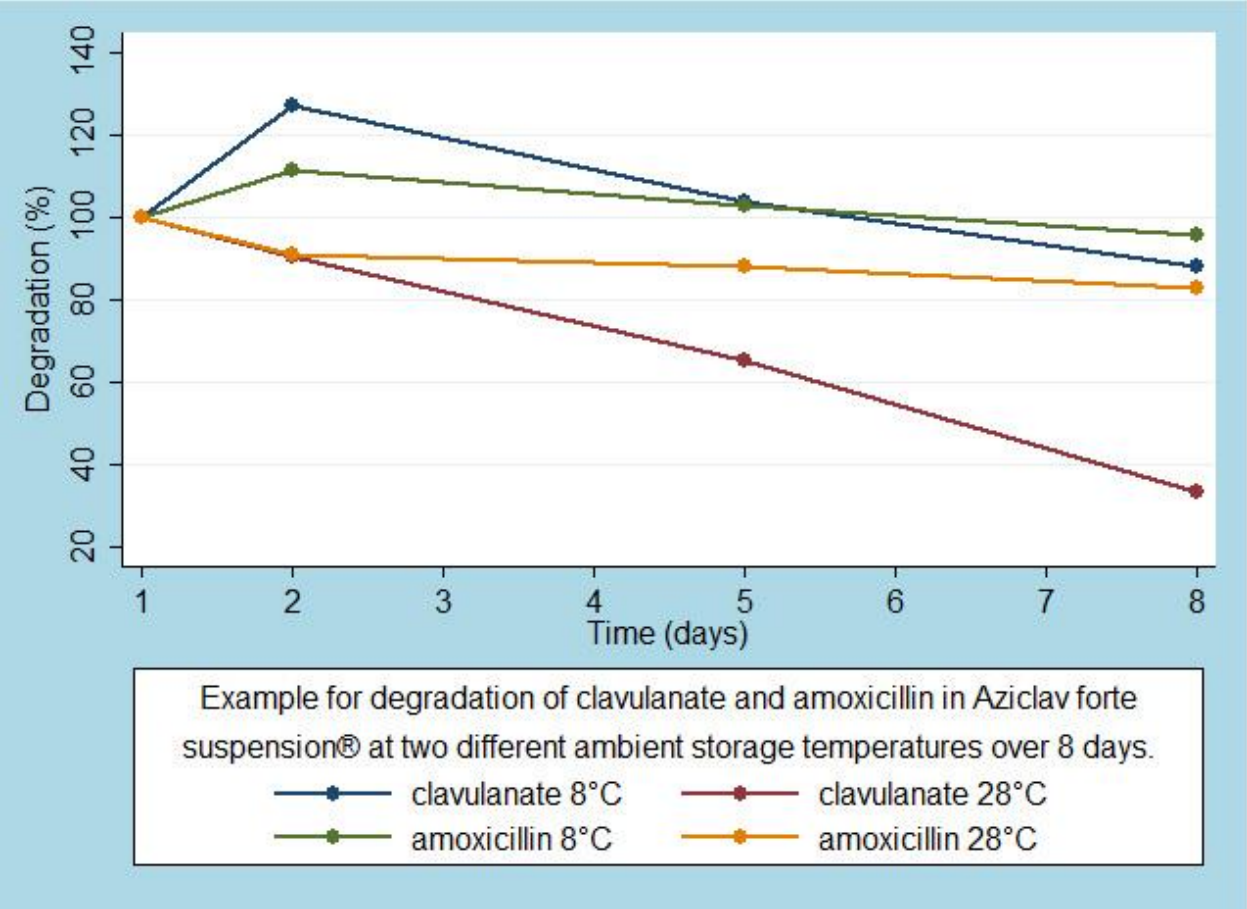
Methods

Oral Amoxicillin (AMX) and AMC formulations were identified from IQVIA-MIDAS wholesale data, and 2015 antibiotic consumption in courses/1000 child-years was estimated in Bangladesh, India, Indonesia, Pakistan, Philippines and Vietnam with an assumed average treatment of 7 days. Costs per course in US-$ standardised to 2015 were estimated from the same dataset. Nationally representative data on access to a refrigerator was extracted from the Demographic & Health Surveys Program. Degradation under different temperature conditions of two different AMC suspensions commercially available in Switzerland was tested. Average degradation (three bottles of each product) was measured during 8 days with ambient temperatures of 8°C versus 28°C.

Results

In India and Pakistan more AMC than AMX courses were sold. In all countries AMC was at least twice and up to 10 times as expensive as AMX. Access to refrigeration was below 45%, even in countries with a high number of sold AMC courses (compared with AMX). In the evaluated co-formulated products, clavulanate showed a maximum degradation of 34% at 8°C, and 73% at 28°C after 8 days. AMX was

largely stable at 8°C but 13% degraded at 28°C after 8 days (see example degradation in **Figure 1**).



Conclusions

Oral amoxicillin-clavulanate suspensions are widely used in six Asian countries classified as middle-income countries by the World Bank. In reconstituted liquid AMC formulations, neither component is satisfactorily stable at room temperature. Storage conditions for stability are likely inadequate for AMC in many households in the six Asian countries of interest.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0079
E-Poster Viewing - May 7-10 - E-Poster Hours

Antimicrobials: resistance and pharmacology

Changing susceptibility of staphylococcus aureus in children with skin and soft tissue infections: a single center experience from 2008 to 2017

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Background and Aims:

Staphylococcus aureus is a major cause of skin and soft tissue infections (SSTIs). This study was aimed to determine temporal trends in antibiotic susceptibility of *S. aureus* in SSTIs patients younger than 19 years.

Methods:

A retrospective observational study was conducted on pediatric wound or cutaneous abscess cultures that grew *S. aureus* between 2008 and 2017. Microbiologic and demographic data were collected and trends in antibiotic susceptibility results were evaluated.

Results:

A total of 935 initial cultures from children during the study period grew *S. aureus*. Overall, 356 (38.3%) isolates were methicillin-resistant *S aureus* (MRSA). Over the study period, *S. aureus* isolates from 2008 to 2017 demonstrated a significant overall trend of decreased susceptibility to clindamycin ($P<0.001$) and gentamicin ($P=0.006$). The rate of clindamycin resistance was increased 3.7-fold, from 10.7% in 2008 to 40% in 2017. MRSA rates remained stable overall, although an initial increase of 18.3% over 6 years of the study was subsequently followed by a decrease of 18.4% between 2013 and 2017.

Conclusions:

Increasing clindamycin resistance among *S. aureus* should raise caution in the use of empirical clindamycin in SSTIs. Clinicians should be aware of regional susceptibility patterns when choosing empirical regimens.

Systematic Review Registration:

N/A

ESPID19-1153
E-Poster Viewing - May 7-10 - E-Poster Hours

Bone and joint infections

Patellar abscess due to citrobacter freundii: case report

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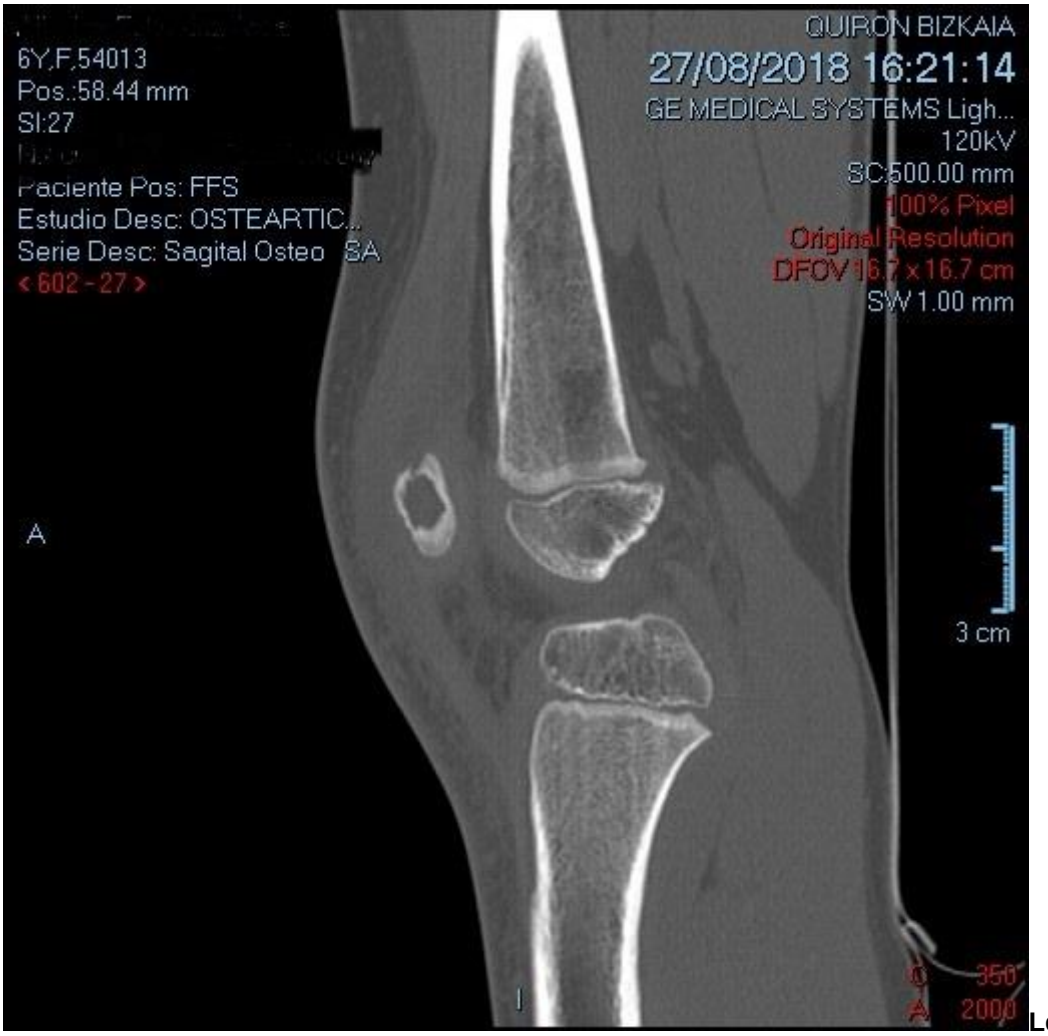
Background

Citrobacter species are known to provoke serious infections in extremes of life and immunocompromise patients. We report a case of osteomyelitis in a healthy child.

Case Presentation Summary

A 6-year-old female, previously healthy, presents to the ER in July 2018, with intermittent knee pain, denying fever, direct injuries or infections. On physical examination she presented tenderness on palpation on the centre of the patella without other inflammatory signs. X-ray was reported normal. The patient returns to the ER three weeks later with increase in pain, edema and erythema, NSAID´s were no longer effective. An MRI and CT of the lower extremity are performed which showed a cystic lytic lesion in the patella of 7.5 mm and surrounded 12 mm of fluid, no signs of malignancy (figure 1). A week later a fine needle aspiration was performed and pathology reported a mixed inflammatory pattern with no signs of malignancy. The culture was positive for *Citrobacter freundii*.

The patient was treated with cefotaxime IV for 7 days, which was sensitive in the antibiogram. Before discharge a new blood culture resulted negative. She was discharged clinically asymptomatic to complete 2 weeks of high-dose oral trimethoprim-sulfamethoxazole. The follow up with MRI 6 months later showed almost complete resolution of the lesion.



Learning Points/Discussion

Citrobacter infections in healthy children are uncommon so it is important to rule out immunocompromise. This case was successfully treated with IV antibiotics and an almost complete resolution of the lesion. However, sometimes surgical removal is required.
To the best of our knowledge this is the first case of bone infection due to Citrobacter species in children reported in Spain.

ESPID19-0843
E-Poster Viewing - May 7-10 - E-Poster Hours

Bone and joint infections

Pediatric spondylodiscitis: a difficult diagnosis

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Background

Pediatric spondylodiscitis is an uncommon disorder. It is an infection of the spine involving the intervertebral disc and the vertebral body. The diagnosis is difficult and often delayed due to the non-specificity of clinical manifestations and children's inability to locate symptoms.

Case Presentation Summary

A 23-month-old girl presents to the Emergency Department (ED) for the fourth time in 10 days with a 2-week complain of abdominal pain and refusal to weight-bear. On physical examination, she had pain on palpation of lumbar spine and preferred to adopt side position. Laboratory showed 11300 leucocytes/mm3, ESR 91 mm/h, and CRP 1,9 mg/L. Lumbar X-ray showed a decreased height of the L1-L2 intervertebral disk. A bone scintigraphy revealed L1-L2 spondylodiscitis. She completed 11 days of intravenous flucloxacillin switching to oral for another 4 weeks. Two months later the x-ray showed L1-L2 narrowing space and after 1 year she was asymptomatic.

A 15-month-old boy was brought to the ED for the second time in 4 days with a 1 week complain of limping and refusal to sit. At the first visit, a lumbar x-ray was performed and read as normal. On physical examination, lower limbs were judged hypotonic. He was unable to remain sited and refused to weight-bear. Laboratory parameters were normal. A lumbar puncture showed no alterations in the CSF. A spine MRI revealed L5-S1 spondylodiscitis. Treatment with intravenous flucloxacillin was continued for 3 weeks and then switched to oral for another 2 weeks, with a significant clinical improvement.

Learning Points/Discussion

The diagnosis of spondylodiscitis should be suspected in children who present with reluctance to sit, stand or walk. The early use of appropriate imaging studies, such as MRI or scintigraphy, may avoid treatment delays and possibly prevent long-term problems.

ESPID19-1132
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Staphylococcus aureus bacteraemia in children: an eight-year retrospective review of experience in a regional tertiary children's hospital

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Background and Aims:

Staphylococcus aureus bacteraemia (SAB) is a significant cause of community-associated (CA) and hospital-acquired (HA) infection. The epidemiology is not well characterised in children and has not previously been studied in Northern Ireland. We aimed to determine the incidence and clinical epidemiology of SAB in children aged <16 years hospitalised at the regional tertiary children's hospital in Belfast, Northern Ireland.

Methods:

A retrospective review of all SAB cases occurring at the Royal Belfast Hospital for Sick Children between January 2010 and December 2017 inclusive was performed. SAB developing greater than 48 hours post admission was defined as HA-SAB.

Results:

During the study period, 107 episodes of paediatric SAB were identified with an average annual incidence of 19.9/100,000 population and 0.97/100,000 population for Methicillin-sensitive *Staphylococcus aureus* (MSSA) and Methicillin-resistant *Staphylococcus aureus* (MRSA) episodes respectively. Forty out of 107 episodes (37%) were identified as HA-SAB and 60% of MRSA episodes were CA-SAB. MRSA isolates demonstrated 100% and 80% resistance to clindamycin and ciprofloxacin respectively. Median age for cases was 20 months (IQR: 4.5-85 months) and over half had comorbid clinical conditions. Bone and joint, soft tissue and device-related infections were the most common clinical syndromes with fever the most common presenting symptom. HA-SAB was more likely in device-related infection.

Conclusions:

Underlying medical conditions and devices represent important risk factors for SAB in children. Incidence of MRSA is low, in-keeping with rates in the rest of the UK and Ireland. Identification of at risk patient populations allows development of targeted improvement plans to prevent paediatric SAB.

Systematic Review Registration:

N/A

ESPID19-0941
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Epidemiology of invasive meningococcal disease in croatia (2009-2018): a single centre study

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Background and Aims:

Invasive meningococcal disease (IMD) is a rare, but potentially life-threatening infection, mostly affecting infants and young children. In Europe, serogroup B (SgB) causes the majority of IMD cases. The serogroup distribution varies by age, region, and it may change over time. We aimed to describe the epidemiology of IMD in the University Hospital for Infectious Diseases (UHID), Zagreb, during 10-year period to monitor seasonal variations, serogroup- and age-specific trends. None of the available meningococcal vaccines is a part of NIP in Croatia.

Methods:

All cases of confirmed IMD treated in UHID from January 1st, 2009 to December 31st, 2018 were included in the study and retrospectively analysed. Confirmed IMD was defined in accordance with EU case definitions. Demographic data were collected from clinical records, while data on serogroup were obtained from microbiological and molecular laboratory.

Results:

There were 226 cases of confirmed IMD, with median age of 3,99 years (range 0,08 – 91,85 years). Most cases were observed in young children aged 1-4 years (28%), followed by <1-year-olds (25%) and 15-24-year-olds (20%). The highest number of cases occured in January and February (16% and 12%, respectively). The majority of cases belonged to SgB (81%), followed by SgC (11%) and SgY (6%). SgB accounted for 88% of IMD cases in children <5 years. Decreasing trend in total IMD and SgB cases was noticed during the study period.

Conclusions:

IMD is a severe infection that predominantly affects young children. SgB remains the most common serogroup among all age groups below 65 years, with the highest burden in children aged <5 years. Determination of the major serogroups and their age and temporal variation is an important step for establishing a vaccine programme targeting *Neisseria meningitidis*.

Systematic Review Registration:

N/A

ESPID19-0516
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Invasive non-candida fungal infections in children during a 10-year period

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Background

Although *Candida* species remain the leading cause of invasive fungal infections (IFI), the spectrum of responsible pathogens is increasing steadily. Our aim was to detect cases of IFI caused by non-*Candida* species in the largest tertiary Greek pediatric hospital.

Methods

A retrospective study was performed from 1/2008-12/2017 regarding IFI caused by non-*Candida* species. Identification of isolates and susceptibility testing were performed according to CLSI methodology.

Results

During a 10-year period, 16 cases of IFI caused by non-*Candida* species were recorded. Four different species were detected: *Cryptococcus* (*C. terreus*-1 case, *C. albidus*-2 cases, *C. uniguttulatus*- 2 cases), *Saccharomyces cerevisiae* (6 cases), *Malassezia furfur* (3 cases) and *Trichosporon asahii* (2 cases). Fourteen isolates were detected in blood samples and 2 in pleural fluids. Six children were hospitalized in neonatal intensive care units (ICU), 2 in pediatric ICU and 8 in hematology/oncology units. *Cryptococcus* species exhibited an amphotericin B MIC value from 1.5 to 4.0 mg/l, while flycytosine and fluconazole showed limited in vitro activity against *C. albidus* and *C. uniguttulatus*. *S.cerevisiae* was susceptible to amphotericin B and fluorocytosine, whereas different rates of resistance to fluconazole and posaconazole were reported. Regarding *Malassezia furfur,* the lowest MIC values were found for itraconazole and voriconazole and the widest MIC ranges were observed for fluconazole.Most of the triazoles were found to have *in vitro* activity against *Trichosporon asahii* but fluconazole didn't.

Conclusions

Emerging and rare IFI are often refractory to conventional antifungal agents. Early detection is essential to provide timely therapy and improve patient's chance of survival.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0454
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Early finegoldia magna associated-infection of the orthopaedic implant of a child with idiopathic scoliosis

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Background

Infections associated with surgical osteosyntesis material are difficult to manage leading to frequent prosthesis removal. Early infections (<3 months) are generally more overt and retention of implants more likely. The most common pathogens that cause orthopaedic implant infections are coagulase-negative staphylococci, *Staphylococcus aureus*, streptococci, and *Enterobacteriaceae*. Anaerobic bacteria can be found, mainly *Propionibacterium acnes*. *Finegoldia magna* is an anaerobic Gram-positive coccus (previously *Peptostreptococcus magnus* until 1999), not previously described in orthopaedic implant infection in paediatric population.

Case Presentation Summary

A 15 year-old boy underwent a programmed surgery for the correction of idiopathic scoliosis: open posterior spinal fusion T2-T12, placing rods and screws. The first days after the uneventful surgery, the patient started with fever but no elevation of acute-phase reactants, and a source for the fever was not found. The 8thday, he started with sero-haematic discharge from the wound. He had a new surgery 14 days after the initial one, samples were taken, and he started with moxifloxacin IV and rifampicin PO. Once isolation of *Staphylococcus epidermidis*, *Propinebacterium* sp and *Finegoldia magna*, moxifloxacin was switched to vancomycin. The patient continued with fever and signs of wound infection, so he underwent another surgery 21 days after the first one, and new samples were taken. After isolation of *F.magna* vancomycin-resistant, he started with piperacilin-tazobactam IV for 7 days; then fever stopped and surgical wound improved. The patient completed a 3-month course of outpatient treatment with amoxicilin-clavulanate PO, uneventfully with retention of the implant.

Learning Points/Discussion

F.magna have to be considered as a potential cause of early orthopaedic implant devices. Sensitivity to vancomycin should be checked if isolation of *F. magna* to optimize treatment. Management may be successful with appropriate prolonged antibiotics, debridement and prosthetic retention.

ESPID19-0444
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Coxiella burnetii as a cause of negative blood culture endocarditis in a patient with congenital heart disease

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Background

Fever of unknown origin (FUO) is a challenge in Paediatrics. Q fever is caused by *Coxiella burnetti*, it is described as a cause of FUO, but it is rarely described in children.

Case Presentation Summary

Eight year-old boy admitted to Paediatric ID department because of FUO, temperature maximum 40ºC, daily, for the last 4 weeks. He developed petechiae on his legs, and hepatosplenomegaly, but nothing else remarkable on physical exam.

Past history: double out right ventricle, interventricular communication and pulmonary stenosis; after last surgery (18 months earlier), patient had a bovine pericardial patch and a prosthetic pulmonary valved conduit. No other relevant medical history; he lived in a rural area, in contact with animals.

Once admitted, blood tests were performed: normal full blood count, CRP 2.68 mg/dL, liver/renal functional test were normal, blood cultures and serologies were taken. Urine dipstick was normal. Chest X-ray was unremarkable, abdominal ultrasound showed homogeneous hepatosplenomegaly, blood cultures came back negative, and the echocardiography didn't revealed images suggesting endocarditis.

A body PET-CT revealed enhancement at prosthetic valve, serology for *C.burnetii* presented high title (>1/8912, phases I&II), and specific PCR for *C.burnetii* in blood was positive. A new echocardiography revealed vegetation at the prosthetic pulmonary valve. Patient started on doxycycline, plus hydroxychloroquine initially but switched to cotrimoxazole after 2 weeks due to gastrointestinal intolerance. He underwent valve replacement surgery and is still under antibiotics to date.

Learning Points/Discussion

Considering all causes of FUO, we should pay attention carefully to past history, physical exam and environmental exposures, especially cardiac surgery and petechiae, which could suggest endocarditis. *C.burnetii* causes negative blood cultures endocarditis and it should be taken into account if patients are exposed to animals or live in rural areas.

ESPID19-0151
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Group a β-hemolytic streptococcus infective endocarditis in a 2 year old: a rare presentation

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Background

β-haemolytic group A streptococcus pyogenes is an uncommon cause of infective endocarditis (IE) post antibiotic era. Most of the cases are reported in adults and intravenous drug abusers. IE due to streptococcus pyogenes in children is extremely rare with only 13 pediatric cases reported in literature so far.

Case Presentation Summary

A 2 year old previously healthy girl was referred in view of high grade fever for 10-15 days and thromboembolic phenomenon. Her blood culture showed growth of group A β haemolytic streptococcus pyogenes sensitive to benzylpenicllin. She was previously treated with oral and IV antibiotics. Her echocardiography showed mycotic aneurysm of sinus of Valsalva and moderate aortic incompetence confirming IE (figure 1). Serial Echos showed increase in size of aneurysm. Findings were confirmed with CT chest. She was subsequently operated for aneurysm repair. Intra-operatively there were perforations of aortic root and coronary cusp which were repaired. Vegetations found on aortic valve were removed and sent for tissue culture which showed no growth. She was treated with five weeks of benzylpenicllin and two weeks of Linezolid. Her CRP gradually decreased from 200 to normal. Her immunology work up was normal. Post surgery recovery was uneventful.

Learning Points/Discussion

Streptococcus Pyogenes IE is extremely rare in pediatric population and has been reported mostly in healthy children with normal heart. Bacteremia can be from previous infections like pharyngitis or skin lesions, however cases have been reported without any preceding infections as in our case. There is a tendency to involve left sided valves unlike IE in intravenous drug users. Presentation is acute and prognosis is excellent. High index of suspicion is necessary.

ESPID19-0919
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Spinal infections in children in slovenia

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Background

Spinal infections (infectious discitis and spondylodiscitis) are rare diseases in childhood and they can present a diagnostic challenge. Significant clinical sequelae, including spinal deformities and segmental instabilities can be devastating for a child.

Case Presentation Summary

Medical charts of 12 children treated for spondylodiscitis at Department of Infectious Diseases, University Medical Centre Ljubljana between 2008 and 2018 were reviewed retrospectively. The mean age of patients was 7,5 years (16 months –17 years) with two distinct age peaks in toddlers and teenagers. Lumbar spine was the most common site of infection.

The main presenting symptom was refusal to walk or limping in toddlers and back pain in older children.

Mean time from the beginning of symptoms to the diagnosis was 22 days (2 –120 days). The main reason for delay in establishing the diagnosis was missed spinal infection in differential diagnosis. On admission mean laboratory value of ESR was 59 mm/h (25–113) and of CRP was 33 mg/l (5–85) respectively.

Blood cultures (*Staphylococcus aureus*) were positive only in two children. Biopsy was performed in two children, in one *S. aureus* was isolated, the other was negative.

All children were treated with antibiotics for at least 6 weeks, none of them needed additional surgical procedure. None of the children experienced any long term clinical sequelae, although in 7 children narrowing of intervertebral disc space was evident
radiologically.

TABLE 1: Characteristics of patients with spondylodiscitis.

SEX	AGE (m,y)	FEVER PRIOR-days	RISK FACTORS	DAYS OF SYMPTOMS	ESR	CRP	MRI level	BIOPSY (pathogen)	PATHOGEN	TREATMENT days		CLINICAL SEQUELAE
										iv	oral	
F	16 m	14	R	14	70	5	L4-5	No	No	21 F	21 F	No
F	16 m	No	No	21	50	40	L3–4	No	No	7 F, 14 C	21 CD	No
M	16 m	No	R	30	48	8	L1-2	No	No	21 F	35 F	No
F	18 m	No	R	5	60	22	L4-5	No	No	4 F, 12 C	29 CD	No
M	24 m	4	No	5	78	34	L3-4	No	No	4 F ,10 C	26 CD	No
M	39 m	4	No	120	25	30	L3-4	No	No	14 F	28 F	No
M	6 y	Yes	I	30	113	66	L5-S1	No	No	14 F	28 F	No
F	12 y	7	R	7	38	6	Th11-12	No	SA	7 F	35 CL	No
M	12 y	No	S	4	38	15	Th4-5	Yes (No)	No	19 F	23 F	No
M	13 y	2	I	6	61	85	Th9-10	No	No	25 F	17 F	N/A
M	15 y	Yes	No	2	52	72	L2-3	Yes (SA)	SA	42 F	/	No
F	17 y	No	S	21	74	18	L1-2	No	No	21 F	21 F	No

LEGEND: F – female, M – male, m-months, y-years, R – respiratory illness in the last four weeks prior, I – injury, S – sports (football), ESR – erythrocyte sedimentation rate (mm/h), CRP – C-reactive protein (mg/l), MRI level – level of infection on magnetic resonance imaging, SA – *Staphylococcus aureus*, F – flucloxacillin, C – cefuroxime, CD – cefadroxil, CL – clindamycin, N/A – not applicable.

Learning Points/Discussion

In a child with unexplained pain, refusal to walk or limping, spondylodiscitis should be suspected, especially with elevated ESR. Particular attention must be paid to the identification of the causative infectious agent, although blood culture is frequently negative. *Kingella kingae* antibiotic coverage should be provided in toddlers especially in those with a history of prodromal illness.

ESPID19-0269
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Streptococcus pyogenes endocarditis with rupture of mitral valve chordae tendineae following varicella associated necrotising fasciitis – case report and review of the literature

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Background

Varicella-zoster virus (VZV) may cause serious and potentially lethal complications such as Group A Streptococcus (GAS) associated necrotizing fasciitis. GAS is rarely described as a cause of infective endocarditis (IE).

Case Presentation Summary

A 5-year-old previously healthy boy presented with varicella and painful livid discoloration on the left buttock on day 3 of illness. Inflammatory markers were elevated. Cefuroxime and Clindamycin i.v. were started. Blood cultures grew *S. pyogenes.* CT suggested fasciitis of the gluteal muscle and urgent surgical debridement was performed confirming necrotising fasciitis. Two further debridements were necessary and vacuum assisted closure was applied. On day 5 of hospitalisation respiratory distress and a systolic murmur were noted. Echocardiography revealed mitral valve prolapse with regurgitation. The child deteriorated further and echocardiography 2 days later showed progressive prolapse of the mitral valve, assuming rupture of the chordae tendineae. Cardiac surgery confirmed IE, the mitral valve was reconstructed and neo-chordae were implanted. No growth of other pathogens was noted. Treatment was adjusted to Amoxicillin and continued for four weeks. He survived.

Learning Points/Discussion

IE is rare in childhood, especially in children without congenital or valvular heart disease. GAS associated IE as a complication of VZV and fasciitis has rarely been described in children. In the past 80 years only 15 cases of IE caused by GAS in children were reported. Acute deterioration secondary to rupture of mitral valve chordae tendineae, as described in our case, has not been reported in the literature yet. Serious complications like these could be prevented by an universal varicella childhood immunization programme which unfortunately is currently not in place in Switzerland.

ESPID19-0130
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Structure of sepsis agents in children

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Background

The purpose of our work is to study the etiological structure of sepsis in children.

Methods

All patients were on treatment at the Children's Infectious Clinical Hospital in Minsk from 2009 to 2017. 200 medical cards of stationary patients aged from 1 month to 18 years were analyzed. In the hospital the whole patient was examined for sterility (prior to the appointment of antibiotic therapy) and / or for meningococcus and according to the protocol of the examination of patients with suspected meningococcal infection - a study of a nasopharyngeal smear for meningococcus, a thick drop of blood for meningococcus, and liquor for meningococcus.

Results

The etiology of sepsis was established in 68.5% of cases, while another 20 patients (10%) had a diagnosis of meningococcal sepsis (meningococcemia) according to clinical and epidemiological data. In 43 patients (21.5%), unfortunately, the etiology of the severe pathological process is not confirmed. Among the verified cases of sepsis Gram negative microorganisms predominated in 85 patients (42.5%): N. meningitides - 64 cases, Ps. Aeruginosa, H. influenzae and Ac. baumannii - 3 children each, Kl. pneumoniae and E. coli - 2 patients each, Achromobacter xylosoxidans, Enterococcus, Stenotrophomonas, E. meningoseptica - 1 child each, Yersinia enterocolitica and pseudotuberculosis - 4 children.

In 18% of the cases, the etiological agent of sepsis was Gram positive microorganisms: staphylococci (10 patients) and streptococci (26 children), 6.5% mixed flora and 3 cases - Candida fungi were the causative agents of sepsis.

Conclusions

Thus, based on the analysis, the following conclusion can be drawn that the main role in the development of both sepsis and septic shock in children hospitalized in an infectious hospital is played by gram-negative microorganisms.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0129
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Meningococcal sepsis in children

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Background

The aim of our work is to study the epidemiological features of meningococcal sepsis in children, clinical and anatomical forms and outcomes of the pathological process.

Methods

A study was conducted of medical records of inpatients with a clinical diagnosis of meningococcemia. The study included 83 patients who were treated at the City Children's Infectious Clinical Hospital, Minsk in 2009-2017.

Results

In 63 patients (75.9%) the diagnosis was confirmed laboratory, in other cases a clinical diagnosis was made on the basis of epidemiological data and / or clinical manifestations. In 56% of cases, meningococcus was detected in the blood, in 17% in the cerebrospinal fluid, in 6% in a nasopharyngeal smear and in 21% in several biological materials. Unfortunately, out of 63 patients, only one third (36.5%) carried out typing of the pathogen: meningococcus type B was detected in 17 cases (74%), type C in 17% and type Y / W in 2 patients (9%).

According to the clinical and anatomical signs (table) in our study, meningococcal sepsis in 39.8% of cases was in the form of septicemia (meningococcemia), in other cases - as a combined form of generalized meningococcal infection (meningococemia + meningitis).

In 44 patients with meningococcal sepsis (53%), the disease was complicated by the development of septic shock, and in 7 (8.4%) - there was an fatal outcome. Among patients with an unfavorable outcome, children of the first 3 years of life prevailed (86%), in 28.5% of cases meningoccemia proceeded with meningitis.

Conclusions

- According to clinical and anatomical signs, in most cases, generalized meningococcal infection proceeded in the form of a combined form - meningococcemia + meningitis;
- In every second patient, meningococcal infection was accompanied by the development of septic shock.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESPID19-1184
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Pericarditis for herpes simplex virus type 7 in adolescent - case report

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Background

Pericarditis is generally self-limited, most of the cases are idiopathic, many of these are viral, but without specific identification of the agent.
It is a case of pericarditis caused by Herpes Virus 7 (HSV-7), isolated in the pericardial fluid and in the blood, with difficult handling due to intercurrences during the treatment. Infection with this virus can cause fever, rash, seizures, meningoencephalitis. There are no reported cases of HSV-7 as a cause of pericarditis in the literature.

Case Presentation Summary

A 12-year-old female, started complaining of chest pain. Chest x-ray was performed with pleural effusion on right base and enlargement of the cardiac area, electrocardiogram was normal and in echocardiogram there was presence of significant pericardial effusion. She presented with fever on the first day in hospital and oxacillin was introduced. She was submitted to pericardiocentesis and the material collected was sent to culture - negative. PCR was performed for virus identification, HSV-7 was isolated in the pericardial fluid and in the peripheral blood, therefore the antibiotic therapy was suspended. Acetylsalicylic acid and Colchicine were introduced. Patient presented again with fever and leukocytosis, after two days of antimicrobial suspension, oxacillin was reintroduced. The anatomic-pathological result from pericardial biopsy showed "Acute pericarditis with neutrophils". The patient presented with increased liver enzymes after 30 days of treatment, considered to be drug hepatitis by acetylsalicylic acid. She came up with leukopenia (1900) and neutropenia, so the oxacillin was replaced by clindamycin and granulocyte colony stimulating factor administered. She completed 21 days of antibiotic therapy with recovery.

Learning Points/Discussion

The biggest issue of this case were the identification of the virus, but after the antibiotic withdrawal, the patient returned to fever, with recovery after 21 days of antibacterial therapy.

ESPID19-1171
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

urinalysis is an important factor predicting poor outcome among children < 90 days of life with invasive bacterial infections

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Background and Aims:

Invasive bacterial infections (IBI) are common and associated with significant morbidity/mortality in febrile children < 90 days. Much data exists on risk for IBI, few have focused on outcomes. Rarely have features at presentation been associated with IBI outcome. Urinalysis (UA) is an integral part of IBI evaluation in these infants, we evaluate UA results as predictor of outcome compared it to C-Reactve protein (CRP) and white blood cell (WBC) count.

Methods:

Retrospective cohort study of infants < 90 days with proven IBI (bacteremia, urinary tract infection (UTI) and meningitis) from Jul 2006 – June 2018. We extracted demographics, pre-existing medical conditions, cultures results (blood/urine/CSF), and laboratory data (WBC, CRP, and UA (for presence of pyuria (>10 WBCs), nitrites/leukocyte esterase). Poor outcome defined as death, meningitis, and long-term sequelae. Association of elevated CRP, WBC, and normal UA and outcome was evaluated.

Results:

We identified 140 IBI infants, one did not have a UA and was excluded; 56 were < 28 days old. E coli (70) and GBS (40) were the most frequent. Poor outcome was identified in 24 patients (1 died, 20 meningitis, 3 died with meningitis) 22/70 with normal UA and 2/69 with abnormal UA ($p<0.0001$). CRP and WBC were not associated with poor outcome. Multivariate analysis adjusting for WBC and CRP showed normal UA associated with poor outcome (OR = 33.27; CI: 4.14-267.17)

Conclusions:

Normal UA was significantly associated with poor outcome in IBI infants, WBC and CRP did not show any association with outcome. Though we only explored infants with proven IBI, a UA should be a valuable tool for the clinician not only to identify UTI but also to predict outcome in febrile infants <90 days old

Systematic Review Registration:

N/A

ESPID19-1119
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

S. Aureus bacteriemia in an immunocompetent teenager: the the role of pet scan in diagnosis

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Background

Bacteremia due to *Staphylococcus aureus* (SAB) is a rare complication in immunocompetent patients. Up to 20% of SABs can be complicated by deep foci of infection.

Case Presentation Summary

A 13-year-old patient previously healthy, consulted in the emergency department for a fever of 40ºC with 10 days of evolution and associated chest pain for 3 days. Maculopapular lesions were found on the patient's lower extremities, left hand and back. A hyperemic oropharynx and fissured lips were observed upon physical examination. No adenopathies were found. Hepatomegaly of 1cm. BT: Leukocytes 11,700 (N85%, L 7%); CRP 260mg / L. AST 148, ALT 177, GGT 208, LDH 446, Nt-proBNP: 322. Negative Streptotest. Chest X-Ray: bilateral pleural effusion with bilateral peribroncovascular infiltrates. Treatment with intravenous cloxacillin and clindamycin was started. Blood culture was positive for methicillin-susceptible *Staphylococcus aureus* (MSSA). Panton-Valentine Leukocidin (PVL) was negative. The study was extended with PET-CT which clarified the presence of several infectious foci: presence of pneumonia; disseminated foci in soft tissues of the lower limbs and larger in the blade of the left sacrum (which was suspected as a possible primary focus).

Learning Points/Discussion

S. aureus can cause localized infections to severe systemic infections. The clinical presentation depends on the presence of toxins, predisposing factors of the patient or virulence factors, such as LPV, which in this case was negative despite the aggressiveness of the infection. At times, their initial clinical suspicion is difficult given that the clinical manifestations of a systemic infection due to S. aureus can mimic several conditions. The use of PET-CT allows the detection of metastatic foci and helps to establish the duration and type of treatment and the evolutionary control of the infection.

ESPID19-1107
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Invasive group a streptococcal infections in children in orange county, california: increasing incidence of a serious disease

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Background and Aims:

Invasive group A Streptococcus (iGAS) infections have significant morbidity/mortality. We reported serious iGAS (1994; 16.6% fatal) mainly associated with varicella. iGAS decreased after varicella vaccine. We have noted an increase in iGAS. Our main objective was to identify changes in incidence of iGAS. Also explore new risk factors for iGAS and laboratory values predictive of iGAS.

Methods:

iGAS from Jul 2006–Jun 2018 was identified and divided into periods A (Jul 06 – Jun 12) and B (Jul 12–Jun 18). We calculated proportion of community acquired GAS BSI per period and compared to other community pathogens (S aureus, E coli, S pneumoniae and S agalactiae). We identified average length of stay (ALOS), intensive care (PICU) admission PICU-ALOS, complications and mortality. We evaluated white blood cell (WBC), platelets, absolute lymphocyte (ALC) and neutrophil (ANC) counts, and C-Reactive protein (CRP) mean/proportion > 30 mg/L as markers of iGAS.

Results:

Rate/10,000 discharges was 42.9 and 38.4 in periods A and B respectively. Proportion iGAS increased 57.1% (7.79 to 12.24); S aureus and E coli increased 2.9%. S pneumoniae decreased 45.2%. No difference noted in severity and laboratory parameters between pathogens, 4 (8.5%) iGAS died, all within 24 hours from diagnosis. Pre-existing medical conditions were identified for all pathogens (28.3% S aureus, 37.9% S pneumoniae, 33.9% E coli, 14.3% S agalactiae but only 16.7% GAS).

	ALOS	% PICU	PICU-ALOS	% PEMC**	WBC	Platelets	ANC	ALC	CRP	% CRP > 30	% Mortality
GAS (n = 48)	11.3 ±12.4	31.2	9.3 ±10.1	16.7	14.5 ±9.8	241.3 ±142.7	11240.8 ±8689.3	1561 ±1878.1	174.8 ±108.3	95.1	8.5
S aureus (n = 159)	10.6 ±8.4	16.8	10.5 ±12.4	28.3	11.2 ±5.8	266.6 ±135.5	7775.2 ±4811.7	1891.2 ±1738.1	129.1 ±106.8	87	0
S pneumoniae (n = 95)	8.2 ±6.8	26.3	6.4 ±6.7	37.9	16.6 ±8.9	328.4 ±139.7	11641.1 ±7424.6	2808.3 ±3035.1	187.5 ±203.9	85.9	0*
E coli (n = 59)	7.5 ±11.3	5	20 ±32	33.9	17.7 ±8.9	314.1 ±156.1	11843.1 ±6718.5	4590 ±6053	132.9 ±103.3	88.9	0
S agalactiae (n= 7)	10 ±2.4	20	4.5 ±2.1	14.3	9.6 ±3.9	279 ±141.9	5163 ±1782.6	3270 ±2395.8	137 ±142.9	66.7	0

* Two patients not included in the population were transferred from outside facilities and died in hour institution < 24 h after admission, including these two patients would result in a 2.1 mortality
** PEMC = Pre-existing Medical Condition

Conclusions:

Incidence of iGAS increased substantially in last 6 years, it is associated with high mortality occurring shortly after presentation. We did not see any patients with preceding varicella. Among survivors, severity of illness is similar to other community pathogens except E coli which is milder. No iGAS specific laboratory markers were identified. Need to raise awareness of this increasing iGAS incidence.

Systematic Review Registration:

N/A

ESPID19-1054
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Unusual infective endocarditis presentation: a 9-year-old boy with acalculous cholecystitis as an early symptom.

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Background

Infective endocarditis (IE) is an unusual, but potentially fatal disease in children. Modified Duke criteria are commonly used for clinical diagnosis. However, despite the current progress, its diagnosis continues to be difficult due to the numerous unspecific symptoms.

Case Presentation Summary

An 9-year-old boy with a minor interventricular communication (MIVC), presented with several days of fever, hepatosplenomegaly, acute phase reactants (APR) elevation and acalculous cholecystitis identified in an abdominal ultrasound. Two echocardiograms had been performed without pathological findings and blood cultures were negative. After five days of intravenous antibiotic therapy with cefotaxime and clindamycin for cholecystitis, he became afebrile, but started with acute glomerulonephritis symptoms (acute renal failure, arterial hypertension, hematuria, nephrotic-range proteinuria and generalized edema) that was handled symptomatically.

Antibiotic therapy was suspended after 10 days, relapsing fever 4 days later with increased APR and worsening of renal function. A new echocardiogram performed, revealed a vegetation on the right ventricle nearby the MIVC. Several new blood cultures were performed, and Methicillin-susceptible *Staphylococcus aureus* was isolated, confirming IE. Treatment with cloxacillin and daptomycin was started, but surgical excision s of the vegetation was decided after confirming septic pulmonary embolism in the 18F-FDG PET/CT and poor clinical and microbiological response to antimicrobials.

Symptoms and complications resolved after surgery and 6 weeks of antimicrobial treatment with a favorable evolution.**Learning Points/Discussion**

The diagnosis of IE is difficult, so we emphasize the importance of maintaining high index of suspicion in febrile children with any cardiological defect and unspecific symptoms. Acalculous cholecystitis is a rare but recognized complication of IE, particularly in *Staphylococcus aureus* bacteremia. 18F-FDG PET/CT should be considered when IE is suspected, and conventional diagnostic tools yield negative results.

ESPID19-1049
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Clinical characteristics of moraxella catarrhalis bacteremia in children

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Background

Moraxella catarrhalis is a common pathogen of the respiratory tract in children but a rare cause of bacteremia. The aim of this study is to analyze the clinical presentation and outcome of children with *Moraxella* bacteremia at our institution during an 18-year period.

Case Presentation Summary

There were 29 cases of *Moraxella* bacteremia (27 *M. catarrhalis* and 2 *M. osloensis*) in 29 children (10 female). Median age was 19 months (range: 1-52). Underlying disease was present in 3 cases (Hyper IgD syndrome, asthma and prematurity). Fever (mean: 38.9º C; median duration: 39 hours) was present in all cases except one, a one-month-old preterm (28 wk) infant with necrotizing enterocolitis (NEC). The Pediatric Assessment Triangle was stable in 25 cases, instable in 3 and one case was dead on arrival. Respiratory symptoms were present in 31% and a rash in 3 cases. Mean WBC: 13,407/μl (range: 5,000-26,500); mean C-reactive protein: 59.18 mg/L. All cases of *M. catarrhalis* were beta-lactamase producers. After the initial assessment, 11 patients were discharged and 17 were admitted to hospital (including 2 in the pediatric intensive care unit: a 2-year-old boy with severe asthma and the preterm infant with NEC). Only 12 children were initially treated with an antibiotic active against M. catarrhalis (intravenous in 8 and oral in 4) and 8 cases received no antibiotics at all. Outcome was excellent with no sequelae in all cases except the one dead on arrival, including those who did not received antibiotics at any time.

Learning Points/Discussion

M.catarrhalis bacteremia occurs mostly in immunocompetent hosts. Most cases go uneventfully and may recover even without appropriate antibiotic treatment, but it can cause an overwhelming, fatal disease.

ESPID19-1040
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Panton-valentine leukocidin staphylococcus aureus endocarditis: how to treat a case with multiple localizations?

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Background

Staphylococcus Aureus (SA) producing Panton-Valentine leukocidin (PVL) are responsible of soft tissues, bone and lung infections with a mortality rate up to 50-75%. Rare cases of PVL-SA infective endocarditis (IE) have been reported in adults.

Case Presentation Summary

We report a case of an otherwise healthy child who developed PVL-SA IE.

A 8-years old boy with a history of hip trauma and boils presented with fever, inability to bear weight, dyspnoea, crepitation and 2/6 systolic murmur on cardiac apex. Initial work-up showed WBC 14,640/µl (79,9%neutrophils), haemoglobin 6.4g/dl, CRP 230.8mg/l, procalcitonin 1.22ng/ml, ESR 120mm/h. Chest CT showed peripheral bilateral excavations of the lungs, and MRI showed osteomyelitis of head of left femur and septic arthritis. The cardiac murmur persisted after blood transfusion and haemoglobin normalization, and transthoracic echocardiography showed severe mitral valve regurgitation. After 72h, blood culture and pharyngeal aspirate resulted positive for SA, sensitive to oxacillin, vancomycin, teicoplanin, TMP-SMX, linezolid, daptomycin. Empirical treatment including association of teicoplanin, meropenem and then TMP-SMX, were started. Successively, PCR for PVL genes resulted positive. On day 6, a linezolid-based regimen was started, because of persistence of fever and bacteraemia. On day 28, despite clinical improvement and negative blood cultures, echocardiography revealed mobile vegetation on anterior mitral leaflet with valve regurgitation and echogenic mass on papillary muscle. Patient was switched to daptomycin and cefazolin with clinical improvement and disappearance of vegetation (suspected asymptomatic pulmonary embolization). Radiological resolution and ability to walk were reached at 7 months follow-up.

Learning Points/Discussion

Treating PVL-*SA* infections with multiple localizations is challenging. Linezolid is active on PVL and a good option for respiratory and bone infections. Daptomycin might be more effective on IE, but is inactive on lung and toxins.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Infective endocarditis: difficulties of differential diagnosis with rheumatic endocarditis

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Background

Infective endocarditis is a rare disease caused by a normal inhabitant of the mouth and human body.

Case Presentation Summary

A 11-year-old girl presented to the hospital with fever and joint pain. She had a history of recent tonsillitis/pharyngitis (2 months prior the admission – not treated, and 2 weeks prior the admission – received amoxicillin for 5 days). In the last 3-4 years the patient had 2-3 episodes of tonsillitis/pharyngitis per year.
There was no previous history of heart disease or rheumatic fever. Family history indicated that her grandmother suffered from rheumatic heart disease.
The physical examination revealed fever (39 C), tachycardia, and systolic murmur with maximal intensity at the apex. There were no stigmata of endocarditis (Osler's nodes, Roth's spots). Laboratory testing revealed anemia (Hb 10.2 g/dl), peripheral white cell count of 6,300/µl (77% neutrophils), erythrocyte sedimentation rate (ESR) of 33 mm/h, C-reactive protein (CRP) 12 mg/dl.
Doppler-echocardiography detected mitral valve regurgitation and asymmetric, thickened mitral valve leaflet. Acute rheumatic fever has been suspected. After following prescribed antibacterial and antiinflammatory therapy, the patient's temperature normalized. Echography repeated after 2 weeks revealed formation of vegetation in the mitral valve. Infective endocarditis was suspected. Blood cultures revealed *S. gordonii* bacteremia, which led to the diagnosis. Surgical treatment was performed: sanation of the infectious process, and mitral valve repair. A culture from the vegetation formation also revealed S. gordonii.

Learning Points/Discussion

In our case differential diagnosis of rheumatic carditis and infective endocarditis was difficult as the case met the Jones criteria (carditis, arthralgia, fever, increased level of CRP, ESR and an episode of recent streptococcal infection). The presence of vegetations allowed to suspect an infective endocarditis. Blood and vegetation cultures confirmed diagnosis of infective endocarditis.

ESPID19-0963
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Suspected kingella kingae outbreak in a belgian day-care center

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Background

With the improvement of culture and molecular techniques, infections by the fastidious gram-negative coccobacillus *Kingella kingae* are increasingly diagnosed. The pathogen is now recognized as a major cause of osteoarticular infections in children. *K.kingae* clusters in day-care facilities have been previously reported, but in limited numbers, and outbreak control measures to apply remain unclear.

Case Presentation Summary

We describe a cluster of 3 acute osteo-articular infections in a Wallonia-based day-care center occurring within a 15 days interval. Case 1 was a 22 month-old boy with femur osteitis, Case 2 a 14 month-old boy with sacroiliitis, Case 3 a 12 month-old boy with knee arthritis. *K.kingae* was the presumed pathogen based on clinical presentation, epidemiological link and positive *K.kingae* NAAT on throat swabs of Case 1 and 2. None of the cases had positive blood-cultures, and deep-site samples were unavailable. All three presented favorable outcomes with antibiotics. Additional information on the cases and the 27 other attendees of the day-care center, including risk factors for infection, were collected (Table1). As frequently described, this cluster was preceded by a hand, foot and mouth disease outbreak. Surveillance of contacts rather than chemo-prophylaxis was chosen for multiple reasons (cluster identified late in epidemic course, viral co-infections resolved, chemo-prophylaxis known for incomplete eradication of carriage etc.). Spontaneous outbreak cessation was observed as no further cases were reported in the 6 months that followed onset.

Table 1: Characteristics of the cases, non-cases, and epidemic cycle

Clinical presentation of cases							
Case	**Clinical syndrome**	**Date of onset**	**Date of diagnosis**	**Days in hospital**	**Micro-biological results[$]**	**Therapy**	**Outcome**
1	Femur neck osteitis	26/Jun/18	9/Jul/18	16 days	NAAT pos. on throat swab	Antibiotics + splint	Favorable
2	Sacroiliitis	29/Jun/18	1/Jul/18	9 days	NAAT pos. on throat swab	Antibiotics + splint	Favorable
3	Knee arthritis	Not reported	8/Jul/18	4 days	NAAT neg. on throat swab	Antibiotics	Favorable

Characteristics and risk factors of the cases & non-cases *(identified among the 30 day-care center attendees)*	**CASES (N=3)**	**NON-CASES (N=27)**
Male/Female	3/0	15/12
Median age [range]	14 [12-22]	19 [12-32 months]
Number (%) with a co-morbidity	0 (0%)	2[&] (7,4%)
Number (%) with viral infection in preceding month[£]	2 (66,6%)	9 (33,3%)
Number (%) with exposure to tobacco	1 (33,3%)	3 (12,5%*)
Number (%) previous hospitalization for infection	1 (33,3%)	4 (16%*)
Number (%) never breast-fed	1 (33,3%)	3 (12,5%*)

Epidemic cycle
Duration of outbreak: 15 days Attack rate: 11.11%. Identification of cluster and report to the regional health inspectors: 10 July 2018 (day 15)

*[$]DNA extraction of insufficient quality to allow for whole genome sequencing; [&] asthma- heart murmur; [£]viral infections during the month of June 2018: gastro-enteritis, stomatitis, hand-foot and mouth disease, upper respiratory tract infection; * data only known for N=25*

Learning Points/Discussion

Although chemo-prophylaxis is generally used in contact-management of *K.kingae* clusters, many questions remain on when it should be prescribed. Outbreaks should continue to be reported in order to compile evidence-based guidelines. In addition, timely reporting of invasive *K.kingae* infections should be considered to allow prompt identification of clusters.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Has awareness of neonatal disseminated herpes simplex virus infection increased amongst uk paediatric specialist registrars (sprs) since 2004?

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Background and Aims:

Disseminated herpes simplex virus (HSV) is a rare cause of sepsis in neonates. It can quickly lead to multi-organ failure and death if left untreated. A study performed in 2004 showed that awareness of this condition amongst paediatric junior doctors was low and needed to be increased. This survey aims to determine (i) current paediatric SpR awareness of the diagnosis and management of neonatal HSV and (ii) whether paediatric SpR awareness of neonatal HSV has increased since this was studied in 2004.

Methods:

An anonymised telephone survey of 30 'on-call' paediatric registrars in hospitals across the UK asking questions related to differential diagnosis and management in a scenario regarding a less than one month old baby presenting with non-specific signs of sepsis.

Results:

All registrars were happy to participate. Only 4 of the 30 registrars who were interviewed initially considered HSV infection as a possible diagnosis in a baby presenting with non-specific signs of sepsis (compared to 0/30 in 2004), and only 1 said that they would send blood for viral PCR as part of their investigations. Abnormal coagulation and deranged liver function tests prompted 10% and 57% respectively to consider and treat for HSV infection in an unwell neonate. All 30 would start treatment with aciclovir if there was a history of maternal HSV infection; however, only 4 said that they would ask about this risk factor when taking the history.

Conclusions:

Although there has been a slight increase in paediatric SpR awareness of neonatal HSV compared to findings from a study in 2004, knowledge of the diagnosis and management of this dangerous condition remains low and needs to be improved.

Systematic Review Registration:

n/a

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E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Mono ? No mono? ; not so easy for clinical differentiation unusual presenting features of typical ebv infectious mononucleosis in a boy.

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Background

TITLE- MONO/ NO MONO; NOT SO EASY FOR CLINICAL DIFFERENTIATION
UNUSUAL PRESENTING FEATURES OF TYPICAL EBV INFECTIOUS MONONUCLEOSIS IN A BOY

Infectious Mononucleosis(IM) is a common clinical syndrome defined by classic triad of fever, tonsillopharyngitis and lymphadenopathy with lymphocytosis .

Epstein Barr Virus(EBV) is the lead aetio-pathogen of IM across ages with variable predominance of clinical features at extremes of age-childhood and senior adults.

A different and diagnostically confusing presentation of EBV IM in an Indian boy with Acute generalized lymphadenopathy, Splenomegaly, Upper airway obstruction

due to symptomatic adenoidal enlargement and lymphocytosis is presented here.

Case Presentation Summary

Anurag,

a 9years old boy presented to OPD with possible IM

with

Uncommon clinical features-

brief fever,
normal throat,
cervical lymphadenopathy- asymmetrical, prominent anterior, tender warm nodes,
absence of skin rash even after amoxycillin;

Uncommon Lab reports- CRP raised, Heterophile negative;

Uncommon behaviour- lymphadenopathy resolving with Antibiotics.

The child improved over next week with confirmatory EBV serology - positive Anti VCA IgM**Learning Points/Discussion**

This unusual case of pediatric EBV Infectious Mononucleosis highlights

confusing variability of common clinical features and

nonspecific early laboratory investigations in EBV IM ;

making EBV serology a dependable and mandatory diagnostic investigation.

ESPID19-0905
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Epidemiological, clinical, microbiological characteristics and management of infants with osteoarticular infections: spanish multicenter study (rioped network)

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Background and Aims:

Osteoarticular infections (OAI) are not very well known in infants and their management is based on small case-series.

Methods:

Prospective study evaluating the epidemiology, clinical presentation and management of infants (<12 months) with OAI from a Spanish cohort (66 hospitals; RIOPed Network); 2015 to 2018.

Results:

A total of 95 patients from 26 hospitals were included. Median age was 245 days (41-304); 56.8% male. Sixty-four patients (67.4%) were febrile on admission, with a median value of inflammatory parameters of 53 mm/h for ESR, 3.4 mg/dL for C-reactive protein and 0.16 ngr/mL for procalcitonin. Twenty-eight (29.5%) patients had acute osteomyelitis, 42 (44.2%) septic arthritis, 18 (18.9%) osteoarthritis and 4 (4.2%) spondylodiscitis. The most frequent sites involved were knee (28.1%)/hip (23.4%) in septic arthritis, femur (36.8%) and foot bones (18.4%) in osteomyelitis and lumbar region (80%) in spondylodiscitis. A microorganism was isolated in 55.7% of cases (22% from blood culture). Most common pathogens were *S. aureus* (35.9%; 5.1% MRSA), *K. kingae* (23.1%), GBS (12.8%) and *S. pneumoniae* (10.3%). Eighty-three patients (87.4%) were hospitalized and 28.4% required surgery (56% elective). Cloxacillin+cefotaxime (40.5%) was the preferred IV antibiotic followed by cefuroxime (29.1%) whereas cefuroxime (47.2%), cefadroxil (19.1%) and amoxicillin-clavulanate (15.7%) were the most prescribed oral antibiotics. Median days of admission and total antibiotic therapy were 10 (7-19) and 28.5 (21-45), respectively. Twenty (22.2%) and 9 (11%) patients developed complications and sequelae, respectively.

Conclusions:

In this study we evaluated a large cohort of infants with OAI. We observed a significantly high frequency of outpatient management, many different sites of anatomical involvement and an elevated rate of *Kingella* isolation. The rate of sequelae was low following a therapeutic approach similar to older children, which may have management implications.

Systematic Review Registration:

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Cardiac Infections

Staphylococcus aureus bacteremic osteoarticular infections in children - the role of panton-valentine leucocidine: single centre 10-year experience

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Background and Aims:

The pathogenesis of osteoarticular infections in pediatric patients is most commonly via hematogenous seeding. The most prevalent pathogen is *Staphylococcus aureus*. We evaluated clinical features, laboratory tests and treatment outcome in acute bacteremic *S. aureus* osteoarticular infections in patients younger than 19 years hospitalized at our institution.

Methods:

We retrospectively reviewed medical charts from children diagnosed as *Staphylococcus aureus* bacteremic osteoarticular infection in a 10-year period. We compared clinical and laboratory characteristics and outcome of patients with osteoarticular infectious caused by Pantone-Valetine leukocydine (PVL) producing strains of *Staphylococcus aureus* (PVL+SA) and those caused by PVL negative *Staphylococcus aureus* strains (SA).

Results:

A total of 16 patients hospitalized at our institution from 2009 to 2018 were enrolled in the study. Among them 6/16 (37,5%) were caused by PVL+SA. All were methicillin sensitive strains (MSSA). Patients with PVL+SA osteoarticular infection had significant higher CRP level, they received longer course of parenteral amicrobial treatment and had significant longer hospital stay as compared with patients with PVL negative SA osteoarticular infection. PVL+SA osteoarticular infection were more commonly presented as acute osteomyelitis (in 50%) as compared with PVL negative SA infection, where septic arthritis (80%) was the most common presentation (table 1).

Table 1. Characteristics of bacteremic *Staphylococcus aureus* osteoarticular infection in children.

	All	PVL+SA	PVL-SA	p value
Number	16	6/16 (37,5%)	10/16 (62,5%)	
Septic arthritis, N (%)	11	3 (50%)	8 (80%)	NS*
Osteomyelitis, N (%)	5	3 (50%)	2 (20%)	
Age, years (median, IQR)	11 (4,2-13,7)	10 (6,7-13,5)	11 (1,8-14,2)	NS*
Male, N (%)	15/16 (93%)	6/6 (100%)	9/10 (90%)	NS*
Fever>38^{0}C, N (%)	15/16 (93%)	6/6 (100%)	9/10 (90%)	NS*
CRP (mg/L), median (IQR)	124 (76-222)	**215 (87-265)**	**104 (57-144)**	0,05**
Leukocyte count, median (IQR)	11,1 (8,3-16,1)	11,8 (9,07-17,00)	10,2 (7,9-17,1)	NS
Positive tissue samples	6/9*** (67%)	3/4*** (75%)	3/5*** (60%)	NS*
Lenght of hospitalization, days, (median, IQR)	20 (16-35)	**34 (24-51)**	**17 (15-23)**	0,01**
Length of parenteral antibiotic therapy, days (median, IQR)	19 (14,5-29,5)	**29 (18-51)**	**17 (14-22)**	0,04**
Length of oral antibiotic therapy, days (IQR, median)	14 (7-21)	21 (17-31)	14 (0-21)	NS**
Surgery	6/16 (37,5%)	3/6 (50%)	3/10 (30%)	NS

IQR-interquartile range

*p-value: Fisher-exact-test

**p-value: Mann-Whitney-test

***tissue samples were taken only in 9/16 children

All patients were treated successfully without recurrence after discontinuation of therapy, without septic complications and without permanent site disability.

Conclusions:

Bacteremic osteoarticular *Staphylococcus aureus* infections were caused by PVL+SA in 37,5% of cases at our institution, similar was reported also by other authors. This study emphasizes the need for PVL testing in all bacteremic *Staphylococcus aureus* pediatric osteoarticular infections to implement appropriate antimicrobial treatment.

Systematic Review Registration:

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ESPID19-0585
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Leuconostoc lactis infections in pediatrics, report of two cases

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Background

Leuconostoc lactis is a Gram positive cocci, resistant intrinsic to vancomycin. Infections by this microorganism are rare and is related to the use of central venous catheters, short bowel syndrome, parenteral nutrition, continuous enteral nutrition, immunodeficient, large burns, and may be involved in polymicrobial processes. Two cases of infection in infants are described by this microorganism, related to central venous catheters, parenteral nutrition and short bowel syndrome.

Case Presentation Summary

The first 2-month-old patient with a history of cerebral palsy in children, a gastrostomy carrier, was admitted to the pediatric intensive care unit (PICU) due to septic shock, respiratory failure secondary to mixed severe pneumonia. On the fifth day of central venous catheter placement, *Leuconostoc lactis* was identified in central and peripheral blood cultures. Linezolid was administered for 10 days and the catheter was removed. At the end of the hospitalization, discharge was uncomplicated. The second patient of 11 months old, with a history of neurodevelopmental delay, short bowel syndrome, was admitted to the emergency room for marasmus; in PICU received meropenem for bacteraemia due to *Klebsiella pneumoniae* with extended spectrum beta-lactamase resistance pattern, fluconazole for fungemia by *Candida parasilopsis* (sensitive to fluconazole), received parenteral nutrition and being in PICU presented endocarditis for *Leuconostoc lactis* for which he received linezolid for 20 days. At the end of the hospitalization, discharge was uncomplicated.

Learning Points/Discussion

It should not be forgotten that *Leuconostoc lactis* infections should be suspected in patients with gastrointestinal pathologies, short bowel syndromes, use of parenteral nutrition, central venous catheter and polymicrobial infections as in the two cases described. The identification and timely treatment must be provided to avoid cases of mortality.

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Cardiac Infections

Base excess and platelet count (bep) score correlation with an outcome of peadiatric invasive meningococcal disease (imd)

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Background and Aims:

Invasive meningococcal disease (IMD) is a severe life-threatening condition with a relatively high case fatality and permanent sequelae rate. Many different prognostic markers and scores have been investigated during the lasts decades in order to predict the outcome of the disease. Lithuania, especially Vilnius district, is one of the regions of Europe where incidence rate of IMD is very high. The aim of our study was to investigate the correlation between the newly developed BEP score and outcome of IMD in children.

Methods:

All children diagnosed with clinically and laboratory confirmed IMD and treated at Children's Hospital* from 2012 to 2018 were included into this retrospective study. Age distribution, clinical manifestation, laboratory data, BEP score, permanent sequelae and the outcome of the disease were analysed.

Results:

A total of 159 patients were included into the study. Children up to 3 yrs. accounted 56.5% of all patients. The most common clinical manifestations were acute meningococcemia (76.7%) and meningococcal meningitis (16.9%). Waterhouse-Friderichsen syndrome was rare (3.8%). In total 15 (9.4%) patients died (mean BEP score was 0.37), 20 (12.6%) developed permanent sequelae and 124 (78%) recovered (BEP score was 0.14 and 0.02 respectively). There was a strong statistically significant correlation between BEP score and the outcome of IMD ($r=0.77$, $p<0.000$). No correlation was found between BEP score and the time between first fever and AB treatment (p=0,114).

Conclusions:

BEP score was statistically significantly higher in patients with lethal outcome as compared to those who completely recovered. This easy calculated score would be very helpful in order to identify patients at high risk of death and could be successfully implemented in Lithuanian hospitals.

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Cardiac Infections

Administration of early and late-commencement sepsis in albania

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Background

The administration of early and late-commencement sepsis and neonatal intensive care entities has not been widely assessed.

Methods

185 highly focused level 1 and level 2 neonatal intensive care entities in Albania were invited to contribute in an internet-based study

Results

The ultimate analysis of the datasets 5 neonatal intensive care entities (response rate 32.3 %) evaluated university hospitals and local neonatal referral centers. The study illustrates probable fields of progress regarding pragmatic cure of infants with late onset of sepsis with vancomycin and cephalosporins, minimum volume of blood sampling for aerobic culture, concern of lumbar valve in any child with blood culture positive late onset of sepsis and drug screening features for gentamicin and vancomycin.

Conclusions

To sum up, this study discloses a considerable hole among current state Albanian guidelines and daily performances in Albanian intensive care units

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0340
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Systemic infection caused by malassezia pachydermatis in infants

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Background

Malassezia pachydermatis (*M. pachydermatis*), a basidiomycetous yeast belong to the genus of Malassezia, is one cause of fungemia in neonates and has been implicated in several outbreaks in neonatal intensive care units. Our study reported four cases of fungemia in infants, due to *M. pachydermatis*, in a neonatal intensive care unit over an 18-month period.

Case Presentation Summary

All patients were preterm with the range of birth weight and gestational age from 490-810 g and 23-26 weeks and had multiple complications. All received fluconazole as prophylaxis before fungemia, occurred at the age from 7-28 day-old with duration of previous central vascular catheters insertion from 7-23 days. All of them received parenteral lipid supplement for nutrition. Symptoms and signs of infection included color change (3), need for re-intubation (1), hypotension (1), leukocytosis (1), bandemia (2), thrombocytopenia (4), and secondary focal infection at lung (1).One infant had concomitant *Staphylococcus aureus* sepsis while fungemia occurred. Two of them had removal or change of the central intravascular catheter and one had lipid emulsion been discontinued. All patients received intravenous anti-fungal treatment consisted with amphotericin B or liposomal amphotericin B for 2-3 weeks and recovered from their *M. pachydermatis* infection.

Learning Points/Discussion

Patients with *M. pachydermatis* systemic infection are very immature infants with ELBW and multiple comorbidities. Prolonged use of central catheters and parenteral lipid supplement are common predisposing factor. Signs and symptoms are nonspecific. While prophylaxis use of fluconazole cannot prevent systemic infection for *M. pachydermatis*, effective systemic antifungal agent may be the most important factor to treat invasive *M. pachydermatis* infection.

ESPID19-0219
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Facial cellulitis in children: cases series

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Background

Facial cellulitis in children usually caused by trauma, insect stings, dental caries, sinusitis, allergic reaction or rarely tumor (neuroblastoma). It could be life threatening, such as visual loss or intracranial infection. Knowing the source and characteristics of the infection is essential in management these children. We present our experience of the clinical source and bacteriological data of facial cellulitis in order to provide the treatment options.

Case Presentation Summary

A total of 16 cases (age range: 2-16y/o) with facial infections were identified with eye swelling (100%), fever (40%), history of sinusitis (56%), trauma (25%), orbital Computed tomography (CT) (68%). Eight cases (50%) had sinusitis and presented with orbital cellulitis. Eight cases (50%) underwent orbital orbitotomy and had evidence of staphylococcus infection from pus culture. All cases had received antibiotic treatment. Vancomycin was administered for Staphylococcus aureus infection with danger triangle site. Third generalization cephalosporin(Ceftriaxone) was administered for sinusitis with covering Streptococcus pneumoniae and Haemophilus influenzae . Ampicillin combination with third generation cephalosporin (ceftriaxone) was better treatment option in considering of drug resistance rate of nontypeable Haemophilus influenza (ntHi). Two cases had corticosteroid treatment. In considering of end point of treatment, we followed Erythrocyte sedimentation rate (ESR) and Platelet count in more severe cases. All cases had good prognosi

Learning Points/Discussion

The location of facial cellulitis could be distinguished by source.

Abscess formation should be treated with incision and drainage. Performing gram stain, instead of culture alone, as early as possible may be useful in the diagnosis.

Complete blood count and differential count had limited help in diagnosis. The orbital CT should be performed in retro-orbital abscess, sinusitis and surgical indication .

The treatment options should be considered source of facial infection and antimicrobial resistance.

ESPID19-0191
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Granulicatella adiacens infections in children

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Background

Granulicatella spp. are uncommon causes of infection. The microorganisms are usually difficult to identify and difficult to treat. *G. adiacens* has been associated with bacteremia and endovascular, central nervous system, ocular, oral, bone and joint, and genitourinary infections. It is aimed to describe the clinical presentations, laboratory characteristics, treatment modalities, and outcomes of pediatric patients with *Granulicatella* spp. infections.

Case Presentation Summary

The study was conducted at a pediatric tertiary care center in Ankara, Turkey. Blood cultures were screened for *Granulicatella* spp. between January 2005 and January 2017 retrospectively. The clinical and laboratory features of patients were documented. During the 12-year study period, 4125 patients with positive blood culture results were investigated. Seven patients (five males and two females) were diagnosed with *G. adiacens* infection (0.1%). The mean age of the patients were 79.5 ± 49.8 months (median: 96 months, range: 10-140 months). Three patients had bacteremia, three patients had catheter-related bloodstream infection (CRBSI), one patient had bacteremia and pneumonia, and one patient had infective endocarditis. Four of the infections were community acquired and three were health-care associated. All patients survived.

Learning Points/Discussion

Granulicatella adiacens might be responsible from invasive infections in children. The majority of reported isolates recovered from blood culture. Because the organisms grow poorly on solid media, they can easily be overlooked. With the discovery of advanced techniques the organism became more detectable. Awareness of clinicians and suspicion and identification of this microorganism by microbiologists are important for prompt diagnosis and treatment.

ESPID19-0125
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Invasive group a streptococcal infections in children

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Background and Aims:

Group A streptococcus (GAS) is a known pathogenic organism mostly responsible for skin and URTIs. Invasive group A streptococcal disease (iGAS) refers to illness associated with the isolation of GAS from a sterile site such as blood, cerebrospinal fluid or pleural fluid. We reviewed the clinical presentation and management of children with iGAS infections admitted to our Children's Hospital in the last eight years.

Methods:

Patients < 18 years of age who had positive isolation of GAS from sterile site cultures over the last 8 years (2010–2018) were identified from the microbiology database. Details on clinical presentation, treatment, outcome and follow up were collected using a structured proforma.

Results:

A total of 57 children had iGAS in the last 8 years; 72 clinical samples from these children grew GAS. The mean age of the children was 5 years. The mean length of stay (LOS) was 11 days. Twelve children (21.1%) were admitted to ICU with a mean LOS of 3.8 days. 4 children (7%) died due to iGAS infection.

Pneumonia was the most common diagnosis; twelve patients had sepsis and six patients (11%) presented with septic shock. Two patients had toxic shock syndrome and nine had chickenpox within the previous month.

Initial antibiotic management was varied, 50% had their antibiotics optimised to IV benzylpenicillin after the confirmation of GAS. The mean duration of IV antibiotics was 8.8 days; the mean duration of subsequent oral antibiotics was 9.6 days.

Most children had a good recovery following treatment with penicillin. 7 Children were readmitted needing a further course of antibiotics.

Conclusions:

Our study highlights the varied symptomatology and management of children with iGAS, which re-enforces the importance of early diagnosis and prompt initiation of appropriate antibiotics.

Systematic Review Registration:

n/a

ESPID19-0121
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

A case of clavicular osteomyelitis secondary to group a streptococcal infection

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Background

Osteomyelitis of the clavicle is rare and is difficult to diagnose in children. We present the case of a 5-year-old child who presented with acute osteomyelitis of the clavicle caused by Group A beta-hemolytic Streptococcus (GABHS).

Case Presentation Summary

A 5-year-old child was admitted with a history of fever, sore throat and left shoulder pain. The child thereafter developed a tender swelling in the region of the left clavicle. Child was started on intravenous (IV) antibiotics. Bloods showed a leukocytosis and high CRP. Blood culture was positive for GABHS. Child received IV benzyl penicillin followed by oral cephalexin. Child developed a swelling in the region of the left clavicle at the end of antibiotic course and was readmitted. MRI clavicle showed osteomyelitis of the medial clavicle with subperiosteal collections. Child had an incision and drainage of the left clavicle collection. Child had 2 weeks of intravenous antibiotics follows by 4 weeks of oral Phenoxymethylpenicillin. Child continued to be well with no further recurrence of symptoms and was discharged from further follow up.

Learning Points/Discussion

Osteomyelitis of the clavicle is a rare condition in children, comprising < 3% of all cases of paediatric osteomyelitis. The commonest bacterial etiology is Staphylococcus aureus. Up to 10% of paediatric osteomyelitis are caused by GABHS, however, there are no published case reports of GABHS clavicular osteomyelitis in children.

GABHS causes invasive infections with significant mortality and morbidity. Early identification helps in nitiation of appropriate treatment.

Learning points:

- Osteomyelitis of the clavicle must be considered in children presenting with a swelling in the clavicular region.
- GABHS is a causative agent in osteomyelitis of the clavicle in paediatric age group.
- Identifying the microbial etiology in these children ensures early initiation of appropriate antibiotic management.

ESPID19-0113
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

The comics study: complications of osteomyelitis in children and its epidemiology in singapore's largest tertiary children's hospital

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Background and Aims:

Osteomyelitis represents a significant disease burden and can be especially debilitating for bone growth and puberty in paediatric patients. In this retrospective study, we looked at the epidemiology and complications of children admitted to our hospital with osteomyelitis.

Methods:

Children under 16 years old admitted from January 1999 to December 2014 with the diagnosis of osteomyelitis proven radiologically and/or microbiologically were included in our study. Data collection was done by reviewing their case notes and laboratory records retrospectively.

Results:

167 patients (58.1% males) met the inclusion criteria. Median age at presentation was 9 years 4 months old. Majority (77.9%) of the patients had acute or subacute osteomyelitis while 33 patients (19.8%) had chronic osteomyelitis, out of which 6 of them had chronic recurrent multifocal osteomyelitis (CRMO). 4 patients had tuberculous osteomyelitis, most of them presented acutely. Pain was the main presenting complaint affecting 87.4% of patients. 17.4% of the patients had concomitant septic arthritis. 20.4% of patients had bacteraemia, with Staphylococcus aureus being the most common organism. Radiological changes were observed in 75.4% of patients. Fever was significantly associated with microbiologically proven osteomyelitis (p=0.004). 63.5% of patients had to undergo incision and drainage. Complications of osteomyelitis were observed in 33 patients (19.8%) during hospital stay or subsequent follow-up, including bone deformities, destructive changes and pathological fractures. Mortality was 1.2% (2 patients).

Conclusions:

Our study identified that at least 20% of patients with the diagnosis of osteomyelitis were left with the long term sequelae affecting bone growth and limb function, and even death. Clinical suspicion aided by radiological and microbiological investigations should be exercised, so that timely administration of antibiotics with subsequent rehabilitative therapies and follow-up can be arranged to minimize complications.

Systematic Review Registration:

Not applicable

ESPID19-0102
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Atypical hand, foot and mouth disease

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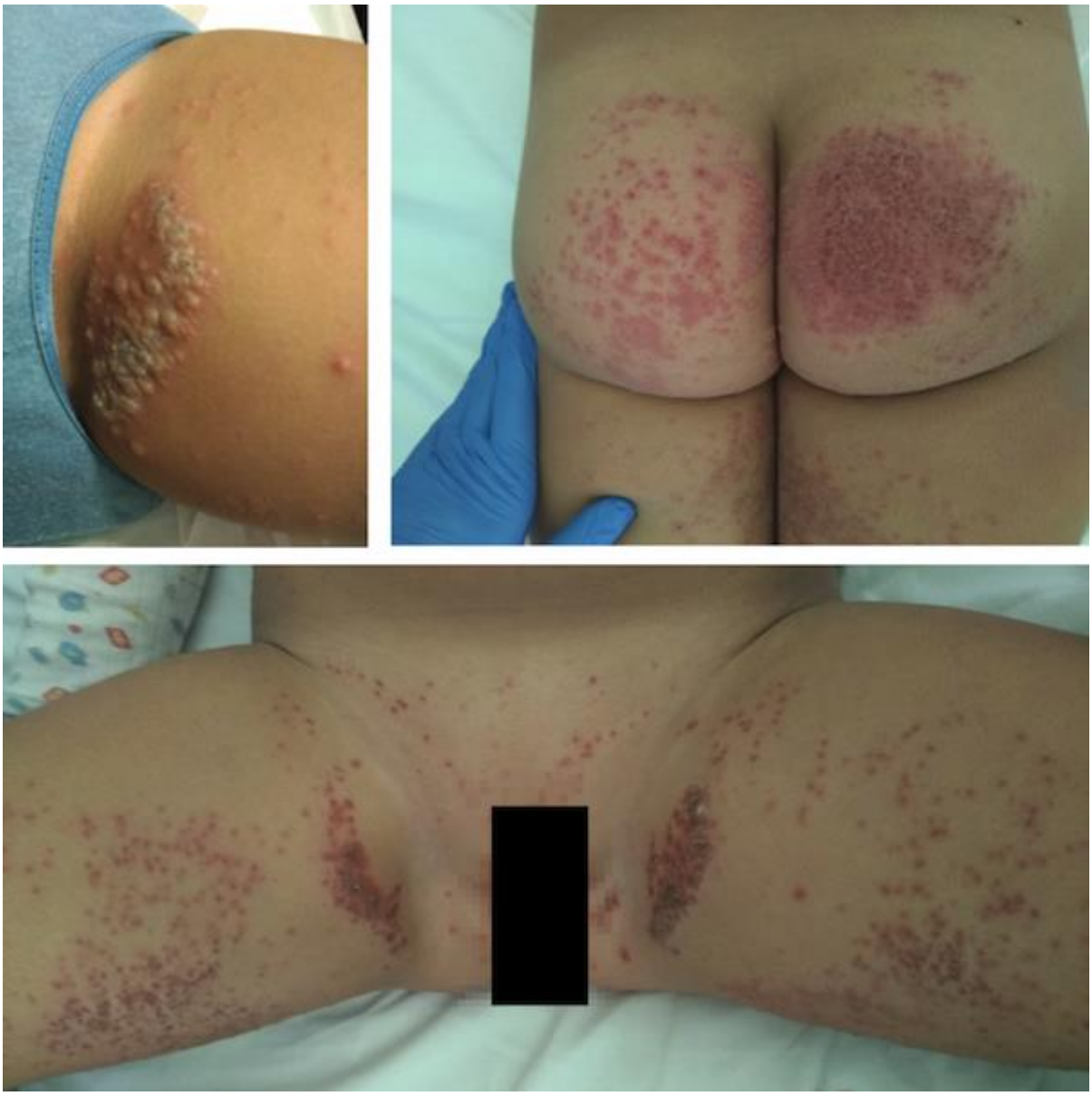
Background

Hand, foot and mouth disease (HFMD) is a contagious viral syndrome, which mainly affects infants and young children, and is caused by different enterovirus serotypes. The viruses are usually transmitted by the fecal-oral route and its typical presentation is oral enanthem and a macular, maculopapular, or vesicular rash of the hands and feet, and sometimes in other locations, such as buttocks, legs, arms, and rarely in genitalia. We here report an atypical manifestation of an otherwise common syndrome.

Case Presentation Summary

A 5 year-old-girl was admitted to the paediatric emergency room with a 24-hour history of erythematous macular lesions in the groin with extreme itchiness. On examination, she had multiple vesicles, some of them already eroded, surrounded by an erythematous halo. Throughout her stay, new macules and vesicles appeared on her genitalia, bottom, hands, mouth and feet; after a period of 24 hours, all lesions had formed into scabs. Given the appearance of the skin lesions and the symptoms, it was hypothesized an atypical HFMD. This case could have been easily mistaken for other clinical entities, such as Eczema herpeticum and Varicella, given that it was an itchy rash, or Henoch-Schonlein Purpura, due to the rash distribution. In this case, given its atypical presentation, a stool sample was collected and the etiological confirmation of an enterovirus infection was obtained through nucleic acid amplification.
The patient remained hospitalized for 2 days with supportive therapy and medicated with antihistaminic only. With no further complications, she was discharged.



Learning Points/Discussion

Currently there is no specific treatment available for enteroviruses. HFMD is usually a self-limited and benign syndrome, however given its potentially severe complications, physicians should be aware of its different presentations.

ESPID19-0080
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

A case of abiotrophia defectiva infective endocarditis presenting as pneumonia

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Background

Abiotrophia defectiva is an extremely rare pathogen of infective endocarditis. This fastidious and aggressive organism is involved in embolic complications and valvular destructions, but septic pneumonia is very rare. We report a case of infective endocarditis caused by *Abiotrophia defectiva* in a 6-year-old boy who presented with fever and right chest pain.

Case Presentation Summary

The patient was diagnosed with perimembranous ventricular septal defect at birth and has been routinely followed up since. The chest radiography revealed patchy haziness in the right middle lobe zone with right pleural effusion at initial presentation while no vegetations were found on transthoracic echocardiography (TTE). Two days later an 11.8 x 7.7 mm vegetation on the anterior and septal leaflets of the tricuspid valve was noted on TTE. Blood cultures grew penicillin-susceptible *Abiotrophia defectiva* and the patient was treated with ampicillin and gentamicin. Despite antibiotic therapy, chest pain recurred and CT pulmonary angiogram revealed multifocal patchy consolidations in the bilateral lower lobes as well as in the left upper lobe. There was no evidence of pulmonary thromboembolism. The vegetation was surgically resected and ventricular septal defect closure was performed. Ampicillin was changed to ceftriaxone due to drug fever and the patient received intravenous antibiotics for a total of 6 weeks and recovered well.

Learning Points/Discussion

Abiotrophia defectiva should be considered in infective endocarditis patients especially those with atypical presentations as complications can occur and surgical management is often required.

ESPID19-0063
E-Poster Viewing - May 7-10 - E-Poster Hours

Cardiac Infections

Characterising the severity of parechovirus infections requiring intensive care admissions during outbreaks at a tertiary paediatric centre

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Background and Aims:

We aim to describe the clinical and laboratory features of severe parechovirus (HPeV) infections in infants admitted to neonatal and paediatric intensive care units in Children Hospital Westmead (CHW): a tertiary paediatric hospital in Australia.

Methods:

Data on all infants admitted to the intensive care units (ICU) from 2013 to 2018 in whom HPeV was isolated in, was collected. We used patient medical charts to collect comprehensive demographic data, length of stay, clinical features, biochemistry results, imaging and therapeutic treatments such as antibiotics, fluid boluses, inotropes and modes of respiratory support. Validated organ dysfunction scores, PELOD and PIMS2 were used to help characterise “severity”.

Results:

We identified 32 patients admitted to the ICU at CHW with HPeV from 2013 to 2018 during the outbreak periods. There was an increase in non-elective admissions to CHW ICUs and a proportional increase in HPEV admissions with incident rate ratio (IRR) of 1.13 (p value of 0.018).19 patients had a CRP >10 and the largest proportion of these patients presented between 2017 and 2018 (n=11). 6 patients required inotrope support. 5 of these patients presented from 2017-18. 7 patients were ventilated of which 4 infants admitted in 2017-18 were ventilated for >48 hours.

Conclusions:

We report an extensive case series on patients with HPeV positive samples presenting to an ICU in a tertiary children’s hospital over three different outbreak periods. We have attempted to define the characteristics of these patients, why these patients required admission to ICU and whether this is an increasing trend with HPeV causing a more severe illness than previously described. We have been able to demonstrate a statistically significant proportional increase in HPeV admissions compared with the overall non-elective ICU admissions.

Systematic Review Registration:

N/A

ESPID19-0683
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Coinfection with hepatitis a and e presenting as acute meningoencephalitis in an adolescent boy

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Background

Infections are still a major problem in the developing countries like India because of poor sewage disposal and economic restraints. Co-infection with hepatitis A and E is reported occasionally in the literature.We report an adolescent boy who presented with acute meningoencephalitis and coinfection with hepatitis A and E.

Case Presentation Summary

An 11 year old boy came to the emergency department of our hospital with complaints of fever,vomiting and headache 4 days and altered sensorium with one episode of uprolling of eye balls on the day of admission. On examination,child was responsive only to deep pain,neck rigidity and kernig's sign were positive.There was no pallor,cyanosis or icterus.Initially child was managed as a case of acute meningo encephalitis with ceftrioxone and acyclovir.Cerebrospinal fluid analysis revealed a total cell count of 80 cells/dl with all lymphocytes,proteins and sugar were normal.MRI brain done was also normal.Child's sensorium started improving but vomitings persisted and urine became dark colored.Thinking about acute viral hepatitis,liver function tests were done which revealed a SGOT-4262 U/L,SGPT-3698 U/L,total bilirubin-4.45 mg/dl,direct bilirubin-3.5 mg/dl.Viral markers were positive for hepatitis A and E.In absence of an alternative etiology,the aseptic meningitis was attributed to the co infection with hepatitis and E. Child's sensorium normalized and vomiting stopped.Repeat LFTs showed a falling trend in SGOT/PT and bilirubin levels.

Learning Points/Discussion

Isolated aseptic meningitis, unaccompanied by hepatitic features is an unusual presentation of a hepatotrophic viral infection. Co-infections should be kept in consideration when someone presents with atypical symptoms or unusual disease course like this presented case.Improving the sanitary conditions and vaccination against hepatitis A is a cost effective way of avoiding these diseases.

ESPID19-0435
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Acute meningitis in pediatric population in last ten years

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Background and Aims:

Meningitis incidence has decreased in last years due to vaccination. Diagnosis and early treatment is the key to avoid high morbidity and mortality, especially in those caused by bacterial agents. The aim of our study is to described clinical and epidemiological characteristics of acute meningitis in our environment which should be useful to diagnose and start treatment (if required) as soon as possible.

Methods:

Descriptive and retrospective study of admitted patients in two hospitals of Madrid with bacterial meningitis (BM) and viral meningitis (VM) between 2006-2016. A total of 181 patients were included: BM: 25(13,8%);VM 156(86,2%).

Clinical, epidemiological and laboratory results were collected and according to bacterial or viral etiology were compared using SPSS 19.0 system (significance level: $p < 0.05$).

Results:

Average of age: 2 months in BM and 59.8 in VM, ($p<0.05$). Similar distribution by sex. Seasonal predominance of spring: 40% of BM and 54% of VM without significant differences. No differences in symptoms(headache,fever) at diagnosis,except low level of consciousness (higher in BM (16% vs 0.6%; $p<0.01$).

There were significant differences in acute phase reactants and cerebrospinal-fluid(CSF) analysis (see figure 1). 22 BM had positive CSF culture (88%), and Enteroviruses real-timePCR were positive in 117 VM(75%). Average length of stay in hospital: shorter in VM (2 days vs 12 days, $p<0.01$)

Figure 1. Lab test and cerebrospinal fluid analysis

		Bacterial meningitis	Viral meningitis	p
Blood test	C-reactive protein (>70mg/L)	40%	5.8%	<0.01
	Procalcitonin (>2 ng/mL)	40%	1.9%	<0.01
Cerebrospinal fluid	White blood cells	275 (RIC 52-1875)	67.5 (RIC 30-186.5)	< 0.01
	Glucose	131 (35-227)	42 (30-62.5)	< 0.01
	Protein	63 (21-67)	54 (48-61)	0,524

Conclusions:

Seasonal predominance of meningitis still exists regardless of the etiological agent. Except for the earlier age of presentation and higher frequency of low level of consciousness in the bacterial ones, symptoms were similar in both groups, so etiology can not be predicted by clinical features. C-reactive protein and procalcitonin should be assessed as tools that help to diagnose and identify meningitis.

Systematic Review Registration:

-Baquero-Artiago F., Hernadez-Sampelayo T., Navarro M.L. Meningitis Bacteriana.An Pediatr Contin. 2007;5(1):22-9

ESPID19-0024
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

A rare case of salmonella typhi meningitis in a four month old infant: a case report

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Background

S meningitis is uncommon cause of gram-negative bacterial meningitis.Clinicians should be alerted on the existence and progression of different pathogens which can cause meningitis. This should be done in order to implement early control measures. These control measures can then be applied to prevent any further complications.

Case Presentation Summary

The case is that of an 4-month-old male infant admitted to the Pediatric emergency unit of the dayanand medical college and hospital,Ludhiana,punjab, with a 2-day

history of excessive crying and fever and 1 day history of lethargy and one episode of seizure.Physical examination revealed a well-nourished infant with a blank, vacant look and a temperature of 38.5°C.Neurological examination revealed bulging anterior fontanel and hyperreflexia.The liver and spleenwere not enlarged.He had been admitted a day earlier with gastro-enteritis and had required rehydration with intravenous fluids in an outside facility.A lumbar puncture done showed turbid cerebrospinalfluid (CSF) with a total white cell count of 450 cells/dl (42 percent were polymorphonuclear cells) and a glucose level of 18mg/dl (blood sugar-115 mg/dl) and Protein was 425mg/dl.CSF culture yielded Salmonella typhi.The isolate was susceptible to ampicillin,ceftriaxone, amikacin,chloramphenicol ,ceftazidime and resistant to cefuroxime.Haematological studies showed the white cell count to be 18,600/mm3 with 70% neutrophils, 23% Lymphocytes and 0.1% eosinophils.Blood culture done at admission yielded growth of Salmonella typhi.On admission the patient was commenced empirically on Ceftriaxone and amikacin, given intravenously.In view of persistant seizures,MRI brain was done which revealed ventriculitis and multifocal vasculitic infarcts.Gradually child started improving and was discharged after 21 days of intravenous antibiotics.

Learning Points/Discussion

- Meningitis can be caused by pathogens that are primarily infecting the gastrointestinal tract.Meningitis in infants can lead to serious sequelae, so early detection and proper treatment is mandatory.

ESPID19-1078
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Detection of bordetella pertussis (bp) by rt-pcr on cerebrospinal fluid (csf) in an infant with acute encephalopathy

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Background

Encephalopathy is an uncommon but serious complication of pertussis. The diagnosis is suggested by cerebral dysfunction manifestations with pertussis infection in the absence of other causes. To date the organism has never been isolated from CSF in the anecdotal cases reported in literature.

Case Presentation Summary

We report the case of a 6 month old girl presented to our third-level hospital with paroxysmal cough and low reactivity.

The patient received just one dose of pertussis vaccine.

Wet cough started about 20 days before hospitalization. After 1 week the cough became paroxysmal and azithromycin and steroid were prescribed by the pediatrician suspecting pertussis.

At the admission she was hyporeactive and drowsy. At the neurological examination no focal deficits were found but moderate neck stiffness was reported.

Electroencephalography showed a bilateral slowing-down rhythm in the temporal, parietal and occipital areas, mainly on the right hemisphere. Cerebral ultrasound findings were normal. The analysis of the CSF revealed no signs of infection. Given the strong suspect of whooping cough, BP PCR was investigated on the CSF and a low positivity was detected, confirmed by a second test. Moreover, PCR and culture for BP on the nasopharyngeal swab were positive. As soon as these data were available, iv steroid, iv immunoglobulin and oral clarithromycin were prescribed.

No cerebral MRI was performed due to anaesthesiology risks correlated to the coughing fits.

During the hospitalization, the patient’s general clinical condition and the neurological status progressively improved. Subsequent EEG performed 11 days after the first one was normal. Follow up examination at 4 months after the initial admission revealed good physical conditions and neurological development.**Learning Points/Discussion**

In children with pertussis and neurological manifestations lumbar puncture with BP PCR investigation should be performed.

ESPID19-0836
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

11-year old boy with excessive sleepiness

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Background

Encephalitis presenting as a moderate change in daily activities is challenging to recognize in the primary care settings, but proper diagnosis is essential for the management.

Case Presentation Summary

An 11-years old boy sought medical attention due to fever, vomiting and head pain for three days. In the absence of evident focal neurological signs, he was diagnosed and managed as a sore throat. After a short period of relief, moderate fever, excessive sleepiness, and mild personality change appeared, and the boy was admitted to a hospital. Moderate pleocytosis in cerebrospinal fluid (CSF), abnormalities in EEG and MRI confirmed the diagnosis of encephalitis. HHV-7 was detected in CSF by Real-Time PCR. The boy was treated with dexamethasone and recovered without sequelae.

Learning Points/Discussion

As behavioral changes can be the first symptoms of encephalitis, pediatricians should take alterations in children's regular activity seriously. Even though the treatment of viral encephalitis generally remains symptomatic and controversial patients with suspected encephalitis should be hospitalized.

ESPID19-0736
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Follow-up immunological evaluation of children older than 3 years affected by an acute central nervous system infection

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Background

Community-acquired bacterial meningitis is a devastating and life-threatening disease, even in developed countries, despite effective antibacterial agents and implementation of childhood vaccination programmes. Aim of this study is to define if children who experienced meningitis, meningoencephalitis and encephalitis have a normal immune system.

Case Presentation Summary

We enrolled patients admitted to Bambino Gesù Children Hospital , Rome, Italy, for meningitis, meningoencephalitis, encephalitis, between January 2006 and June 2016 and re-evaluated at day hospital follow-up. Follow up consists in pediatric visit, vaccine status evaluation and laboratory exams to investigate the immune status. 126 participants had been identified. Of those, we excluded 30 patients affected by VZV, 34 patients younger than 3 years old at the follow-up evaluation, 6 patients because of comorbidities, 15 patients because of incomplete data. Our final sample included 42 patients, with a mean age of 9,81 years old. At least one immunological alteration ain most of our sample (74%, 42/57). Considering immunological exams, Fenotipe B changes and immunoglobulin level alterations were the most observed. In particular, 47,6% had alterations in B cell proliferations test, 26,2% had any Fenotipe B changes. Moreover, we observed lower values of IgG and IgM in patients younger than 5 years old and younger than 4 years old respectively. Finally, CD3, CD19 and CD16/CD56 were lower than reference value considering patients older than 12 years old.

Learning Points/Discussion

The immune system plays an important role in determining the course and outcome of the diseases.
An immune evaluation is suggested in children if a single episode of acute central nervous system infection occurs because our preliminary results may indicate that they may have subclinical, but measurable immunological alterations.
Quantitative assessment of B cells, IgA, IgM and IgG should be performed.

ESPID19-0634
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Central nervous system complications of varicella-zoster virus in childhood: a 12-years' experience of a pediatric hospital

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Background

The varicella zoster virus (VZV) is a neurotropic herpesvirus. About 14%-20% of all pediatric varicella hospitalizations are due to neurologic complications.

Methods

Descriptive study of children admitted with neurological complications by VZV in a tertiary pediatric hospital, between 1st January 2006 and 31th December 2018. Epidemiological, clinical, therapeutic and evolution data were analyzed.

Results

40 children (10.7%) of 375 varicella hospitalizations had neurologic complications (median age 36 months; 65% male). Of these 80% were previously healthy, 12/40 (30%) received previous oral acyclovir and one child was vaccinated. The time between rash onset and neurologic symptoms ranged from 1 to 4 days (median 4 days). Clinical syndromes included seizures (n=15), acute cerebellar ataxia (n=14), transient changes in neurological examination (n=2), encephalitis (n=3), acute disseminated encephalomyelitis (ADEM) (n=2), stroke (n=2), *Guillain-Barre* syndrome (n=1) and acute cerebellar edema (n=1).There was a trend for severe complications in older children (45 vs 36 months; p=0,086) and in children who received previous oral acyclovir (5/9). Median days between onset of rash and neurological symptoms were higher in patients with severe disease (8 *vs* 3days; p=0.026). All patients with severe disease underwent treatment with intravenous acyclovir. 7/9 of children with severe illness had either a motor deficit (4) or disturbed consciousness (3). Residual neurologic sequelae (hemiparesis) at one year occurred in one patient with hematologic disease undergoing bone marrow transplantation and ischemic stroke.

Conclusions

Nervous system complications are rare in childhood and can follow primary VZV infection even after vaccination or antiviral prophylactic therapy. Although severe illness can occur, the majority recover without neurologic sequelae.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0540
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Neuropsychological and internalizing problems in acute central nervous system infections after follow-up evaluation

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Background

Acute central nervous system (ACNS) infections such as meningitis, encephalitis and cerebellitis are related to considerable rates of morbidity and mortality despite the availability of effective antimicrobial therapy and the improvement of survival rates. Although physical and neurological complications have been most described, less is known about neuropsychological sequelae and residual behavioural problems after ACNS infection. In details, few studies focused on psychopathological impairment such as internalizing (ID) and externalizing disorders (ED) following ACNS infection. Aim of our study is to find out if internalizing problems may affect ACNS infections survivors in order to prevent further disabilities.

Case Presentation Summary

Participants were a consecutive sample of 84 survivors of childhood ACNS infections, admitted to the Bambino Gesù Children's Hospital, Rome, Italy, from June 2013 to June 2015 and then re-evaluated at follow-up. Both patients and their parents underwent a psychological interview during a follow-up control. The tests performed varied according to patient's age and ability to collaborate with the psychologist who administered the tests. The following tests were administered to participants: the Leiter international performance scale – revised (Leiter-R), the child behaviour checklist (CBCL), the K-SADS-PL test. Our study revealed that 20% of ACNS survivors developed anxiety disorders and 10% subclinic anxiety during the follow-up evaluation.

Learning Points/Discussion

Patients admitted because of ACNS infections may develop anxiety disorders during the follow-up.
An early detection of neuropychological and internalizing problems is important for disease prevention and control efforts.
Specific psychological tests should be introduced as routine screening for psychological disorders and cognitive deficits in ACNS survivors in order to prevent mayor psychological sequelae.

ESPID19-1148
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Pediatric anti-n-methyl-d-aspartate receptor encephalitis: case series

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Background

Anti–*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a severe form of encephalitis with specific neurological features that is increasingly recognized in children and adolescents worldwide. In the pediatric population symptoms are similar to those in adults, but seizures, behavioral changes and movement disorders are more prominent and occurrence of underlying tumor is lower. We describe clinical features and treatment outcomes of seven children with anti-NMDAR encephalitis treated at University Hospital for Infectious Diseases in Zagreb.

Case Presentation Summary

A total of 7 children were treated between September 2012 and September 2018. The median age was 9 years and 8 months (range 10 months-17 years); 5 of them were female. All cases presented with seizures, depressed level of consciousness and movement disorder; insomnia was observed in 85%; behavioural changes, memory deficits and hallucinations in 71%; autonomic instability and language dysfunction in 57% of cases. The diagnosis was confirmed by positive anti-NMDAR antibodies (serum and CSF). Three patients required mechanical ventilation (duration 4-14 days). No patient had a tumor. One infant had a biphasic disease with HSV encephalitis followed by NMDAR encephalitis (22 days after). Although one patient had clinical improvement after corticosteroids, others (after initial immunoglobulins/total plasma exchange therapy) were treated with second-line therapies: cyclophosphamide (n=5) and rituximab (n=2). All children had substantial recovery; relapses were not observed.

Learning Points/Discussion

Our case series outlines common clinical features of pediatric anti-NMDAR encephalitis. Good clinical outcomes were observed in all children after first or second-line treatment; full recovery with only minor deficits were present in more than half of the cases. This disorder is likely under-recognized and should be suspected in children with neuropsychiatric deficits because early recognition and prompt treatment are essential to obtain full recovery in these patients.

ESPID19-1021
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Enteroviral meningitis in children

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Background and Aims:

Enteroviruses (EVs) are the most common cause of aseptic meningitis in children. This study aimed to identify the epidemiological characteristics, clinical features and cerebrospinal fluid (CSF) findings associated with EV meningitis.

Methods:

We performed a 5-year retrospective study of 57 children, treated at a tertiary children's hospital, with positive CSF EV polymerase chain reaction (PCR) and negative blood and CSF bacterial cultures.

Results:

The median age was 13.7 months (IQR 1.92-67.87 months). Forty two (73.7%) patients were male. Although EV menengitis were encountered throughout the year, most occured during summer and spring months. Fever, vomiting, rash, irritability were the most pronounced symptoms. Pleocytosis with the predominance of lymphocytes was observed in 45/57 of specimens and 12/57 did not have CSF pleocytosis. The median CSF white cell count was 80 cells/mm^3 (IQR 2.5-241 cells/mm^3). The median age of the patients that has no cell in CSF was 13.8 months (IQR 2.94-50.13 months). The median hospital stay was 6.5 days (IQR 5-9 days) and all of the patients were received empiric antibiotics. All patints had a favorable clinical outcome without complications.

Conclusions:

Although EVs generally responsible from benign aseptic meningitis, the clinical presentation may not differentiate from bacterial meningitis. CSF pleocytosis may not be seen especially in young infants.

Systematic Review Registration:

No

ESPID19-1007
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Meningitis caused by reactivation of latent varicella-zoster virus infection in an immunocompetent adolescent.

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Background

Varicella-Zoster Virus (VZV) causes chickenpox, which is the primary infection that usually occurs in childhood. The virus remains latent in dorsal root ganglia or cranial nerves and may reactivate years later to cause shingles. Here we report an adolescent who developed VZV meningitis due to reactivation of the virus 12 years after chickenpox.

Case Presentation Summary

A previously healthy 17-year-old adolescent was admitted to the Department of Pediatric Infectious Diseases with fever, headaches and occasional vomits. On admission he presented with meningeal signs: neck stiffness and upper Brudzinski sign. Lumbar puncture was performed and cerebrospinal fluid (CSF) was examined showing pleocytosis of 522 cells/mm3 (93% lymphocytes) and protein concentration of 170 mg/dL. A routine evaluation of lymphocytic meningitis excluded enteroviral meningitis, tick-borne encephalitis, and Lyme disease. Although ten days after the admittance his body temperature was normal and meningeal signs were absent, the patient constantly reported intense headaches. A control lumbar puncture revealed pleocytosis of 178 cells/mm3 and protein concentration increased to 162 mg/dL. A further detailed virologic examination of the CSF revealed the presence of VZV-DNA by PCR. Head MRI scan has not revealed any important abnormalities in the brain. Treatment with acyclovir was initiated for the next 21 days resulting in a full recovery. Patient had a history of uncomplicated chickenpox at the age of 5 years. A thorough evaluation for immunodeficiencies revealed a selective immunoglobulin A deficiency without any symptoms to date.

Learning Points/Discussion

Although rare, Varicella Zoster Virus may reactivate to cause central nervous system disease.

ESPID19-0995
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

A retrospective analysis of aseptic meningitis in children in years 2016-2018

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Background and Aims:

Aseptic meningitis (AM), usually caused by enteroviruses, is an important cause of hospitalization in children. We aimed to compare laboratory test results, duration of hospital stays, and the seasonality of AM caused by various pathogens.

Methods:

The study is a retrospective analysis of medical records of children with AM hospitalised in the Department of Paediatric Infectious Diseases at the Medical University of Bialystok during 3 consecutive years.

Results:

Enteroviral meningitis comprised 57% (94/165) of all cases. In 2017 coxsackieviruses predominated (26/33) and the majority of infections occurred in the midsummer. In 2018 more infections were caused by echoviruses (31/37) and there was a shift towards autumn. Infections caused by *Coxackie* B5, as compared to *Echovirus* 30, were associated with higher plecytosis and protein level in CSF. Tick-borne diseases were recorded mainly in summer and were the second cause of AM - 28% (47/165). Enteroviral meningitis was associated with significantly shorter duration of hospital stay compared to other etiologies.

Conclusions:

As the frequency of enteroviral infections remains stable, routine testing for enteroviruses in patients with aseptic meningitis might significantly shorten the duration of hospitalization. Tick-borne infections remain a significant cause of meningitis in endemic areas and should be considered a possible cause of meningitis. Interestingly, differences in CSF pleocytosis and protein concentration between *Coxsackie* B5 and *Echo* 30 indicate that the viruses possibly differ in virulence.

Systematic Review Registration:

N/A

ESPID19-0985
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Ignored cause of bell's palsy.

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Background

Lyme disease is an infectious disease caused by the bacteria Borrelia burgdorferi sensu lato. B. burgdorferi is transmitted to humans by a bite from an infected tick. Lyme disease occurs in three stages: early localized, early disseminated and late disseminated. Neural system is involved in 5-10% of cases. As Armenia has recently been determined as an endemic region for Lyme disease, we emphasize the importance of early detection.

Case Presentation Summary

A 10-year-old boy admitted to hospital with severe pain around his right ear (posterior auricular region), absence of motority of right part of his face, lagophthalmos, inability to wrinkle brow, drooping mouth (inability to smile and pucker), which started a day before hospitalization. Three weeks before the patient has been bitten by a tick and erythema migrans was developed around the right ear in a week. Early anamnesis was unremarkable, he only had viral meningitis in 2015. The patient also complained of headache but meningeal signs were absent. Paralysis of right facial (VII) nerve was seen.

Laboratory data: IgM antibodies against borrelia as well as immunoblotting were positive. Other laboratory tests (CBC, Biochemistry of blood) were unremarkable.

Neuroborreliosis was diagnosed.

The treatment started with Ceftriaxone 75 mg/kg IV for 21 days and methylprednisolone 1mg/kg for 7 days.

Learning Points/Discussion

To inform population of the RA and medical workers that Armenia is an endemic zone for borreliosis and to provide population with epidemiologic services. Also to review protocols for examination and treatment of neuropathy, encephalitis, myelitis.

ESPID19-0980
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

A five-year retrospective study of pediatric bacterial meningitis in s.Orsola-malpighi bologna hospital, northern italy.

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Background and Aims:

Acute bacterial meningitis (BM) is a medical emergency. However, the mortality and morbility of the illness vary according to the geographical location and the ability of clinicians to suspect BM and quickly start the therapy. In Italy Haemophilus Influenzae (Hib) vaccination is compulsory, while Streptococcus Pneumoniae (SP) and Neisseria Meningitidis (NM) are strongly recommended.

Methods:

We retrospectively reviewed the medical records of children diagnosed with BM, based on the presence of suggestive clinical symptoms and a positive bacterial culture in cerebrospinal fluid, aged between 1 month to 14 years, in a tertiary care hospital in Bologna (Italy) during a 5-year period (2014-2018).

Results:

A total of ten cases of BM (8/10 cases under 12 months of age), out of about 100.000 accesses to our Emergency Room were identified.

SP (4/10) and NM (3/10) were the most commonly isolated pathogens. One case of tuberculosis meningitis occurred. One single case of Hib was related to the only patient who had not been vaccinated. About clinical manifestations of BM, 5/10 patients were admitted with the classical triad of fever, altered mental status and nuchal rigidity. Fever was present in all cases, in 7/10 occurred 24 hours before admission. A bulging fontanelle was identified in 4/10. Most patients (7/10) underwent cranial neuroimaging. A third-generation cephalosporin was used in 7/10 of cases. The most common complications were subdural empyema (3/10) followed by seizures (2/10). One patient died.

Conclusions:

In our limited experience, an effective immunization programme, a clinical suspect in feverish infants and a prompt treatment of BM still remain the main challenges for a good outcome.

Systematic Review Registration:

N/A

ESPID19-0928
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Acute encephalitis in a pediatric intensive care unit

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Background and Aims:

Acute encephalitis is a serious infection of children associated with significant morbidity and mortality. It presents with a broad spectrum of symptoms and often requires intensive neuro-cardiopulmonary support. The aim of this study was to evaluate the clinical profile and the outcome in pediatric patients admitted in a PICU with acute encephalitis.

Methods:

Retrospective study of patients with acute encephalitis admitted in a single tertiary PICU from 01/01/2013 to 30/09/2018.

Results:

During the study period, 19 patients with acute encephalitis were admitted. Median age was 4.5 years (2 months-16 years) and males accounted for 63%(12/19).Fever was the predominant symptom (89,5%,17/19), followed by seizures(79%,15/19) and mental status impairement (68,4%,13/19). 9 patients presented with focal neurologic deficits(47,4%).Other symptoms included headache, speech and psychiatric disorders. CSF was indicative in 53% of the patients applied (8/15), and neuroimaging and EEG studies had pathological features in 47%(9/19).

A pathogen (primarily virus) was identified in 42.1% (8/19) of patients: 3 cases of HHV-6, 2 cases of measles, 1 of H1N1, 1of HSV-1 and 1 case of Mycoplasma pneumonia. There were indications of autoimmune encephalitis/ADEM in 5 cases, but only 1 had positive NMDAR in CSF).

The majority of patients (18/19) received antiviral agents, and 8(42.1%) received corticosteroids and/or intravenous immunoglobulin. Ventilatory support was needed in 14 patients (74%) and 3 patients (16%) required inotropic support due to cardiopulmonary compromise.

Median duration of stay in PICU was 6 days (1-23 days). Mortality rate was 16% (3/19), while 56.2% (9/16) of patients presented neurological sequelae.

Conclusions:

Acute encephalitis remains a medical emergency, with significant mortality and morbidity in pediatric patients. Definite etiologic diagnosis is challenging, since it remains unknown in up to 60% of the cases.

Systematic Review Registration:

0

ESPID19-0860
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

A rare cause of severe rhombencephalitis

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Background

Rhombencephalitis (RE) is a rare syndrome of multiple causes and variable prognosis. The etiologic categories of RE include infections, autoimmune diseases and paraneoplastic syndromes. Among viral agents, enterovirus 71 and herpes simplex virus (HSV) are the most common causes.

Case Presentation Summary

A previously healthy four-year old girl was admitted with fever for four days and somnolence and ataxia since few hours before medical observation. On admission, meningeal signs were suspected and a facial asymmetry was observed. In few hours, she developed flaccid paraparesis and arreflexia. Routine hemogram, blood gas and serum electrolytes were normal. Drug's use was excluded and CT was normal. LP was performed and CSF showed increased proteins (68,5mg/dL) and leukocyte count (263,2/mm^3, mainly mononuclear cells) with normal glucose and no organisms seen on the gram stain. Ceftriaxone and acyclovir were initiated. EEG was normal and MRI showed RE and extensive myelitis. Ampicillin and methylprednisolone were then started. CSF PCR for enterovirus and HSV were negative, as well as stool PCR for enterovirus. Three days after hospital admission, clinical worsening occurred with respiratory distress and dysphagia. Chest X-ray was normal and intravenous immunoglobulin was initiated, with clinical improvement. Epstein-Barr virus (EBV) serology was compatible with recent infection (IgG>200U/mL and IgM 0.4U/mL). CSF PCR for EBV was strongly positive. The patient started a rehabilitation program with mild improvement of the initial clinical condition.

Learning Points/Discussion

This case emphasizes the role of EBV in the pathogenesis of infectious neurologic disorders. The invasion of the nervous system by EBV-infected cells only occasionally produces significant neurologic disease and the highest mortality rate occurs among patients with isolated brainstem involvement. An adequate multidisciplinary rehabilitation program should be early initiated.

ESPID19-0850
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Multiplex pcr may have the potential to reduce hospitalization and unnecessary antibiotics in febrile young infants with viral meningitis

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Background and Aims:

Young infants with fever commonly present to the emergency department. Given the risk for serious bacterial infection, many undergo invasive testing, receive empiric antibiotics and are hospitalized. Yet, viral infection, particularly enterovirus, is the major cause of viral meningitis, with parechovirus emerging as an increasingly recognized pathogen. We report on molecular diagnostic testing of the CSF of young febrile infants.

Methods:

147 febrile infants, up to 3 months of age, 1/1/2016 through 12/11/2018 underwent a sepsis work-up at an Israeli hospital. Fifty-nine frozen samples underwent additional multiplex PCR [Allplex meningitis V1-V2, Seegene (12 viral pathogens)]. Meningitis was defined by either the detection of a pathogen and/or pathological cell count. Six bloody CSF samples precluded pleocytosis evaluation.

Results:

Forty-three of the fifty-nine infants (73%; 95% CI: 61%-84%) had meningitis whereas 16/59 (27%; 95% CI: 15-39%) had other infectious diagnoses. All CSF bacterial cultures were negative. Allplex confirmed viral meningitis in 38/43 (88%) of the CNS infections - 33/43 (77%) enterovirus, 5/43 (12%) parechovirus. Of samples appropriate for evaluation, 4/4 of the parechovirus and 15/29 of the enterovirus were without pleocytosis. There were no significant differences between the clinical features (e.g., bulging fontanelle) and laboratory testing (e.g., inflammatory markers) of patients with enterovirus and parechovirus meningitis. Length of stay did not differ between the viral meningitis and other infectious diagnoses patients, OR=0.615, [95% CI: 0.2-1.9], p=0.39).

Conclusions:

Enterovirus meningitis constitutes a common cause of meningitis in the young febrile infant. Given the absence of pleocytosis in a proportion of enterovirus and parechovirus meningitis cases, clinicians should consider multiplex array of CSF with normal cell count. An expedient viral meningitis diagnosis has the potential to decrease antibiotic use and length of stay.

Systematic Review Registration:

N/A

ESPID19-0632
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Listeria meningoencephalitis in an immunocompetent child

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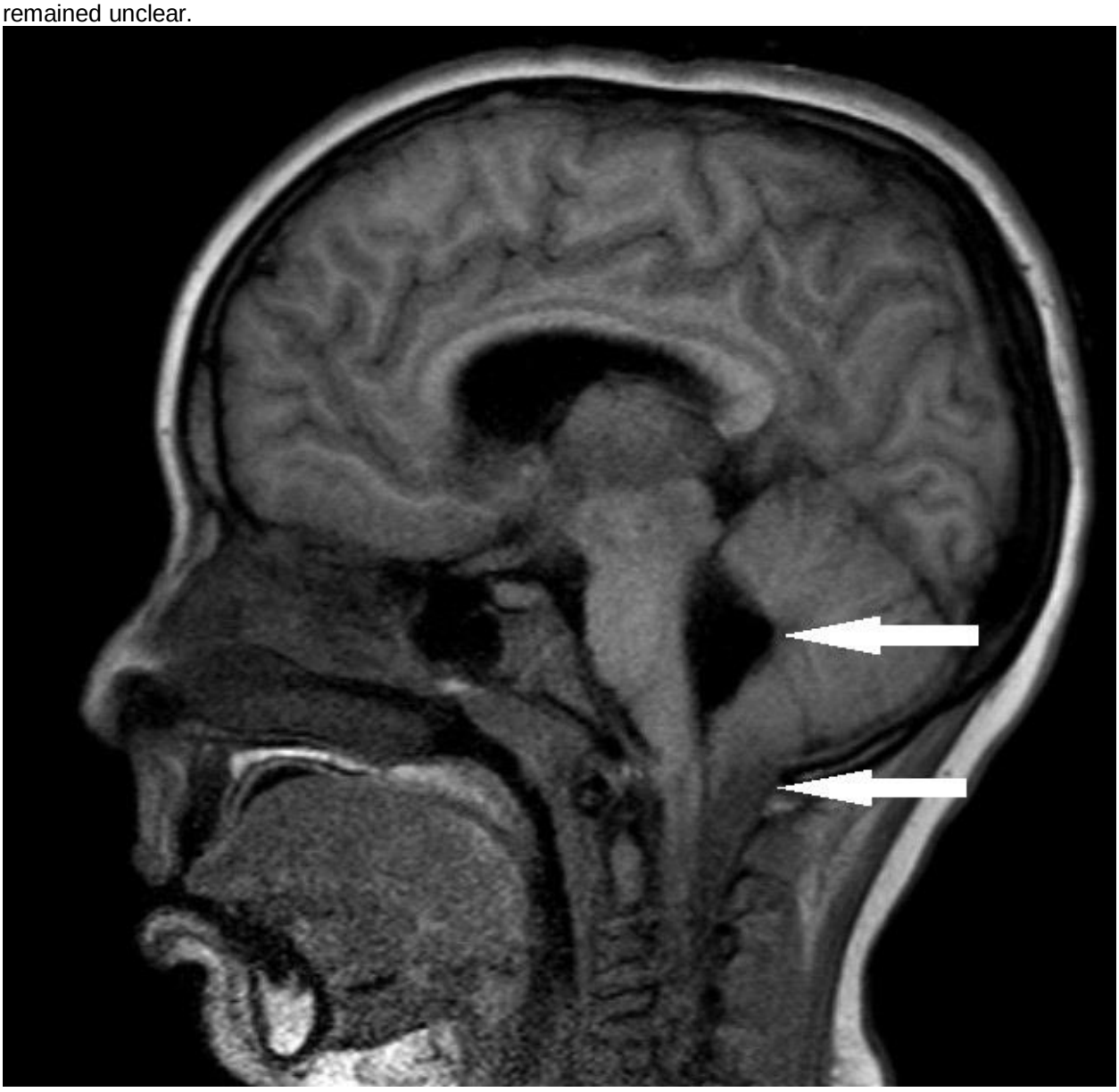
Background

Listeria is an important cause of severe meningitis/encephalitis in elderly, neonates and patients with immunosuppression. CNS infections due to listeria are rare in immunocompetent children. We present a 7-year old previously healthy female patient with acute meningitis/encephalitis and hydrocephalus due to Listeria.

Case Presentation Summary

A 7-year old healthy girl presented to a local emergency room with one day history of fever, headache and vomiting. Lumbar puncture (LP) was unsuccessful. Vancomyin, ceftriaxone and acyclovir were initiated and the patient was transferred to another institution. On the second day of hospitalization (day 2), she developed altered mental status and LP was attempted again. CSF results showed glucose at 2 mg/dl, protein at 246 mg/dl, leucocytes at 199/mm^3 with 66% lymphocytes. MRI of the brain showed acute ischemia in left parieto-occipital lobe. Blood culture grew *Staphylococcus capitis,* considered as contaminant. On day 5, the patient had developed apnea leading to intubation. Head CT showed new-onset hydrocephalus at which point the patient was transferred to our facility for neurosurgical intervention. CSF's Gram stain results were then reported by the outside facility as Gram-positive rods followed by initiation of ampicillin and gentamicin. Patient received external ventriculostomy and later posterior fossa decompression for brain stem herniation and worsening obstructive hydrocephalus (figure, arrows). Final CSF cultures showed *Listeria monocytogenes*. She was treated with ampicillin/genatmicin for total 3-4 weeks. She suffered impaired mobility and cognition. The definitive source of Listeria

remained unclear.



Learning Points/Discussion

Listeria is a rare but possible cause of meningoencephalitis in immunocompetent children. It's important to add ampicillin empirically in suspected bacterial meningoencephalitis patients not responding to conventional therapy. Although hydrocephalus is usually a late complication of bacterial meningitis, it can occur in the acute phase in listeria meningitis.

ESPID19-0621
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Admission c-reactive protein in childhood bacterial meningitis

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Background

CRP levels rise in response to inflammation and are typically high in invasive bacterial infections (>20mg/L). In bacterial meningitis (BM) the inflammation of the meninges can lead to intracranial complications, neuronal injury or death. We aimed to study the admission CRP and the prognostic value of CRP measurements done during treatment of childhood BM.

Methods

The BM patients comprise from a prospective clinical trial of children aged 2 months to 15 years admitted to the Paediatric Hospital of Luanda, Angola. CRP was measured from whole blood finger-prick samples on day 1-2 (n=234) and on day 3-4 (n=154) of treatment. When CRP exceeded the level 160 mg/L it was marked as being 161 mg/L. The results were compared to other patient, clinical and outcome data.

Results

The median CRP on day 1-2 was 161 mg/L (IQR 33) and on day 3-4 133 mg/L (IQR 79). CRP on day 1-2 was positively correlated with respiratory rate on admission (Rho 0.145, p=0.037), CSF leukocyte count (Rho 0.206, p=0.002) and CSF protein (Rho 0.163, p=0.022). A negative correlation was found with platelet count (Rho −0.354, p=0.036), day 1-2 haemoglobin (Rho −0.14, p=0.036) and CSF glucose (Rho −0.135, p=0.042). CRP on day 1-2 and day 3-4 correlated negatively with the time of death measured in hours after start of cefotaxime treatment (Rho −0.122, p=0.049 and Rho −0.45, p=0.019 respectively).

Conclusions

A high admission CRP in childhood BM correlates with diagnostic BM CSF findings, anaemia and thrombocytopenia. The higher the initial CRP the sooner the patient died. Our inability to get the exact value for CRP exceeding 160 mg/L may have distorted the results and explain the lack of other prognostic information given by CRP.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT01540838

ESPID19-0542
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Post-varicella ischemic stroke 25 years after the stroke

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Background

In healthy children, chickenpox (varicella) usually have a benign course. Complications of the disease also include defects of the central nervous system. Transient cerebellar ataxia is the most frequent manifestation. Ischemic stroke occurring several weeks to months after the onset of the disease is a very rare complication.

Case Presentation Summary

An 8-year old boy without significant findings in both family and personal medical history, 7 weeks after developing symptoms of chickenpox , a sudden onset of dysarthria occurs, with objects dropping from his right hand, insecurity when walking. In the course of several hours the boy developed complete manifestations of right-sided hemiparesis. Afebrile, CT of the brain 8 hours after the first manifestations, with negative findings. After 2 days, a CT revealed ischemic findings along a. cerebri media. The findings did not progress after the beginning of the treatment. The clinical condition improved slowly, requiring long-term intensive rehabilitation.

25 years after the vascular stroke, residual findings of postmalatic pseudocyst persist on the left in the ganglion area. Mild signs of right-sided hemiparesis persist, manifested in particular in the upper extremity. We point to the MR finding and clinical picture a quarter-century after the disease.

Learning Points/Discussion

Varicella is an infectious disease which in immunocompromised patients may have a serious course. Complications are more frequent in adulthood. A rare complication is ischemic stroke, which occurs a later time after acute manifestations of the disease. The prevention of chickenpox and associated complications is offered by vaccination against the varicella-zoster infection. Similarly, vaccination against herpes zoster prevents the infection and the possible, although rare complication in the form of ischemic stroke in older people.

ESPID19-0410
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Intrathecal colistin therapy to treat multi drug resistant gram negative central nervous system infection in paediatric patient

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Background

Acinetobacter baumannii has emerged as an important multidrug-resistant (MDR) healthcare-associated pathogen. Meningitis caused by these MDR pathogen is a real challenge to treat in critical care units. Intraventricular(IVT) or intrathecal (ITH) administration of colistin appears to possess a major role in the treatment of A. baumannii meningitis/ventriculitis.

Case Presentation Summary

A 8 years old child admitted in intensive care unit following road traffic accident with fracture of paranasal sinuses,CSF rhiorrhea and altered sensorium. He was intubated and mechanically ventilated. On 6th day there was febrile spike, TLC 22800, increased tracheal secretion, x-ray chest showed right lower opacity. Considering a case of ventilator associated pneumonia (VAP) inj meropenem started empirically. Culture grew *Acinetobacter baumannii* sensitive to colistin (MIC<0.5) but resistant to meropenem. Inj colistin added with the existing regime. Patient became afebrile after 48 hours.

On 11th day patient again developed febrile spikes with drowsiness and neck rigidity. Lumbar puncture was done, CSF cloudy, cell count-460 (92% neutrophils), protein 78mg/dl, sugar 31mg/dl,all of which suggestive of bacterial meningitis. gram stain:few gram negative coccobacilli. considering a case of Acinetobacter meningitis, intrathecal colistin started alongwith iv colistin and inj meropenem stopped. Culture grew same *Acinetobacter sp* with same antibiotic sensitivity. Patient extubated on day17th. The treatment continued for a period of two weeks with intermittent screening culture of CSF, till it became microbiologically negative.

He was discharged on 27th day with normal TLC, resolution of chest x-ray shadow and a neurologically & hemodynamically stable condition.

Learning Points/Discussion

Patients with central nervous system infection by MDR Acinetobacter baumannii isolates susceptible to colistin may benefit from adjunct intrathecal colistin therapy, along with iv colistin as colistin can not achieve adequate CNS penetration after iv administration.

ESPID19-0372
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Fusibacterium nucleatum causing multiple brain abscesses in immunocompetent child.

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Background

Fusobacterium nucleatum is frequently found in dental plaque and can cause gum disease. However there have been very rare reports of the bacteria causing multiple brain abscesses in the immunocompetent.

Case Presentation Summary

Case Summary

A previously well 15-year-old boy was referred by his GP with a one day history of weakness of his right arm, reduced hand grip and paraesthesia.

He had complained of frontal headaches for 2 days with nausea and vomiting for 24 hours.

Examination revealed a boy awake, alert and making coherent conversations.

He had no slurring of speech or diplopia, and fundoscopy was normal.

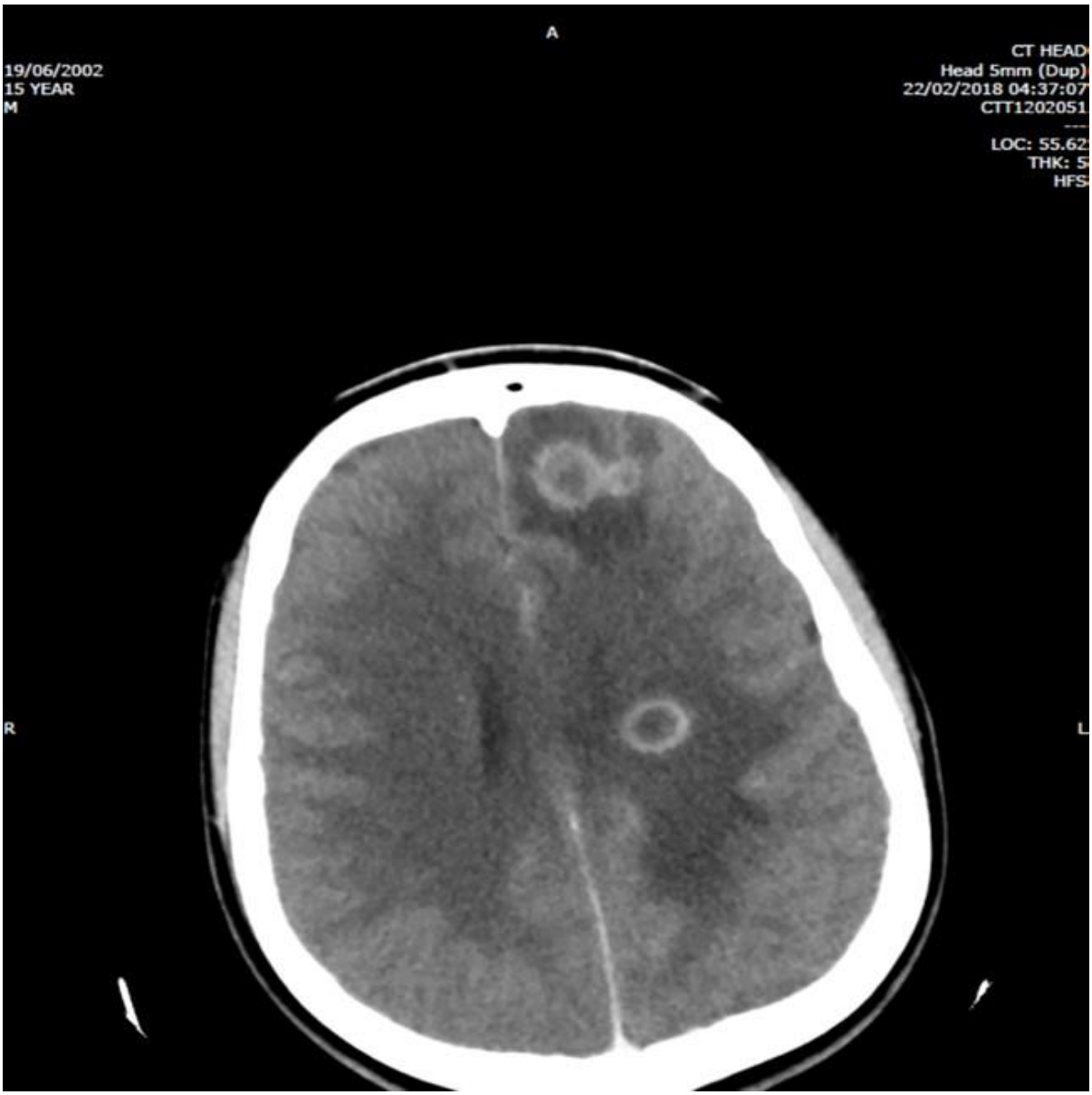
Positive finding on examination was reduced power in his right upper limb with weakness of hand grip and loss of right arm reflexes.

On admission, he was noted to have a respiratory rate of 16, with a Heart rate of 62 and a blood pressure of 140/71. He reported a pain score of 7/10.

He developed a generalised tonic clonic seizures, which self-abated after about 2 minutes.

Investigations

CT scan of his head had showed “Multiple rounded ring-enhancing lesions demonstrated at multiple sites through both cerebral hemispheres.” (see figure 1).



MRI scan confirmed the same finding.

His blood count showed a WBC of 24.7 with a Neutrophilia of 20.3. Echocardiogram showed structurally and functionally normal heart.

Treatment

He was expediated to our neurosurgical centre, where he underwent stealth guided right parietal craniotomy with aspiration of abscess.

Abscess grew Fusobacteium nucleatum (FNUC).

He received a six-week course of IV Ceftriaxone and Metronidazole and a 2 week course of oral Cephalexin and Metronidazole.

Outcome and follow up

He had complete resolution of symptoms and restoration of full function of his right limb.

Learning Points/Discussion

In treating multiple brain abscesses, duration of antibiotics therapy is guided by regular clinical and radiological assessments.

ESPID19-0245
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

High frequency of paediatric facial nerve palsy due to lyme disease in a geographically endemic region

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Background and Aims:

Idiopathic facial nerve palsy (FNP) is an uncommon but important presentation in children. Lyme disease is known to be a common cause of FNP in children. The UK region of Hampshire including the New Forest has a high incidence of Lyme disease. We conducted a retrospective review of the investigation and management of FNP, including serologic testing and treatment for Lyme disease at the regional children's hospital.

Methods:

A retrospective chart review was conducted of children under 18 presenting between 01/01/2010 and 31/12/2014 with a presentation of FNP. Patients with known neurological co-morbidity, known iatrogenic or traumatic cause were excluded. Data were collected on demographics, initial presentation, investigations including Lyme Serology; and management including antibiotics, antivirals and steroids.

Results:

A total of 64 patients were identified, with an even proportion of male and female patients and a median age of 8.5 years (IQR 3.8-11.7 years). A history of rash was present in 4.7%, tick bite in 14% and recent travel to, or residence in the New Forest in 39%. Lyme serology was performed in 83% of patients, and of these 43% returned showed a positive result. Antibiotics were prescribed for 77% of patients, oral steroids for 28% and aciclovir for 8%. No children had associated symptoms of meningitis and none underwent lumbar puncture.

Conclusions:

Lyme disease was found to be a significant cause of FNP in this endemic area of the UK, with a large degree of variability in management. Regions with endemic Lyme disease should consider introducing local guidelines supporting routine investigation and management for FNP, including and empiric treatment for Lyme disease in accordance with national guidelines to improve care and reduce variability.

Systematic Review Registration:

NA

ESPID19-0232
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Decompressive craniectomy and partial temporal lobectomy for herpes simplex virus encephalitis with refractory intracranial hypertension in an adolescent and literature review

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Background

Herpes simplex virus (HSV) encephalitis is uncommon but has a reported mortality of 10-30%. Some patients develop brainstem herniation syndrome because the virus has a predilection for the temporal lobes despite prompt treatment with aciclovir. We describe our case and provide a full literature review surrounding neurosurgical intervention in severe HSV encephalitis.

Case Presentation Summary

We report a case of HSV encephalitis in an adolescent who presented with fever and seizures then developed worsening encephalopathy (despite appropriate antiviral therapy) due to severe cerebral oedema and subfalcine herniation on CT, refractory to medical management.

Investigations

Cerebrospinal fluid: 78 WCC/mm^3 (12 neutrophils/mm^3 , 66 monocytes /mm^3 , 10 red blood cells /mm^3), protein 0.64g/l, glucose of 3.3 mmol/l (plasma glucose 5 mmol/l), PCR - Type 1 DNA HSV identified

MRI [DWI] (day 3) – Reduced diffusion in right temporal lobe suggestive of tissue hypoxia

MRI [intraoperatively] (day 7) - Midline shift due to cerebral oedema involving the right temporal lobe (**figure 1)**

CT [postoperatively] (day 7) - Resolution of midline shift He underwent a decompressive craniectomy with partial right temporal lobectomy followed by intensive neurological, psychological and educational rehabilitation. He has no physical deficits but some residual neuropsychological issues. Neurosurgical intervention appears to be uncommon in HSV encephalitis: only four other children are reported to have had a similar procedure, all with favourable outcome (Glasgow Outcome Score 4 or 5).

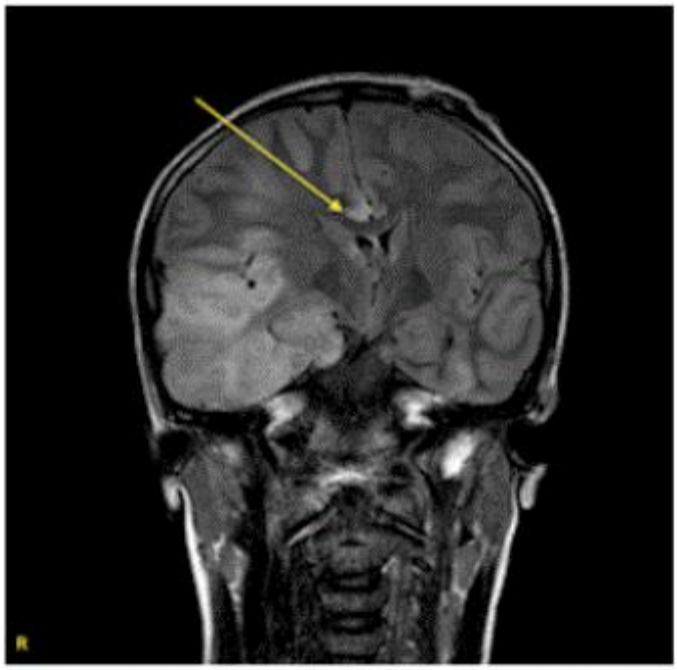

Figure 1: Intra-operative MRI (T2 FLAIR sequence) on day 8 of the illness after introduction of external ventricular drain, showing midline shift with subfalcine herniation (arrow) with persistent hyperintense signal and oedema involving the right temporal lobe.

Learning Points/Discussion

- Focal involvement of the temporal lobe is common in HSV encephalitis, sometimes leading to raised intracranial pressure and brain herniation syndrome

- Decompressive craniectomy and temporal lobectomy can be life saving in cases of HSV encephalitis, with good outcome

ESPID19-0197
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

'keep an eye out' for tetanus in humanitarian settings

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Background

Children in humanitarian settings are at risk of tetanus due to injuries and poor vaccination coverage.

Case Presentation Summary

A 6 year old boy in a remote region affected by conflict suffered a penetrating eye injury with a retained fragment of wood. He attended hospital with a discharging and grossly inflamed eye, with no vision. He was given IV antibiotics and pain relief, and removal under anaesthesia was unsuccessful. He then developed possible facial asymmetry and difficulty eating, and then trismus, followed by generalised rigidity and spasms.
Generalized tetanus was diagnosed, potentially preceeded by cephalic tetanus (defined as trismus with cranial nerve involvement), having missed prophylaxis. A grave prognosis was expected, given that proximity of the wound is associated with higher mortality.
He was treated with tetanus immunoglobulin, diazepam IV hourly (infusion pumps unavailable) and morphine PRN. Despite this he deteriorated, developing autonomic disturbance, hyperthermia and possible aspiration pneumonia.

Unexpectedly, he gradually improved and after 4 weeks of nursing care in a darkened room, NG feeding and weaning diazepam, he gradually improved and was discharged very happy, albeit with vision in only one eye.

Learning Points/Discussion

Case reports of cephalic tetanus after eye injury are rare, and we could not identify any in children.
This case highlights the importance of tetanus in humanitarian settings, and of prompt vaccination and immunoglobulin in penetrating injuries with unclear vaccination history
The eye may be 'overlooked' as a high risk entry point.

Keep an 'eye out' for Tetanus in humanitarian situations + give prompt prophylaxis

ESPID19-0142
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Invasive meningococcal disease in a limited resource country

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Background and Aims:

Although meningococcemia is less common presentation of invasive meningococcal disease, it continues to cause high case fatality and long term sequelae.

The aim of this study was to analyze invasive meningococcal disease in children in Kosovo.

Methods:

This retrospective study enrolled children treated for meningococcal septicemia with or without meningitis during years 2009 – 2018.

Results:

Of 40 children treated for invasive meningococcal disease (IMD), 19 cases (47.5%) manifested meningococcal septicemia (MS) and 21 cases (52.5%) manifested meningococcal septicaemia with meningitis (MSM). Duration of symptoms <12 hours had 6 children with MS (15%), <24 hours had majority of cases 32 (80%) while duration of symptoms >24 hours had only two cases with MSM (5%). There were no statistical differences concerning gender, 20 females and 20 males with 9 vs. 10 cases of MS. Children living in urban places (n=19) developed more often MS (58%) compared to children living in rural places (38%). The median age of patients was similar in both groups [MS = 3.0 years old (9 months – 16 years)] and MSM = 3.2 years old (9 months – 14 years)]. Children with MSM were treated more often with empirical therapy with Penicillin G (67%) while 33% with Ceftriaxone. Children with MS were treated with penicillin G (53%) and Ceftriaxone (47%). Extended skin haemorrhages with peripheral necrosis of fingers and toes manifested four children, two in each group with amputation of necrotic parts in one child with MS. There were no deaths in children who manifested MSM, while there were two deaths in children with MS (M=10.5%).

Conclusions:

Meningococcemia manifested almost in half of patients with invasive meningococcal disease, continues to be a life threatening disease for children in Kosovo.

Systematic Review Registration:

N/A

ESPID19-0126
E-Poster Viewing - May 7-10 - E-Poster Hours

CNS infections

Severe parechovirus infections

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Background

We describe a case series of three children with Human Parechovirus (HPeV) infection over a period of one year. All of them had evidence of Parechovirus infection in their CSF, blood, nasopharyngeal aspirate and faeces.
HPeV infection can range from mild flu-like symptoms to severe sepsis and aseptic meningitis. Transmission of HPeV occurs through the fecal-oral and transplacental routes and by respiratory droplets.

Case Presentation Summary

	CASE 1	CASE 2	CASE 3
AGE	9 days	2 weeks	17 days
MAIN PRESENTING SYMPTOM(S)	Irritability and fever	Irritability and fever	Irritability and fever
ASSOCIATED MORBIDITY	Encephalitis	Hypocalcaemia Vitamin D deficiency	Cardiac arrest
INITIAL DIAGNOSIS	Presumed sepsis	Presumed sepsis	Presumed sepsis
WCC (highest)	17.6	24	12.6
CRP (highest)	49	26	<5
BLOOD – HPeV PCR	Positive	positive	Positive
CSF PCR	Positive	Positive	Positive
NPA or THROAT SWAB	Positive	Positive	Positive
FAECES or RECTAL SWAB	Positive	Positive	Positive
INITIAL TREATMENT	IV antibiotics and IV antivirals	IV antibiotics and IV fluids	IV antibiotics and IV antivirals
PICU ADMISSION	Yes	No	Yes
LENGTH OF ADMISSION	12 days	7 days	7 days
IMMEDIATE OUTCOME PRIOR TO DISCHARGE	None	None	None

Learning Points/Discussion

All patients had irritability and fever. Of the three children, two needed PICU admission for ventilatory and circulatory support while the third patient required HDU admission. One had a confirmed diagnosis of encephalitis on MRI and also had a tonic seizure. In all three, there was evidence of disseminated infection.

Conclusion:

HPeV is an uncommon cause of illness in young children but can lead to potentially serious complications in the immediate setting and near future. There is little or no data about its prevalence and long term outcomes. Treatment is supportive and testing should be part of sepsis work up.

ESPID19-1140
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Group b streptococcus infection: a 10-year retrospective study

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Background and Aims:

Streptococcus agalactiae [Group B streptococcus (GBS)] is a common cause of neonatal sepsis. GBS colonizes the gastrointestinal and genital tract of a significant percentage of pregnant women. GBS infection is classified in early-onset disease (EOD) and late-onset disease (LOD). Incidence of EOD has declined due to intrapartum antibiotic prophylaxis (IAP); however, LOD is not prevented by IAP.

Methods:

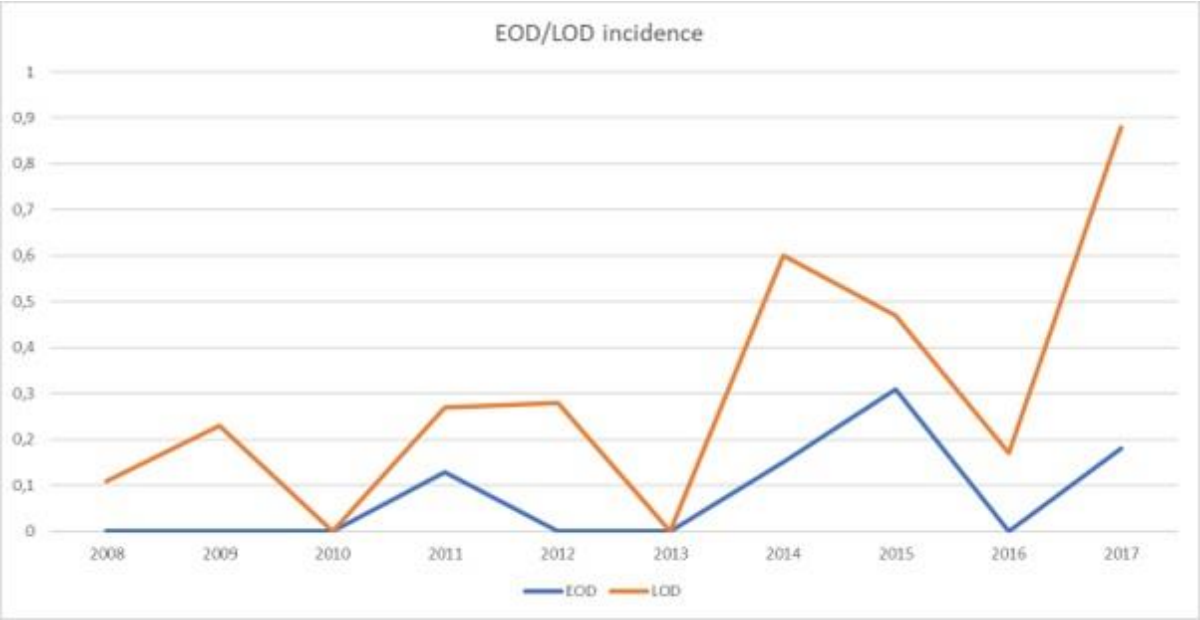
We conducted a retrospective review of GBS infection cases in our hospital from 2008 to 2017. Epidemiological data, risk factors and tendency were reviewed.

Results:

72.157 children were born in our hospital during this period. 5 EOD (0.07 per 1000 live births) and 20 LOD (0.27 per 1000 live births) were presented. Tendency of EOD and LOD is shown in Figure 1.

In the EOD group, rectovaginal swab was negative in 3 of them and unknown in 2 (no prophylaxis). All were vaginal deliveries. Regarding the type of infection; 3 had sepsis, 1 meningitis and 1 bacteraemia. GBS was isolated in the blood culture of all of them. No sequelae were found.

In the LOD group, rectovaginal swab was positive in 6 (all received correct prophylaxis), unknow in 4 (no prophylaxis) and negative in 9. There were 14 vaginal deliveries (70%) and 6 C-sections (30%). The type of infection was sepsis in 16 (80%), meningitis in 10 (50%), cellulitis in 2 (10%), UTI in 1 (5%) and bacteraemia in 1 (5%). 1 had a recurrent episode. Neurodevelopmental sequelae were present in 2 children (9%). No deaths occurred.



Conclusions:

We have lower EOD incidence, but similar LOD incidence and type of infections compared to other series. LOD is associated to a high morbidity. New strategies should be developed to avoid *S. agalactiae* LOD.

Systematic Review Registration:

N/A

ESPID19-1112
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Congenital syphilis: a case series

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Background

Vertical transmission of syphilis is an important public health problem in Brazil. In 1995, Brazil and other countries from Latin America and Caribe made the commitment to create an action plan for the elimination of congenital syphilis (CS). Despite the efforts, the incidence rate of CS raised from 2.4 for each 1,000 live births in 2010 to 6.8 for each 1,000 live births in 2016.

Case Presentation Summary

There were ten cases of CS attended by the pediatrics infectious disease team at a tertiary hospital in Brazil from 2013 to 2017. Nine of these children were born from inadequately treated or untreated mothers.
Diagnosis occurred right after birth in the inpatient setting in 6 cases. Only one child was asymptomatic. Neurosyphilis was diagnosed in 2 newborns. The other 3 cases had more than one clinical finding : periostitis (n=2), hepatomegaly (n=2) and one presented a rash with involvement of hands and soles.
There were 4 CS cases diagnosed after discharge from the maternity hospital (17 to 60 days old). Clinical findings were: skin rash (n=3) and periostitis (n=3). Laboratory tests showed anemia in 2 children.
All CS cases were treated with 10 days of penicillin, most (n=9) with aqueous crystalline penicillin G. One newborn received procaine penicillin G after exclusion of neurosyphilis.

Learning Points/Discussion

Maternal treatment with penicillin is 98% effective in preventing CS among pregnant women with syphilis. This case review highlights the importance of prenatal care in preventing CS cases.
It is important to notice that 4 newborns were discharged from the hospital without being diagnosed or treated for CS. This emphasizes the importance of testing for syphilis at the maternity, as it is preconized by the Brazilian ministry of health.

ESPID19-1102
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Postnatally acquired cytomegalovirus infection: the unpausterized human milk dillema

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Background

Postnatally acquired cytomegalovirus infection (CMV) in preterm infants through unpasteurized human milk (UHM) can manifest with sepsis-like symptoms, often self-limited, but some might require antiviral treatment.

Case Presentation Summary

Case 1: A 745g male was born at gestational age of 25-weeks due to premature labor and rupture of membranes. The mother seroconverted for CMV during 2nd trimester of pregnancy, amniocentesis tested negative for CMV-PCR and all initial screening of the newborn, including urine CMV-PCR, were negative, making congenital infection less likely. During hospitalization, he was fed with UHM. At 6 weeks of life he presented with abdominal distension and hepatosplenomegaly. During investigation, acute CMV infection (IgM and IgG positive) was diagnosed, and he was successfully treated with a 21 days ganciclovir/valganciclovir course.

Case 2: A 2400g male was born at gestational age of 35-weeks. Three days before delivery, the mother presented fever, hepatitis and thrombocytopenia and was diagnosed with acute CMV infection (IgM positive and IgG inconclusive). C-section was performed due to oligohydramnios. The infant was born with no clinical signs of CMV infection and initial screening revealed IgM negative and IgG positive (close to indeterminate range). UHM and breast feeding was not authorized.

Learning Points/Discussion

CMV is shed in UHM in up to 96% of CMV seropositive mothers. Preterm infants can be infected through UHM. The main risk factors for symptomatic disease are extremely low birth weight, early transmission and low gestational age (<32 weeks), as in case1.

Several reports found an association between high CMV viral load in UHM and transmission risk, hence our cautions about feeding case 2 with UHM.
Effective prevention of CMV transmission can be achieved through pasteurization of human milk, but can lead to nutritional loss.

ESPID19-0805
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Vaccination status for influenza, pertussis and measles in pregnant women in south greece

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Background and Aims:

Vaccination for pertussis and influenza is recommended for all pregnant women. It is also important for pregnant women to be immune for measles before pregnancy, especially in a period of measles epidemics. Appropriate immunization status of pregnant women could reduce the morbidity of both women and neonates. The aim of the study was to record the immunization status of pregnant women in a south Greek city.

Methods:

This was a prospective study which was performed in the Departments of Pediatrics, General Hospital of Sparti, Greece, from January to August 2018. Mothers who gave labor in the hospital during this period participated in the study. Questioners were completed after personal interview with the pregnant women, and checking their personal vaccination record, with their consent.

Results:

Among the 161 pregnant women who participated in the study, 93 (57.7%) were of Greek origin, 96 (59.6%) were occupied with the household and 29 (18%) had higher education. Regarding immunization status for measles, 55 (34.1%) women had been fully vaccinated with 2 doses of vaccine (monovalent or MMR) in their childhood. Only 2/161 (1.24%) women were vaccinated against pertussis and influenza during pregnancy after pediatrician's motivation, whereas 157 (97.5%) stated that had no information over this issue from their pediatrician or gynecologist. 2 (1,24%) women were advised to get vaccinated during pregnancy from their pediatrician but refused to do so.

Conclusions:

The above results demonstrate that a significant percentage of pregnant women and their neonates are vulnerable for measles, while there is almost absence of immunization for pertussis and influenza during pregnancy. Consequently, there is urgent need to educate healthcare professionals and inform pregnant women regarding vaccination issues during pregnancy.

Systematic Review Registration:

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ESPID19-0711
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Retrospective analysis to study prevalence of congenital cmv infections at a tertiary care referral centre in india

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Background and Aims:

Human cytomegalovirus is the leading non-genetic cause of congenital malformation and continues to be underdiagnosed.Diagnosis of congenital CMV(cCMV) infection is established by the presence of CMV-specific IgM/PCR in cord blood/ infant's blood/saliva/urine in the first 3 weeks of life. Studies regarding prevalence of birth defects due to congenital CMV infection are limited in India. We did a retrospective study to estimate the incidence of cCMV in new-borns at our centre from 2009-2018.

Methods:

In the present study neonates with signs and symptoms compatible with acute CMV infection referred to SGPGI, Lucknow,India between Jan 2009 to April2018 were analysed.

Inclusion criteria: Neonatal hepatitis, small for gestational age, microcephaly, petechiae, purpura, chorioretinitis, hepatosplenomegaly. Exclusion criteria: Inherited microcephaly, hepatitis due to metabolic cause, petechiae due to sepsis. Samples from neonates(n= 287) within 21 days of birth comprising foetal blood (n:246), cord blood(n:4), urine(n:2) were tested in Clinical Virology laboratory to establish the evidence of cCMV infection by PCR(35) and /or detection of CMV specific IgM(252).

Results:

IgM antibodies were found in 50 out of 252 samples(19.84%) and PCR assay was positive for CMV in 15/35 (42.85%). Congenital CMV was found in 22.64% neonates cumulatively. Congenital CMV related clinical manifestations in the present study showed jaundice as the most common clinical feature followed by hepato-splenomegaly, bronchopneumonia, anaemia. Other infectious causes were not studied.

Conclusions:

The high prevalence of cytomegalovirus in the general population, unpredictability of transmission, and asymptomatic nature of the disease in otherwise healthy women challenge prevention and treatment efforts. Appropriate timing of sampling, sample treatment, usage of validated assays under quality assessment conditions, and correct interpretation of the results are all essential for obtaining a reliable diagnosis.

Systematic Review Registration:

not applicable

ESPID19-0378
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

The challenges of laboratory diagnosis of congenital syphilis

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Background

Congenital syphilis (CS) is highly transmittable (70 to 100%). Non-treponemal tests are used for initial screening while treponemal tests (TT) are more specific and used to confirm the diagnosis. TT can stay positive up to 18 months of life if transplacental maternal transmission occurred, so they are commonly used in following up after birth.

Case Presentation Summary

A preagnant woman had a 1:32 VDRL test on the first and second trimester of pregnancy, received 3 doses of Benzathine penicillin on each occasion, but still presented with VDRL 1: 4 at delivery. VDRL of the newborn was 1:2 and he received one dose of Benzathine Penicillin. The patient presented negative VDRL tests with 1 and 3 months of age. At 8 months of age, the boy presented with lesions on the palms of the hands and soles of the feet, and gingival petechiae. He had a positive test for Coxsackie B4 virus, a positive VDRL 1: 256 and positive treponemal test. CSF was normal with negative VDRL. The infant received 10 days of Crystalline Penicillin. IgM FTA-abs was negative.

Learning Points/Discussion

Our patient had skin lesions with positive Coxsackie serology which make us hypothesize that the current VDRL can be false positive by cross-reaction with the viral infection. Another plausible explanation is that the patient has CS, with negative VDRL at 1 and 3 months of life due to the prozone effect. There is also the possibility of acquired syphilis, as the grandmother had syphilitic roseola. The FTA-abs IgM test with negative result doesn't rule out syphilis. However, if this result were positive, we could determine a recent infection. Diagnostic elucidation will require monitoring with treponemal test.

ESPID19-0370
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Combined treatment in pregnant women with fetal cmv infection and high risk of symptomatic disease

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Background

Cytomegalovirus hyperimmune globulin (CMV-HIG) and oral valacyclovir have been tested for the treatment of fetal CMV infection, but there is no experience in combination treatment.

Methods

From April 2017 to December 2018, we offered “double therapy” to pregnant women with CMV infection during the first or second trimester and viral load in amniotic fluid above 10^5 copies/ml.

"Double therapy" consisted of: valacyclovir 2g/6h until the end of pregnancy and CMV-HIG (200 UI/kg). Additional monthly doses were used in case of ultrasonographic or MRI evidence of persistent fetal involvement. Neurological and hearing evaluation of infants were performed at birth and during follow-up.

Results

We enrolled 10 pregnant women with primary infection (9) or reactivation (1) and detection of CMV-DNA in amniotic fluid (mean $4.9x10^6$ copies/ml). Mean gestational age was 12.9 weeks at infection and 24.6 weeks at start of treatment. Double therapy was well tolerated, and no significant adverse effects were documented.

Five pregnant women presented abnormal ultrasound or neuroimaging findings; in three cases the immunoglobulin cycle was repeated. In the other five women, imaging studies were normal.

Four women are still in treatment and six gave birth to full-term newborns (two with weight<p10), all with normal physical examination. Four neonatal imaging tests confirmed prenatal findings (ventriculomegaly, periventricular cysts-2- and germinolysis). Two newborns without prenatal imaging abnormalities showed mild findings in the postnatal period (lenticulostriate vasculopathy and white matter hyperintensity). One newborn had unilateral hearing loss. All received oral valganciclovir and have a normal psychomotor development (mean follow-up of 7.5 months).

Conclusions

These preliminary data suggest that combined treatment with oral valacyclovir and CMV-HIG is well tolerated and could be a therapeutic alternative in pregnant women with fetal CMV infection and high risk of symptomatic disease.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0128
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

A review of the current practice of intra partum antibiotic prophylaxis in nigeria and sub saharan africa

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Background and Objective

A review of the current practice of Intrapartum Antibiotic Prophylaxis in Nigeria and Sub Saharan Africa

Intrapartum Antibiotic Prophylaxis(IAP) is a potentially life-saving intervention, preventing neonatal and maternal infections. Policies existfor screening of women for infections and the intrapartum use of antibiotics especially in developed countries. In Africa, there is a high variability in the organisms causing infections andpossibly the policies for IAP. We review the literature for the practice of IAP in Sub-Saharan Africa.

Methods

Methodology

A search was conducted on Pubmed with the terms “Intrapartum AND antibiotic* AND (prophylaxis OR prevention) AND Africa”. We also searched African Journals online with a similar theme. A survey was conducted among Obstetricians in tertiary health facilities in Nigeria.

Learning Points Discussion

Results

Most screening programmes were for group B streptococcal disease(GBS) in the developed world. In Southern Africa, they show similar GBS infection rates. In Nigeria, A prevalence of 0.06 per 1000 livebirths was seen in a systematic review, but a prospective study found a carriage rate of 8.6% for GBS, like other studies in Nigeria (8% to 11%) and IAP prevented neonatal sepsis in 100% of cases. Inappropriate laboratory methods and early-onset of mortality in GBS are cited as reasons for the low GBS reports in Africa. There were no published universal policies on screening and IAP.

The survey results showed that most tertiary health facilities in Nigeria have a policy of selective IAP, the most common indication being PROM. Find the details below.

Conclusion

There is no consistent practice of IAP in most of Sub Saharan Africa, in Nigeria most hospitals administer IAP on a case by case basis, probably due to inadequate information regarding carriage of microorganisms.

ESPID19-0373
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Descriptive epidemiology of neonatal invasive infections with streptococcus b in a french department, 13-year retrospective study

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Background and Aims:

Streptococcus B (SB) is one of the most common causative bacteria in serious newborn infections and justifies a preventive strategy based on maternal antibiotic prophylaxis perpartum. However, the incidence rate is stagnating in France. The objective of our study is to estimate the frequency and describe the clinical manifestations of early invasive infections (EII) and late (LII) at SB in Gironde over a period of 13 years.

Methods:

This is a multicenter retrospective survey from January 1st, 2005 to December 31st 2017 among children under 5 months hospitalized in department of Gironde. Invasive infections were defined by septic status associated with a SB positive central bacteriological specimen.

Results:

There were 71 cases of II (26 EII, 37% and 45 LII, 63%). The estimated incidence rate in 2017 is 0.47 per 1000 births (EII: 0.12 and LII: 0.35), which corresponds to the national data of the EPIBAC network. Of the 46 bacteremias, 36 were "clear", 7 were accompanied by dermohypodermitis, two had osteoarthritis (hip and knee) and one had pneumopathy. Meningitis accounted for 25 cases (EII: 8 and LII: 17). Of the 24 samples sent to the CNR, 17 isolated EII strains belonged to the ST17 hypervirulent clone and one isolated from LII also had this profile. All GB were sensitive to amoxicillin, 12 strains were resistant to clindamycin (5 early and 7 late). The overall mortality is estimated at 7% (EII: 1, LII: 4).

Conclusions:

The number of II to GB has tended to increase since 2005 and the number of EIIs has exceeded that of LII. The II to SG becomes a different pathology, affecting rather the child of 3 weeks of life. The future probably lies in maternal vaccination.

Systematic Review Registration:

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ESPID19-1145
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Incidental finding of acquired cytomegalovirus in two cases of neonatal cholestatic jaundice

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Background

Infectious causes have been implicated in approximately 11% of neonatal intrahepatic cholestasis (NIHC) cases, cytomegalovirus (CMV) being the commonest. Two complex preterm infants with conjugated hyperbilirubinaemia were incidentally found to be CMV-DNA positive and will be discussed to highlight the controversies surrounding acquired CMV.

Case Presentation Summary

Case 1:

24^{+2}wk female (576g) with a history of chronic lung disease (CLD), patent ductus arteriosus (PDA), 2 episodes of NEC requiring prolonged parenteral nutrition (PN) and a laparotomy. Required treatment for E-coli and Staphylococcus haemolyticus bacteraemias and also had an intracerebral intraparenchymal bleed, stage three ROP and persistent thrombocytopenia.

Case 2:

24^{+3}wk male (716g) with CLD, PDA, intracerebral intraventricular bleed and 3 episodes of NEC with prolonged exposure to PN. Also treated for a coagulase negative staphylococcal bacteraemia.

CMV infection was diagnosed on day 76 and day 99 of life respectively. Pathogenesis was likely a perinatal infection or acquired from expressed breast milk. Newborn blood spots and CSF testing were negative for CMV. Urine sent at birth on case 2 was CMV-PCR negative. Both were given valganciclovir treatment because of high CMV-DNA levels, multi-system involvement, worsening hepatitis and relative immunosupression.

Evaluation of cholestasis is challenging in extreme preterms due to its multifactorial nature, non-specific clinical features, patient's potential to deteriorate and the risk of missing important pathologies like biliary atresia.

Learning Points/Discussion

Different diagnostics and seroprevalences causing difficulty-evaluating CMV results.

Presence of CMV IgM only suggests this virus may-be the etiologic agent, treatment can be controversial.

Conflicting evidence regarding using CMV-DNA values as an indication to treat.

Literature suggests spontaneous recovery is expected unless severe systemic disease occurs - decisions should therefore be individualised.

Consider the appropriate follow-up of infants with acquired CMV.

Should we test for CMV in cases of recurrent NEC?

ESPID19-1144
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Cellulitis as an indicator of bacteremia in the neonatal period: a group b streptococcus late onset disease

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Background

Cellulitis-adenitis syndrome is a rare clinical manifestation of group B *Streptococcu*s (GBS) late- onset disease. Its significance lies in the fact that local infection may be the only initial sign of systemic infection that is often concurrent with meningitis. Soft tissue involvement (cellulitis - adenitis) can sometimes be the only initial manifestation of GBS infection

Case Presentation Summary

A 22-day-old infant was seen in the ER for 72 hours of irritability. Upon arrival, the patient presented with a rectal temperature of 39.8 C and tachycardia (210 bpm). His perinatal history revealed no incidences. Vaginal smear was GBS negative. Blood test with absence of infectious parameters. Ampicillin and gentamicin were started. Twelve hours after admission erythema and inflammation suddenly appeared from the left inferior preauricular region to the submandibular angle, with serous secretion in the left external auditory canal. There was an increase in infectious parameters and blood culture was reported positive for GBS. The CSF culture and otic secretion were negative for GSB. Cefotaxime and ampicillin were started. Cervical ultrasound showed extensive adenopathy in the left sternocleidomastoid area. No involvement of the mastoid region in CT scan. Clinical improvement was seen after 3 days of treatment.

Learning Points/Discussion

Cellulitis has been described as an indicator of bacteremia in the neonatal period, and may be the only sign. In children under 3 months of age with a local infectious focus, especially if accompanied by regional adenitis, should suggest the possibility of bacteremia and CNS involvement, making it essential to perform a blood culture and lumbar puncture. Early diagnosis and treatment may improve the potentially poor prognosis of these patients. Therefore, the need to rule out central nervous system involvement by studying cerebrospinal fluid is highly recommended

ESPID19-1128
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Hiv exposed uninfected children and group b streptococcal disease in madrid

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Background and Aims:

The number of HIV exposed uninfected (HEU) children is increasing over time. It has been shownthat HEU children have higher susceptibility to severe infections during the first years of life due toimmune dysregulation. In high-income countries, these studies are scarce.

The aim of this study is to compare the incidence and clinical presentation of GBS infection in HEU and non-exposed infants.

Methods:

Retrospective observational study done in 4 hospitals in Madrid from 2008 to 2017. Cases of GBS infections (blood and CSF culture) under 90 days of life were identified from the microbiology records. Perinatal and clinical data were collected from the medical history, as well as exposition to HIV.Data was analysed with SPSS program.

Results:

GBS infections were described in 113 infants born from HIV-uninfected mothers (113/146850;0.076%). In the same period, 1 HEU infant had a neonatal GBS infection (1/291;0.3%).The Odds Ratio was 4.477, with no significant difference (X^2 Fisher correction 0.2).

The HEU infant was a female, with an early neonatal sepsis and meningitis. The mother came from Equatorial Guinea, HIV was well controlled and treated before and during pregnancy. HIV prophylaxis was given to the child.

Regarding clinical presentation of GBS infection in HIV-unexposed infants, 9 had meningitis (0,006%). Compared to HEU, Odds Ratio was 56.2, with a significant difference (X^2 Fisher correction 0.02).

Conclusions:

In our study, HEU presented a higher incidence of GBS infection, not statistically significant, probably due to the size of the population. It is to remark that HUE infant presented a severe infection with meningitis, which was extremely rare in non-exposed infants.

Systematic Review Registration:

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ESPID19-1118
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Mother-to-child transmission of hiv in a tertiary portuguese hospital

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Background and Aims:

The possibility of transmission of HIV from a HIV-positive mother to her child during pregnancy, labour, delivery or breastfeeding ranges from 15% to 45% in the absence of any intervention. Since the introduction of antiretroviral therapy (ART), mother-to-child transmission(MTCT) of HIV has successfully been reduced. Preventive measures such as routine screening in pregnancy, early use of ART in pregnant HIV-infected women and post-exposure antiretroviral prophylaxis in newborns at risk, contributed to prevent that transmission.

Methods:

Review of the medical records of newborns whose mother was HIV-positive and were born in a tertiary Portuguese hospital between January/2011 and December/2018.

Results:

During the analysed period, there were 25012 pregnancies, with 25461 newborns, 74 (2.9‰) from an HIV-positive mother. The mother median age was 32yo (19-42), 90.5% portuguese and the majority infected by sexual transmission (85%). The diagnosis was made previously to the pregnancy in 78%(74% on triple ART). Mother viral charge at labor was <20copys/ml in 60.8%, and <1000copys/ml in 34% with a median CD4 count of 617/mm3 (68 to 4861). AZT was administered to the mother during the labor in 97%. The median gestational age was 38weeks (30-41), 18.9% preterm, 50% males, with median weight at birth of 2922.5g (1400-3860) with 6 newborns small for gestational age. None were breastfed. One died due to complications of prematurity, all did prophylaxis during at least 4 weeks and none were infected.

Conclusions:

There were no cases of MTCT in our centre in the last 8 years. There were a significant number of infections detected during pregnancy, leading to the later onset of therapy. Newborns at risk should start prophylaxis as soon as possible and should keep close follow up until the infection is excluded.

Systematic Review Registration:

N/A

ESPID19-1113
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

The impact of congenital cmv infection on clinical presentation of cryopyrin-associated syndrome (caps)

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Background

CAPS is a group of rare, heterogeneous autoinflammatory syndromes: familial cold autoinflammatory syndrome, Muckle-Wells syndrome (MWS) and most severe Neonatal-onset multisystem inflammatory disease (NOMID/CINCA). They are associated with a gain-of-function mutation in same NLRP3 gene encoding the major component of interleukin 1 (IL1) inflammasome – cryopyrin. Diseases are characterized by IL1β-mediated systemic inflammation and clinical symptoms involving skin, joints, central nervous system, and eyes. We report a congenital CMV infection in a patient with mutation in NLRP3.

Case Presentation Summary

First child of healthy parents presented with macular skin rash and increased inflammatory markers a day after her birth. Congenital CMV infection was confirmed on day 7 and she was treated for 3weeks with ganciclovir. Fever, skin rash and inflammatory markers resolved slowly over few weeks. Bursts of skin rash persisted in later months and at immunological assessment at 12months elevated inflammatory markers with persistent CMV viremia was found. On ophthalmologycal reevaluation at 18months bilateral optic disc oedema appeared. Repeated brain MRI that previously showed subtle subcortical nonmyelinated regions was suspicious for additional raised intracranical pressure which wasn't confirmed with spinal fluid evaluation.

With reapperence of periodic fevers autoinflammatory syndrome with CNS involvement was suspected and confirmed genetically. However, mutation in NLRP3 gene in our patients was previously described in milder clinical syndrome – MWS.

Treatment with interleukin 1 receptor antagonist – anakinra, resolved the periodic fevers, rashes and inflammatory markers in a few days. Optic disc oedema improved within weeks and CMV became undetectable within months.**Learning Points/Discussion**

Congenital CMV infection had an important influence on clinical presentation in our patient with CAPS. We believe that timing and etiology of infections can influence the severity of clinical presentation in identical genetic mutation of immune system.

ESPID19-1109
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Infants born to mothers with infectious risk factors: an observational study

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Background and Aims:

Sepsis in the new-born is a relatively common and potentially serious condition. Children are early admitted for antibiotic treatment and it is important to consider the risk factors for early suspicion of the possibility of an infectious process. The management of asymptomatic new-borns with infectious risk factors remains one of the most controversial problems in the perinatology. Our objectives were to determinate the prevalence of chorioamnionitis and neonatal sepsis and to analyse the characteristics of mothers with infectious risk factors and their newborns.

Methods:

A cross-sectional, epidemiological, observational and descriptive study of 686 mothers diagnosed with chorioamnionitis and their newborns was conducted at the “Complejo Hospitalario Universitario Insular Materno Infantil” of Las Palmas de Gran Canaria from January 2014 to December 2017.

Results:

The prevalence of maternal chorioamnionitis was 3.76%. Of their newborns, 3.1% had symptoms suggestive of neonatal sepsis. However, 2.2% developed neonatal sepsis confirmed by positive blood culture. *Escherichia coli* was the most frequently isolated microorganism (60%). Mothers of newborns with positive blood cultures had fewer obstetric visits, more hours of rupture of membranes and a history of preterm labour. The group of new-borns with positive blood culture had a lower gestational age, higher C-Reactive Protein and symptoms of sepsis with statistically significant differences.

Conclusions:

A significant percentage of newborns were admitted to hospitalization (80.3%) and Neonatal Intensive Care Unit (12%) for empirical antibiotic treatment, even though only 3.1% of them had any symptoms suggestive of neonatal sepsis and 2.2% had a positive blood culture.

Systematic Review Registration:

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ESPID19-1104
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Asymptomatic congenital cmv in a hiv positive newborn: clinical dilemmas

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Background

There is consensus in the benefit of treating symptomatic congenital cytomegalovirus (cCMV) infection according to international guidelines, however, recommendations for asymptomatic cCMV, especially in HIV exposed newborns, are lacking.

Case Presentation Summary

Full term infant, born from a 23 years old mother, HIV diagnosed during pregnancy in stage N1, starting ART at 16 weeks gestation with emtricitabina + tenofovir + raltegravir, decreasing HIV viral load (VL) to 52 copies/mL at week 36. Elective C section was performed at week 38 with fully completed prevention of mother-to-child transmission (PMTCT) protocol (mother:intrapartum ZDV, newborn: oral ZDV and breastfeeding contraindication). HIV blood PCR and urine CMV isolation were positive within 48 hrs of life. CMV disease was assessed in the newborn by CSF analysis, CBC, liver function tests, brain and abdominal ultrasound, ophthalmoscopy, and BERA, resulting all normal. Case was categorized as asymptomatic cCMV. CMV blood VL was 990 copies/ml (Log 3), and negative in CSF before starting treatment at day 24 of age, with valganciclovir for 6 weeks. CMV VL of 88 copies/mL (Log 1.5) was achieved after two-weeks of treatment. HIV was confirmed with a second positive PCR. Infant was classified on stage B1 (CD4 count 2550 cel/ul – 39%) and other opportunists were ruled out. ART started at 6 weeks of age with AZT+3TC+LPV/rtv. Satisfactory evolution and remain asymptomatic at 4 months of age with appropriate response to therapy.

Learning Points/Discussion

Fulfillment of PMTCP protocol decreases the risk of HIV acquisition to 1-2%. CMV infection may lead to more rapid progression of infant HIV infection, which was the reason to prescribe CMV antiviral treatment, despite being asymptomatic. There are still many questions regarding appropriate timing and length of treatment in cCMV and HIV coinfection.

ESPID19-1094
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

A case series of newborns with postnatal cmv infection

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Background and Aims:

Human cytomegalovirus (CMV) is still one of the major viral causes of birth defects and subsequent neurological and sensory disorders (hearing impairment, cognitive and motor development, slow development, etc.). Due to diverse clinical manifestations of disease, together with findings of genetic variability and differences in growth of various CMV strains, hypotheses of different pathogenic potential of CMV strains exist.

The aim of the study was to assess clinical presentation and outcome of postnatal CMV infection in neonates.

Methods:

A retrospective study including newborns with postnatal CMV infection who were hospitalized at the Neonatal intensive care unit of the Division of Gynecology and Obstetrics, University Medical Centre Ljubljana from January 1, 2013 to December 31, 2017 was performed. Inclusion criteria were gestational age <39 weeks and/or birth weight <1500g, and proven postnatal CMV infection in urine, plasma or blood.

Results:

There were 34 patients with postnatal CMV infection, 15 (44%) boys and 19 (56%) girls. Twelve (35%) were treated with valganciclovir or ganciclovir, other 22 (65%) did not receive treatment. The decision to institute treatment was at the discretion of the physician in charge. Only 4 (33%) of those treated had severe manifestations (i.e., respiratory distress), others had splenomegaly, hepatosplenomegaly and did not differ from neonates not receiving treatment.

Conclusions:

The results of our study show that treatment of postnatal CMV infection in neonates depended on clinical judgement and not on specific criteria. Genotyping of the isolated CMV strain could prove useful in identifying more virulent strains requiring treatment.

Systematic Review Registration:

Ongoing

ESPID19-1029
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

The rate of waning of maternal antibodies against toxoplasma gondii in uninfected infants

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Background and Aims:

Congenital toxoplasmosis can cause a disease with severe symptoms at birth. More commonly, however, newborns are asymptomatic and if left untreated may develop symptoms of the infection years later. Serological screening of new-born babies born to mothers exposed to the parasite during pregnancy gives a chance to identify infected babies and initiate treatment. The absence of specific IgM or IgA antibodies, which are the mainstay for diagnosing congenital toxoplasmosis, is common. Therefore, the diagnosis must be based on the IgG antibody response. However, passively acquired maternal antibodies make that approach difficult. Here we analyse the rate of waning of maternal antibodies against *Toxoplasma gondii* in uninfected infants.

Methods:

The study is a retrospective analysis of medical records of children consulted in the Outpatient Clinic of Bialystok Children's Clinical Hospital at the Medical University.

Results:

We analyzed lab test results of 67 infants and their mothers exposed to the parasite during pregnancy. Infant and maternal IgG levels correlated well ($R=0.78$, $p<0.001$). The median half-life of maternal antibodies was 30 days (interquartile range (IQR), 24-35 days). The median time of antibody waning was 85 days (IQR, 62-123 days). In 63 infants (94%) maternal antibodies persisted less than 6 months.

Conclusions:

The rate of waning of maternal antibodies against *Toxoplasma gondii* in uninfected children is rather rapid. It indicates that any presence of specific IgG antibodies in infants older than 6 months should rise a suspicion of congenital infection.

Systematic Review Registration:

N/A

ESPID19-1025
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Measles in neonatal age: clinical manifestation in two cases.

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Background

Measles in neonatal age is rarely reported. Congenital infection may cause variable clinical pictures from asymptomatic to skin rash, pneumonia and neurological complications with up to 27% mortality.

Case Presentation Summary

We reported two cases of neonate with measles infection.

Case#1: The mother with coryza, fever and conjunctivitis in 34th gestational week developed exanthema the day before delivery (Positive IgM and negative IgG anti-measles). At 35+1/7 weeks of gestational, she gave birth by spontaneous delivery a 2200g male infant, Apgar score 6 at 1min and 10 at 5min. The baby received polyclonal immunoglobulin, although no clinical signs of measles infection were observed. Serum anti-measles IgM were negative, but RT-PCR resulted positive for measles B3-genotype in urine and saliva. Clinical outcome was favourable, we incidentally detected bilateral hypo-echogenic adrenal lesions that regressed one month later.

Case#2: The mother presented fever, cough, Koplick's spot 15 days after giving birth to a full-term boy (weight 2620g). On admission the newborn did not evidence any clinical signs of measles. Immediately, polyclonal immunoglobulin was administered. Laboratory work-up showed negative serology and urine sample resulted positive for B3-genotype in RT-PCR. Two days after immunoglobulin injection, the baby developed neutropenia (410/µl), fever, CRP 27.7 mg/l and poor perfusion, blood culture and spinal puncture were performed and an empirical treatment with ampicillin and gentamicin was started. After isolation of methicillin-resistant *Staphyloccus Epidermidis* in cerebral fluid therapy was shifted to vancomycin. Filgrastim was administered with neutrophils increase and recovery.

Learning Points/Discussion

Neonatal measles may have variable clinical features. As reported for children (Lo Vecchio ADC 2019), B3-genotype may cause neutropenia in neonatal age. Immunoglobulin prophylaxis in newborn may have a role in preventing or attenuating symptoms.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Congenital toxoplasmosis and cmv coinfection in a 13-month old asymptomatic girl

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Background

Infections acquired during prenatal period can be asymptomatic; may cause mortality or may present with morbidity in later periods. Here, we present a 13-months asymptomatic girl with the diagnosis of congenital toxoplasmosis and cytomegalovirus (CMV) co-infection.

Case Presentation Summary

Healthy 13-month-old patient was referred to our clinic with the suspicion of congenital toxoplasmosis due to detection toxoplasma scar on the left posterior pole of her right eye on routine ophthalmologic examination. She was born by cesarean section at the 39th gestational week whose nurse mother was healthy without any history of disease in pregnancy. Neonatal audiologic examination and neuromotor development up to date were normal. Patient's serum toxoplasma IgG antibody and her mother's serum toxoplasma IgM and IgG antibody were positive. Her immunoglobulin levels and lymphocyte subset analysis were normal. In the coinfection screening; urine CMV polymerase chain reaction (PCR) test was positive. Computerized brain tomography yielded linear calcifications in the left frontal lobe anteromedially and coarse calcifications in the bilateral caudate lobes and left temporal lobe(Fig-1). CMV PCR and toxoplasma PCR were negative in cerebrospinal fluid. However,PCR analysis of dry blood sample taken in the early neonatal periodwas positive for CMV. Control audiologic examination showed unilateral sensorineural hearing loss. Treatment was started due to diagnosis congenital toxoplasmosis with primetamine, folinic acid and clindamycin since there is no sulfadiazine. In the third week of treatment, clindamycin was discontinued as sulfadiazine was provided. Valganciclovir was added to the treatment for congenital CMV infection. The patient who is in the 4th month of the treatment continues to be uncomplicated.

Learning Points/Discussion

Any patient diagnosed for congenital infections should be investigated for co-infections since the early initiation of treatment can preventthe development of late sequelae.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Congenital rubella syndrome - diagnostic challenges

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Background

We present the case of an infant with intrauterine growth restriction and significant birth defects including congenital bilateral cataracts. A diagnosis of congenital rubella syndrome (CRS) was suspected but incorrectly discounted in the presence of a positive 2nd trimester maternal IgG. Subsequent investigations, maternal history and retrospective analysis led to a delayed diagnosis of CRS.

Case Presentation Summary

Baby A was born at 34 weeks gestation. Her mother had recently arrived in the UK from Tanzania and booked late at 19 weeks. Her booking bloods were normal. Serology showed immunity to rubella. An anomaly scan at 20 weeks noted that the baby was small but anatomically normal. On serial scans the baby's growth was slow. In the neonatal unit she was noted to have a systolic murmur, bilateral cataracts, (figure 1) corneal clouding, petechiae, micrognathia, and a high arched palate. Cranial ultrasound demonstrated Grade III intraventricular haemorrhages. An echocardiogram revealed a PDA and ASD. Karyotype, array CGH, TORCH screen and a metabolic screen were sent. On further exploration of the history, her mother had a mild illness with rash in early pregnancy. At 2 weeks of age baby A's salivary sample was positive for Rubella RNA and a diagnosis of CRS was made. Repeat analysis of maternal booking blood tests detected a high IgG titre and equivocal IgM result, consistent with recent infection. Baby A stayed on NICU for 6 months due to complications associated with CRS.

Learning Points/Discussion

Serology results for rubella should not be interpreted in isolation; clinical judgement, and the clinical picture should also be considered. Bilateral congenital cataracts require a careful workup for associated abnormalities and underlying medical conditions. Investigation of possible congenital or perinatal infections should involve multidisciplinary teams.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Congenital tuberculosis by multidrug resistant strain after in vitro fertilization: case report and review of the literature

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Background

Genitourinary tuberculosis (GU-TB) leading to infertility in women is common in regions with high TB burden. *In vitro* fertilization (IVF) is an effective treatment to improve fertility, and its increasing availability may create the potential for congenital TB (CTB) to emerge as a significant problem.

Case Presentation Summary

A 30 week gestation preterm girl, conceived by IVF and born to an immigrant from India, developed pneumonia at 1 month of age. With antibiotics the infant improved. At 3 months of age, fever developed and respiratory status worsened. Antibiotic regimens for presumed nosocomial pneumonia lead to transient improvement. Bronchoscopy and lung biopsy facilitated the diagnosis of pulmonary TB with a multidrug resistant strain. Endometrial TB with identical strain was diagnosed in the infant's mother. Both responded satisfactorily to treatment with 2nd line anti-tubercular medications.

Learning Points/Discussion

We identified 20 cases of CTB following IVF in 16 women described in the literature. About two thirds of women (64%) were born in TB high burden countries, and most (88%) had inflammation or obstruction of fallopian tubes. No TB test was performed in two thirds (69%) and positive test results in 3 women did not lead to TB treatment. Almost all infants (95%) were premature; most (70%) had only pulmonary TB while 30% had disseminated disease. The median age (range) at onset of TB-relevant symptoms were 28.5 days (1-98). Most (80%) recovered with anti-TB treatment. Clinicians caring for infants, conceived by IVF, with progressive, unexplained respiratory illness should maintain a high index of suspicion for CTB. TB testing should be included in the diagnostic evaluation of infertile women with TB risk factors.

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Congenital and perinatal infections

Motor development curves and item map by difficulty order of gross motor function of a child with cerebral palsy due to congenital zika virus infection

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Background

Motor development curves have been widely used to describe gross motor development among children with cerebral palsy (CP). When used in association with item mapsby difficulty order of the gross motor function, the information helps rehabilitation teams planinterventions based on the neurologic potential of those children. Currently, there are few studies about long-term disabilities in this specific population.

Case Presentation Summary

A male child diagnosed with quadriplegic spastic CP and congenital microcephaly due to congenital ZIKV infection confirmed by serology (positive IgM) and according to the criteria of the Brazilian Ministry of Health (MOH) surveillance system. This child was followed longitudinally for 2 years in a reference Rehabilitation Center in Salvador, Brazil. At 2 years of age, the GMFM-66 score indicated the child had reached approximately 90% of his potential motor development limit. According to motor growth curves, his GMFM-66 score was compatible with GMFCS level V. The item map by difficulty order highlighted that the child's emerging skillswere still around in the lower gross motor abilities at this age. In combination, these results evidenced the child's severe impairment in gross motor development and poor motor prognosis.

Learning Points/Discussion

This case report underscores the need for long-term follow-up studies in this field to understand how congenital ZIKV infection impacts motor development in the affected population. In cases of CP diagnosis due to congenital ZIKV infection, the motor development curves based on GMFM-66 score should be used together with item maps by difficulty order toplan and improve individual rehabilitation programs. Until now, no study addressed these aspects of motor assessment and/or motor prognosis.

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Congenital and perinatal infections

Long-term sequelae of children with cmv congenital infection in gran canaria island (spain)

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Background and Aims:

Cytomegalovirus (CMV) is the leading cause of congenital infection in developed countries, and causes important long-term sequelae, especially neurosensory hearing loss and neurological disorders. Our aim is to describe long-term sequelae of children with a diagnosis of CMV congenital infection in our hospital.

Methods:

Retrospective descriptive study of cases of CMV congenital infection diagnosed on Gran Canaria (Spain) from 2010 to 2018. Data of obstetric antecedents, diagnosis of infection, image studies, treatments and sequelae were collected.

Results:

Sixteen congenitally infected infants were identified. Eleven (68.7%) presented a symptomatic infection at birth (most frequent were hepatomegaly, purpura with thrombocytopenia and jaundice), 2 were detected by screening in HIV-positive women, in 2 the mothers had a clinical picture during pregnancy. One case had a pathologic ultrasound fetal image. Eight (72%) were preterm infants. Infants with a symptomatic infection received treatment (intravenous ganciclovir and/or oral valganciclovir).

At follow-up, 6 (37.5%) had neurological sequelae: 3 had mild and 3 moderate sequelae. The sequelae were identified at age 6-18 months. One infant presented cataracts and only one child had a sensorineural hearing loss. Among children with symptomatic infection at birth, 45% (5/11) had sequelae versus 25% (1/4) of asymptomatic infants.

Cerebral ultrasound imaging and CT or MRI were normal except in 3 cases in which cerebral calcifications or white matter alterations were identified. These 3 children had moderate sequelae and all had a symptomatic infection at birth.

Conclusions:

In our study only children who presented moderate sequelae had alterations shown in image studies. Neurological sequelae were detected in the first 2 years of age. Intensifying multidisciplinary protocols in long-term follow-up in our center is necessary to improve the diagnosis of sequelae and the prognosis of these children.

Systematic Review Registration:

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E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Prevention of mother-to-child transmission (pmtct) of hiv - 10-year polish observations

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Background and Aims:

The effectiveness of prevention of mother-to-child transmission (PMTCT) of HIV was analyzed.

Methods:

258 mother-child pairs were included between 2006 and 2015. Maternal HIV infection was detected no later than perinatally. The duration and the type of the prophylaxis, the maternal HIV viral load during pregnancy, and the type of labor were analyzed.

Results:

Complete prophylaxis (during pregnancy, delivery, and in the newborn) was adapted in 70% of cases, in 3% of cases no prophylaxis was administered. 88% of women received antiretroviral treatment during pregnancy, 74% received ZDV during labor. The prophylaxis was administered in 97% of the newborns. Six (2%) of the children were HIV-infected. No child became infected when the full prophylaxis was applied, or when maternal treatment was initiated before the 14th week of gestation, and in none of 163 mothers who had undetectable HIV viral load in the last weeks of gestation. The child infection rate was 3% for children of mothers in which the treatment was initiated from 14th week of gestation, 11.5% for cases when the prophylaxis was used only in neonate and/or during labor, and 16.5% in children without any prophylaxis. Inclusion of the antiretroviral drugs in later weeks of gestation was associated with a higher risk of infection ($p = 0.02$). The risk was lower when a planned caesarean section was performed (1%) compared to the natural delivery (6.3%, $p = 0.03$).

Conclusions:

The risk of vertical HIV transmission is low. An effective treatment of a woman before pregnancy or initiation of the treatment from the beginning of the second trimester of pregnancy are the most important factors for prevention of MTCT of HIV.

Systematic Review Registration:

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ESPID19-0575
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Cerebrospinal fluid (csf) immunoglobulins are significantly increased in neonates born to mothers with gestational zika virus clinical symptoms

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Background

Congenital Zika virus (ZikV) infection has recently been recognized as a disease with neurological alterations. Increased CSF protein has also been reported, particularly among patients born with microcephaly. We measured different immunoglobulins in the CSF of neonates exposed to ZikV during foetal life and compared these results with measurements performed in the CSF of control neonates.

Methods

We identified 16 neonates who underwent lumbar puncture (LP) in the CSF Laboratory in Salvador, Brazil, during the ZikV epidemic (December 2015 to March 2016). All mothers reported ZikV clinical symptoms (rash, fever, myalgia, arthralgia) during gestation. Then (November 2017 to September 2018), we identified neonates who underwent LP in the same Lab and fulfilled criteria to be controls: age ≤4 days, CSF White Blood Cell count ≤8/mm^3, CSF protein ≤132mg/dL, CSF Red Blood Cell count ≤1,000/mm^3, neither central nervous system illness, nor congenital infection, nor microcephaly. CSF immunoglobulins were measured (mg/L) by targeted mass spectrometry in Rotterdam, The Netherlands and compared as median (p25th-p75th).

Results

Out of 85 neonates investigated to be included as controls, 14 were included and were tapped due to sepsis (n=6), maternal syphilis (n=5), seizure, fever without source, and maternal acute cytomegalovirus infection (n=1 each). Congenital syphilis and cytomegalovirus infection was safely ruled out. Table 1 shows the comparison. Eight (50%) cases had congenital microcephaly. When the comparison was repeated including only cases without microcephaly, similar results were found.

Conclusions

Neonates exposed to ZikV infection during gestation intensely produce different amounts of immunogloblulins in CSF, irrespective of having congenital microcephaly.

Clinical Trial Registration (Please input N/A if not registered)

N/A

Table 1. Comparison of CSF immunoglobulins (median [p25h-p75th]) between neonates exposed to Zika virus during fetal life, with or without congenital microcephaly, and controls

CSF proteins	Controls n=14	Cases with and without microcephaly n=16	P	Cases with microcephaly n=8	Cases without microcephaly n=8	P
IgA-SAVQ (mg/L)	0.65 (0.5-1.03)	6.8 (1.5-48.3)	<0.001	25.1 (6.0-89.6)	1.6 (1.0-16.4)	0.011
IgA-YLTWASR (mg/L)	1.5 (1.4-1.7)	12.5 (2-75)	0.001	50.2 (10.3-80.8)	2.1 (1.5-15.3)	0.05
IgG-DTLM (mg/L)	716 (504.5-914.9)	1091.8 (851.1-1358.2)	0.002	1163.3 (985.2-1683.1)	969.3 (567.5-1278.6)	0.088
IgG-DTLM I (mg/L)	913.9 (761.5-1268.8)	2165 (1414-2935.8)	<0.001	2574 (1706-3593.3)	1425.3 (1292.3-2854.1)	0.014
Ig kappa (κ)-SGTA (mg/L)	6378.8 (5040.6-9918.7)	13812.6 (10392.9-17794.8)	<0.001	14851.1 (13251.0-21760.8)	12375.0 (9562.5-15914)	0.02
Ig kappa (κ)-TVAA (mg/L)	820.9 (671.2-1268.0)	1938.2 (1571.8-2466.5)	<0.001	2311.7 (1776.4-2723.3)	1667.5 (1362.5-2053)	0.06
Ig lambda (λ)-SYSC (mg/L)	1108.6 (941.7-1509)	2161.1 (1766.6-4297.6)	<0.001	3952.5 (1937.3-6792.7)	1841.6 (1549.8-2361.7)	0.005
Ig lambda (λ)-YAASS (mg/L)	424.5 (358.3-589.6)	754.6 (591.5-1594.9)	0.001	1391.2 (728.8-2194.3)	677.7 (430.5-901)	0.034
IgM (mg/L)	1.3 (0.9-1.9)	47.8 (3.3-173.3)	<0.001	135.3 (59.7-655.5)	3.8 (1.9-29.8)	0.009

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Congenital and perinatal infections

Cerebrospinal fluid (csf) inflammatory markers are significantly decreased in neonates born to mothers with gestational zika virus clinical symptoms

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Background

Congenital Zika virus (ZikV) infection has been recently recognized as a disease with potential neurological illness. We measured different biologically active proteins in the CSF of neonates exposed to ZikV during foetal life and compared these results with measurements performed in the CSF of control neonates.

Methods

We identified 16 neonates who underwent lumbar puncture (LP) in the CSF Laboratory in Salvador, Brazil, during the ZikV epidemic (December 2015 to March 2016). All mothers reported ZikV clinical symptoms (rash, fever, myalgia, arthralgia) during gestation. Then (November 2017 to September 2018), we identified neonates who underwent LP in the same Lab and fulfilled criteria to be controls: age ≤4 days, CSF White Blood Cell count ≤8/mm^3, CSF protein ≤132mg/dL, CSF Red Blood Cell count ≤1,000/mm^3, no Central Nervous System illness, no congenital infection, nor microcephaly. CSF proteins were measured by Lumos Fusion Orbitrap by shot gun mass spectrometry in Rotterdam, The Netherlands and compared as medians (p25th-p75th).

Results

Out of 85 neonates investigated to be included as controls, 14 were included and were tapped due to sepsis (n=6), maternal syphilis (n=5), seizure, fever without source, and maternal acute cytomegalovirus infection (n=1 each). Congenital syphilis and cytomegalovirus infection were safely ruled out. The median (p25th-p75th) age (days) was 2 (1-3) and 3 (1-4) among cases and controls, respectively. Table 1 shows the comparison of CSF proteins.

Conclusions

Distinct cell mediators, including biotinidase, are down-regulated among neonates exposed to ZikV infection during gestation. Biotin intake may be useful for these patients.

Clinical Trial Registration (Please input N/A if not registered)

Table 1. Comparison of CSF proteins (median [p25h-p75th]) between neonates exposed to Zika virus during foetal life and controls

CSF proteins	Controls n=14	Cases n=16	P
Alpha-1-antitrypsin	34 (33-34.3)	31 (29.3-32.0)	<0.001
Alpha-1-acid glycoprotein 1	7.5 (7-9.3)	7 (6-7)	0.012
Alpha-1-acid glycoprotein 2	6 (6-7.3)	6 (5-6)	0.02
Osteopontin	6 (5.8-7.3)	3 (2-4)	<0.001
Metalloproteinase inhibitor 2	3.5 (3-4.3)	3 (1-3)	0.007
Superoxide dismutase	3 (2.8-4.3)	2 (1-2.8)	0.003
Neuromodulin	5 (2.8-6)	1 (0-2)	<0.001
Cell growth regulator	3 (1.8-4)	0 (0-1)	<0.001
Disitegrin and metalloproteinase	1 (1-2)	1 (0.3-1)	0.019
Macrophage colony-stimulating	1 (1-2.3)	0 (0-1)	0.014
Biotinidase	2 (1-2)	0 (0-1)	0.001
Osteomodulin	1 (0-2)	0 (0-0)	0.001
Macrophage colony-stimulating fator 1	1 (0-1)	0 (0-0)	0.001

ESPID19-0539
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

What lies behind microcephaly?

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Background

A prenatally acquired cytomegalovirus (CMV) infection may have serious consequences in the form of microcephaly with various neurological implications.

Case Presentation Summary

Child with congenital microcephaly, hypotrophy and a postnatally confirmed CMV infection (serum aCMV IgM 9.8 AU, standard value up to 0.84 AU, urine CMV PCR 13x10.6 and 50x10.3 copies/mL) treated with ganciclovir, with cortico-subcortical atrophy and pontocerebellar hypoplasia diagnosed later with MRI testing. Due to progressive microcephaly, delayed psychomotor development and neurological symptomatology in infancy, clinical picture and serological findings were assessed as CMV infection towards the end of pregnancy. The infant's mother was later diagnosed as well. After confirmation of the CMV infection in the child, the CMV viral load was identified in the mother (serum aCMV IgM 0.80 AU with negative result, aCMV IgG 250 AU, standard values up to 5.99 AU, urine CMV PCR 1,120 copies/mL).

The further clinical development of the child was significantly different from what is expected in the case of an infant with CMV infection. The MRI finding (pontocerebellar hypoplasia, neocortical atrophy) was an indication for molecular genetic examination which confirmed the TSEN54 gene with pathogenic founder mutation c.919G>T (p.Ala307Ser) in the homozygous condition, which is the most frequent cause of type 2 pontocerebellar hypoplasia (PCH2).

Learning Points/Discussion

A congenital CMV infection leads to severe CNS, vision and hearing defects, 85-90% of newborns with a congenital CMV infection are asymptomatic at birth, 5-15% of children developing neurological disability or hearing defect in the years to come. The implementation of screening in newborns would allow for the diagnosis of asymptomatic children. Studies involving the application of a specific vaccine are ongoing as part of the prevention of maternal infection and the subsequent transplacental transmission of the virus.

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Congenital and perinatal infections

A preparatory audit of neonatal sepsis management at a large tertiary neonatal unit in harare, zimbabwe

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Background and Aims:

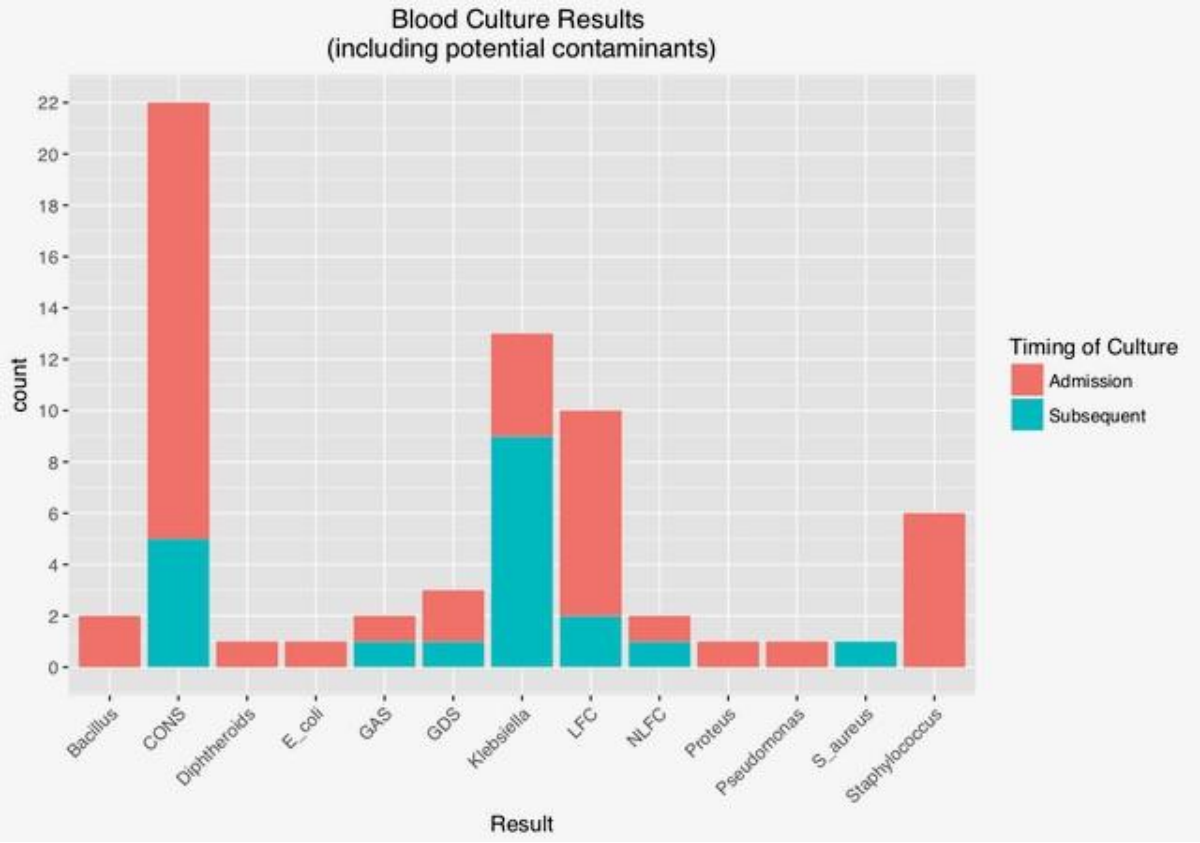
Neonatal sepsis kills 700000 infants annually. In low-income settings, diagnosing infections can be challenging. We aimed to evaluate investigation and management of neonatal sepsis at baseline prior to interventions aiming to improve quality of care at Harare Central Hospital (HCH) Neonatal unit.

Methods:

We carried out a prospective audit of babies admitted over 4 weeks using local guidelines (based on World Health Organization 2016 evidence) as the gold standard. Data were collected daily from admission to final outcome from medical records noting episodes of suspected sepsis, investigations and management. All babies admitted from 8.5.18 to 5.6.18 were included.

Results:

459 babies were admitted over 28 days, with outcomes available for 458. 369(80%) were inborn with 115(25%) Caesarean deliveries. 361(78%) survived to discharge, 95(21%) died, 2 were transferred (1 unknown, 0.2%). Suspected sepsis was the most common admitting diagnosis(82%) and implicated in 90% of deaths. 449(98%) received antibiotics, mean/median duration 9 days(IQR 8-12). Inpatient therapy was 1243/1000 patient days. Blood cultures were sent in 44%(196/445) of those starting antibiotics on admission of which 65/196(33%) received results (median time-to-result 6 days, IQR 5-9).Only 7/196(3.5%) cultures sent impacted on therapy. There were 75 episodes of subsequent sepsis in 54(12%) admitted babies. 7/36(20%) positive cultures led to an appropriate change in therapy. *Klebsiella pneumoniae*/Lactose-fermenting coliforms were common pathogens even at admission, all but one of which was resistant to third-generation cephalosporins(Figure).



Conclusions:

Sepsis is an important contributor to mortality on the neonatal unit, but may be overdiagnosed/overtreated with extensive antibiotic use. Highly resistant Gram-negative organisms were frequent. Culture results were rarely available in a clinically useful timeframe, hampering isolation procedures, likely contributing to ongoing spread of resistant nosocomial infections. Low-cost technological interventions could speed up time-to-results.

Systematic Review Registration:

N/A

ESPID19-0402
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Clinical characteristics of infants exposed to varicella infection around the newborn period: a case series

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Background

Varicella infection around the neonatal period occurs within 4-6 weeks of life, where neonates may be infected in utero, at birth, or after birth. When maternal varicella develops more than 5 days before delivery and gestational age is 28 weeks or more, newborn's disease severity is modified by transplacental transfer of maternal IgG antibodies. If maternal symptoms occur 1-4 weeks before delivery, approximately 50% will be infected. Incubation period ranges from 10–14 days. Symptoms appearing within 10 to 12 days of life are addressed as perinatal varicella, those after 12 days considered as postnatal infection.

Case Presentation Summary

Ten newborns exposed to varicella infection were hospitalized in pediatric isolation ward. Gestational age were 33-40 weeks, birthweight 2400-3700 grams. Diagnosis of varicella was clinically based; lesions consisted of crops containing vesicles at various stages. No serology test was applied. Perinatal exposure occurred in eight infants, three who didn't develop clinical symptoms were regarded as varicella exposed infants, with mother's symptoms appearing at 4, 6, and 14 days before delivery. Five developed vesicles within 1-12 days of life where maternal varicella occurred 1-7 days before delivery. Two infants developed clinical disease at 20 and 23 days of life considered as postnatal varicella where mothers showed symptoms one week before and 14 days after delivery respectively, the former started acyclovir one day after delivery. All were treated with acyclovir. Four cases with maternal varicella occurring ≤3 days before delivery developed pneumonia, necessitating ampicillin and gentamycin. One was associated with secondary skin infection, another with late preterm and low birthweight infant experienced hypoglycemia. None died.

Learning Points/Discussion

Infants born to mothers with chickenpox may not develop clinical disease. Maternal varicella occurring ≤3 days before delivery were associated with complications.

ESPID19-0393
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

A newborn with severe combined immune deficiency, maternal t-cell engraftment and cytomegalovirus (cmv) pneumonia

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Background

Severe combined immune deficiency (SCID) is a rare primary deficiency affecting 1:50000 live born.These babies appear normal at birth and then start having severe infections, pneumonia by PCP, adenovirus, CMV and RSV, chronic viral diarrhea, malabsorption and failure to thrive.

Case Presentation Summary

A male baby born to third degree consanguineous Muslim couple was shifted to neonatal unit in view of respiratory distress and mild asphyxia. Mother was 4th Gravida with 3 abortions. There was no family history of infant deaths or recurrent/severe infections. Mother was negative for HIV. He required minimal amount of Oxygen for his respiratory distress. There were no dysmorphic features and systemic examination was normal.

He received Piperacillin Tazobactum from day 5 for late onset sepsis and pneumonia which were changed to Meropenem and Amikacin in view of clinical worsening and meningitis. There was recurrence of pneumonia on day 25 when blood counts were reviewed (Fig1).

Blood Counts

Day of Life	Hb	TLC	Platelet	DLC	Neutrophil count	Lymphocyte count
Day 1	14.3	6500	2.71	$N_{52}L_{27}$	3.3 X 10^3	1.8 X 10^3
Day 5	13.6	3100	2.24	$N_{52}L_4$	**1.6 X 10^3**	0.1 X 10^3
Day 25	13.3	4300	5.19	$N_{60}L_3$	4.4 X 10^3	0.6 X 10^3
Day 54	10.3	17200	3.42	$N_{70}L_4$	12. 1X 10^3	0.7 X 10^3

Immunoglobulin Profile

Immunoglobulin	Value (mg/dl)	Age specific reference
IgG	328	(250- 906 mg/dl)
IgM	<5	(17-105 mg/dl)
IgA	<5	(1.3-53 mg/dl)

Flow cytometric Immunophenotyping for lymphocyte subsets SSC vs CD45

Lymphocyte subset	Day of Life 25*	Day of Life 54**	Normal range
% CD3+ (T lympho)	0.2% (1-2)	93.31% (658)	60-85% (2300-7000/cumm)
% CD19+ (B lympho)	32.4% (198)	0.03% (0-1)	04-26% (600-19000/cumm)
% CD56+ (NK cell)	-	0.14% (0-1)	03-23% (200-1400/cumm)

***Impression: B lymphocytes have dim to moderate expression. T cells are negligible.**

****Impression: B lymphocytes are absent. T subset shows maternal engraftment.**

In view of persistent lymphopenia and x ray appearance of viral pneumonia a clinical diagnosis of immune deficiency was made. Bronchoalveolar lavage fluid and urine were positive for CMV PCR. Child was started on Gancyclovir. On confirmation of diagnosis of SCID (B-T-NK-), child was given intravenous immunoglobulin and fluconazole and cotrimoxazol prophylaxis. A repeat flow cytometry was suggestive of maternal T cell engraftment. The baby expired on day 75 because of persistent pneumonia and sepsis.

Learning Points/Discussion

Lymphopenia noted on CBC may be a clue towards SCID. These patients require work up for unusual organisms. Patients with SCID may have low normal absolute lymphocyte counts due to presence of maternal lymphocyte. SCID infants do not usually reject maternally engrafted cells. Since these T cells are usually non-functional, they do not alter the course of the disease.

ESPID19-0375
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Congenital varicella syndrome: a case report

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Background

Congenital varicella syndrome (CVS) is an extremely rare disorder of newborns, following maternal varicella infection during 6-20 weeks of gestation. The most frequent presentation of CVS are cicatricial skin lesions, limb hypoplasia, muscle atrophy, malformation of the digits, psychomotor retardation, microcephaly, cortical atrophy, Horner's syndrome and various eye abnormalities, including cataracts, chorioretinitis and microphthalmos.

Case Presentation Summary

10 months old girl presented to our clinic with a 4 day history of fever and rash.
From the past history: the girl was born by normal vaginal delivery at 32 week of gestation with birth weight 3200g. Mother had chickenpox at 17th week of pregnancy and was not treated with antivirals. As a newborn she developed vesicles on her face and trunk, chorioretinitis from the right side. CVS was diagnosed and she was treated with IV Acyclovir 80 mg/day for 1 month, followed with oral Acyclovir for 5 months. She developed scar on retina.
The rash consisted of discrete papular lesions on her left leg, which progressed over 72 hours to a vesiculobullous lesions across the L5-S1 dermatomes, with overlying yellow crusting. She had cicatricial skin lesion on her forehead. Neurological examination was normal; movements of the leg were limited and painful. Varicella zoster virus (VZV) was detected by polymerase chain reaction in bullae fluid.
Current admission was due to reactivation (herpes zoster) of varicella. Treatment with IV acyclovir was started immediately. After all bullous elements were crusted treatment regimen was changed from IV to oral for 3 months.
During 1 year follow up the girl showed no symptoms of relapse.

Learning Points/Discussion

Infants with CVS could present with reactivations requiring antiviral treatment.

ESPID19-0356
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Gestational and congenital tuberculosis in a low-burden country

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Background and Aims:

Tuberculosis (TB) during pregnancy is rare, but it can represent a serious hazard for pregnant women and newborns.

Methods:

We reviewed clinical data of patients diagnosed with gestational and congenital TB in a tertiary hospital in Spain during 12 years (2007-18).

Results:

We included 11 women who received TB treatment during pregnancy, 5 had started before conception and 6 afterwards (median gestational age 18 weeks, IQR 8.5-19). All patients were immigrants (4 from Morocco, 4 Latin America, 3 other). Eight patients (73%) were diagnosed with pulmonary TB, 2 with adenitis and one with miliary TB. Polimerase chain reaction (PCR) was positive in all patients, culture in 71% and acid-fast smear in 44%. All received TB treatment (90% including pyrazinamide) for 6 -12 months with good outcomes.

All newborns were asymptomatic; two were preterm (both 35 WGA) and one small for gestational age. TST (n=11) and IGRA (n=8) were negative in all infants tested. All imaging results (7 abdominal ultrasound, 6 chest radiograph) were normal and all microbiological studies (4 patients: acid-fast smear, culture and PCR of gastric aspirates) negative. Only two newborns received isoniazid prophylaxis for 3 months. All patients but one completed one year follow-up, without developing latent or active TB.

During the study period, two infants (8 and 36-day-old) were diagnosed with microbiologically-confirmed congenital TB (pulmonary and miliary). Both mothers were diagnosed with genital TB afterwards by endometrial biopsy.

Conclusions:

In Spain, gestational TB affects mainly immigrants. TB treatment appears to be safe for the fetus and diminishes greatly the risk of vertical transmission. All infants with congenital TB in our study were born to mothers with genital TB who had not been diagnosed during pregnancy.

Systematic Review Registration:

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ESPID19-0337
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Cases of vertical transmision of hiv in gran canaria island (spain) in the last 18 years

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[3]Hospital Universitario de Gran Canaria Doctor Negrín, Microbiology Department, Las Palmas de Gran Canaria, Spain

Background and Aims:

Vertical transmission (VT) of Human Immunodeficiency Virus (HIV) has been drastically reduced in developed countries, but still exists with incidence of around 1.5%. Our objective is to describe cases of VT of HIV diagnosed in our center from the introduction in 2000 of a new protocol which included the highly effective antiretroviral treatment in pregnancy.

Methods:

Retrospective descriptive study of cases of HIV TV diagnosed on Gran Canaria (Spain) from 2000 to 2018. Data of pregnancy, deliveries, treatment and evolution were collected.

Results:

We registered 159 newborns (NB) from a total of 140 HIV-positive women. Of these, 3 (1.88%) cases of VT of HIV were detected.

The first one was a medically unsupervised pregnancy and no maternal infection was detected. The child was diagnosed with acquired immune deficiency syndrome at 5 years of age.

In the second case, the VT was in a newborn with fetal gastroschisis. The mother was diagnosed at week 34, and started treatment. A cesarean was done and the NB was treated and was given formula.

The third case was an unsupervised pregnancy with diagnosis at delivery, with positive viral load (VL) in just two samples of the NB in the first days of life and with early intensive antiretroviral treatment. In the follow-up the NB lost the antibodies, the treatment was terminated at 2 years of age and the VL remained undetectable 6 years later.

Conclusions:

The incidence of VT of HIV on the island is in line with the national incidence (1.88%); however, one case had a very late diagnosis. The infection was resolved in another case after an early intensive treatment. We must be alert to possible cases in order to apply effective prophylactic measures.

Systematic Review Registration:

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ESPID19-0236
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Risk of infection and prognostic outcomes in neonates born from precipitate labor with out-of-hospital delivery

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Background and Aims:

Precipitate labor (PL) is defined as expulsion of the fetus within less than three hours of uterine contractions. PL usually took place outside the delivery units due to unexpected timing of labor. PL is known to associate with higher rates of maternal complications and problems of neonates. The aim of this study was to investigate the risk of infection and prognosis of neonates born with out-of-hospital delivery (OHD).

Methods:

We enrolled PL neonates with OHD at the Department of Pediatrics, MacKay Children's Hospital, from January 2004 to December 2017. We retrospectively reviewed maternal history, birth records, clinical courses and laboratory data.

Results:

A total of 158 newborns were enrolled. The overall rate of OHD was 0.22%. Twenty-nine patients (18.4%) underwent non-sterile umbilical cord care. Six patients (3.8%) had developmental delay, and five of them (3.2%) had seizure disorder. Nine patients (5.7%) had positive cultures, and two of them (1.3%) had bacteremia. In the multivariate analysis, gestational age (OR, 0.75; 95% CI, 0.56–0.99; p = 0.047) was the factor associated with infection. Forty-nine women (31%) did not receive any prenatal examinations, and 10 women (6.3%) were even unaware of pregnancy. The newborns with OHD had younger maternal age, higher rates of prematurity, and higher rates of early-onset infection (OR, 5.12; 95% CI, 1.26–20.83; p = 0.011) than those born in hospital.

Conclusions:

Poor prenatal care and social issues as teenage mothers were not uncommon in PL. Support resources should be provided to the vulnerable populations. Preterm delivery is related to PL, and gestational age is the factor associated with infection. Early-onset infection rate of neonates with OHD is higher than general population, so those who born out-of-hospital should be hospitalized for observation.

Systematic Review Registration:

Not applicable

ESPID19-0108
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Intrauterine growth restriction among patients exposed in utero to zika virus with and without microcephaly

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Background

Congenital infections are associated with intrauterine growth retardation (IUGR). We aim to investigate the possible association between IUGR and microcephaly in children of mothers with probable Zika virus infection during pregnancy

Methods

We recruited mother-infant pairs between May 2015 and October 2017 in a pediatric infectious disease clinic in Rio de Janeiro. Inclusion criteria required that either the mother reported Zika infection symptoms during pregnancy or the infant presented with clinical or imaging features of Zika virus infection. Exclusion criteria included detection of an alternative cause for the patient's presentation or negative polymerase chain reaction assays for Zika in all specimens tested within 12 days from the beginning of maternal symptoms. Microcephaly was characterized by <3 z-score on WHO/Intergrowth curves at birth. The presence of microcephaly and its relationship to the presence of IUGR (based on pregnancy sonogram) was assessed by Fisher exact or Mann-Whitney test. Maternal and pregnancy-related information was were collected and we used logistic regression in order to adjust for possible covariates also associated with IUGR.

Results

Out of the 41 included neonates, 19 (46%) were diagnosed with microcephaly. The mean maternal age at the birth was 21 years old. Among the 12 patients with IUGR, 8 had history of microcephaly (p=0.03). When adjusting for history of maternal tobacco use during pregnancy (p=0.58), maternal alcohol use during pregnancy (p=0.16), other congenital infection (p=0.39), and income (p=0.13), microcephaly was still associated with IUGR (p=0.02)

Conclusions

Our study corroborates the hypothesis that microcephaly associated with congenital Zika virus infection was associated with IUGR

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESPID19-0030
E-Poster Viewing - May 7-10 - E-Poster Hours

Congenital and perinatal infections

Congenital cytomegalovirus: case series and their follow-up

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Background

Cytomegalovirus infection affects 0.5-2% of newborns and is the most important congenital infection associated with non-genetic hearing loss and mental retardation. Our country lacks local data due to the non-performance of universal hearing screening and the underdiagnosis of cytomegalovirus in oligosymptomatic/asymptomatic newborns.

Case Presentation Summary

There were 23 congenital cytomegalovirus with urine PCR positive test around 14 days of life. The incidence was 0.07%. The majority were males (14), gestational age average was 37 weeks (27-41), birth weight average was 2844 g (1965-4105) and ten were small for gestational age. Clinical characteristics were: neurological disorders 78.3%(18), genetic syndrome 30.4%(7), microcephaly and convulsive syndrome 13%(3) each and necrotizing enterocolitis (NEC) 8,7%(2). At diagnosis the exams highlights: chorioretinitis 4.3% (1) and hearing loss 17.4% (4). They had alterations in cerebral ultrasounds 63.2%(12/19) and magnetic resonance 66.6%(4/6). Were treated: 69.5%(16), 9 ganciclovir for 6 weeks and 7 valganciclovir for 6 months. The adverse more important was neutropenia with ganciclovir.

Oftalmologic evaluation: 65.3%(15) followed-up with fundus, all normal.
Otorhinolaryngologic evaluation: 69.5%(16) followed up, 5 had hearing loss (3 of them with normal hearing screening at the beginning).
Neurologic evaluation: 78,3%(18) followed-up, 13 had alterations, 1 patient was normal until 18 months and had language delay at 36 months.

Learning Points/Discussion

This study present valuable information on the most relevant clinical characteristics these patients and highlighting the precocity of the diagnosis. 8% presented NEC as a non-usual presentation and which could be under diagnosed. Three normal patients at the time of admission evolved to hearing loss, emphasizing the importance of long-term follow-up due to the appearance of late sequelae. An improvement in the diagnosis could favor early intervention, especially in hearing loss.

ESPID19-0651
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Faecal s100a12: a useful biomarker in the assessment of childhood acute gastroenteritis

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Background and Aims:

Acute gastroenteritis is one of the most common infections in children. Differential diagnosis between viral and bacterial gastroenteritis is often difficult. Faecal calprotectin (FC), faecal lactoferrin (FL) and faecal S100A12 are stool biomarkers of intestinal inflammation. Although faecal markers are good indicators of inflammatory bowel disease (IBD), they are not specific for IBD; elevated levels have also been found in other diseases, such as infectious gastroenteritis (IG). The aim of this study was to explore the usefulness(?), value?? of faecal biomarkers in children with acute gastroenteritis.

Methods:

Prospective case-control study conducted from 01/2017 to 03/2018. Epidemiologic and clinical data was collected from patients and controls. Faecal biomarkers (calprotectin, lactoferrin, S100a12) were measured using enzyme-linked immunosorbent assay (ELISA).

Results:

A total of 36 patients with clinical diagnosis of acute gastroenteritis and 36 age-matched healthy controls were included. Viral gastroenteritis was diagnosed in 62% of patients. Boys exceeded girls (58.8%). The concentrations of FC , FL and faecal S100A12 were higher in patients (1490±1913μg/g; 75.7±72.6μg/g; 28.3±25.3μg/g, respectively) than in controls (632±1535μg/g; 17.7±42.2μg/g; 6.5±11.6μg/g, respectively) (p<0.0001), whereas C-reactive protein was non-statistically significant between the two groups (35mg/dl±46) vs (35mg/dl±41). Faecal S100A12 was significantly lower in children with viral compared to bacterial gastroenteritis according to logistic regression (p=0.04).

Conclusions:

Faecal biomarkers, such as calprotectin, lactoferrin, and S100A12 are predominantly derived from neutrophils, easily detectable in faeces, and, apparently, indicators of intestinal inflammation. Among the faecal biomarkers studied, only S100A12 was associated with the origin of acute gastroenteritis in children.

Systematic Review Registration:

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ESPID19-1151
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Intussusception as a complication of adenovirus and rotavirus coinfection

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Background

Intussusception is one of the most common causes of intestinal obstruction in young children. Approximately 90% are younger than two years old, with only up to 4% occurring in children over 10 years old. Outside the typical age range, it is likely associated with a pathologic lead point, which may include reactive lymphoid hyperplasia secondary to infection. A strong association with adenovirus infection has been shown in a variety of populations.

Case Presentation Summary

A previous healthy 11-year-old girl presents to the emergency department (ED) with a history of peri-umbilical intermittent abdominal pain,recurrent vomiting and 5 episodes of diarrhea that evolved to bloody stools within hours of evolution. At admission she was prostrated, pale and tachycardic. Her mucous membranes were tacky and her abdomen revealed nothing but hyperactive bowel sounds. Blood test revealed 17.600/uL leucocytes with 80,7% neutrophil count and RCP < 0,1 mg/dl. During the ED stay she developed more intense abdominal pain that prompted an abdominal ultrasound which revealed an intussuscepted ileum into the proximal portion of colon, that not disappeared during the exam. On the urgent exploratory laparotomy that she was submitted an ileum-ceco-colonic intussusception was noted, ending on a terminal ileum-colonic resection. The stool analyses isolated both adenovirus and rotavirus.

Learning Points/Discussion

Adenoviruses are important human pathogens, being associated with a broad spectrum of clinical diseases that the clinician must be aware of. There are some findings that viral infection plays an important role in the development of intussusception. Infection with adenovirus is a strong predictor of it. We therefore wish to alert to one of the possible complications of adenovirus/rotavirus coinfection, which in our case occurred in a less common age group.

ESPID19-1030
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Sapovirus: an emerging virus to consider

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Background and Aims:

Gastroenteritis caused by sapovirus is one of the most common cause of this desase in childre being infants more afected. The clinic of sapovirus is fever diarrea and vomits what can cause dehydrtation and an increase of hospital admision. Te aim of our study is knowing the characteristic and evolution of childre to whom have been isoleted sapovirus in stools in last year.

Methods:

We have reviewed clinical histories about children at whom sapovirus was isolated in stools knowing abaout the episode , analyzing the age, sex, duration of sympthoms, the presence of fever and the need of hospitalization.

Results:

We got a sample of 7 patients, 57% were male and, 43% females, the average of age was 2.39 years. 71% of patients presented diarrea, what it seems to indicate that it was a causal finding, only 1 patient presented vomits and 57% patients the illness was accompanied by fever.
For 29% of patients was necessary the hospital admision but it is worth noting than in one of them it was due to another cause, not just diarrea and the other one needed intravenous fluid. The average of duration of sympthoms was 3 days.
The 29 patients came from abroad.

Conclusions:

Gastroenteritis caused by sapovirus is frequent in infants perhaps due to stool testr are made more frequently in this gruop of age. We must pay attention to thi virus as a possible emerging pathegen since rotavirus vaccination, is making usually in our countries. It seems the clinical course of the illness does not differ so much from another virical gastroenteritis being a self-limitted desease in almost all cases just with oral rehydratation.

Systematic Review Registration:

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ESPID19-0892
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

A case of pediatric strongyloides stercoralis and salmonella enteritidis mixed infection in a non-endemic country

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[3]Children's City Clinical Hospital № 6, Deputy chief doctor, Dnipro, Ukraine

Background

Pediatric co-infections are emerging clinical problem due to their ascending prevalence and tendency to amend typical clinical presentation of particular diseases, which tangles the accurate estimation of etiology, complicates the management process and negatively impacts the outcome. Given the climatic changes, significant migratory flows and international tourism, tropical helminthiases, previously not common in Ukraine, are a real threat to the public health, especially in combination with other pathogens.

Case Presentation Summary

We observed a case of strongyloidiasis and salmonellosis in a 5 month old female infant who had had no history of visiting any sub-or tropical territory of the globe. The girl came from a socially unprotected layer of society and was abandoned by her homeless parents immediately after admission. The girl presented with severe toxic manifestations, diarrhea, developmental delay, moderate-to-severe malnutrition and dehydration, and maculopapular rash on the trunk and lower extremities. Direct light microscopy of feces revealed Str. stercoralis in the number of more than 10 mobile larvae per high-power field, at different stages of evolution. Bronchial lavage fluid contained no larvae of Str. stercoralis. Fecal culture revealed group D S. enteritidis. Chemotherapy with ceftriaxone IV and oral albendazole resulted into elimination of both pathogens.

Learning Points/Discussion

The given case of S. enteritidis and Str. stercoralis co-infection and C relative should be considered as a "probable case" of autochthonous Str. stercoralis infection, as it was not confirmed by more reliable diagnostic methods (e. g. PCR for Str. stercoralis DNA) and due to questionable epidemiological history. To improve the diagnosis of endemic parasitic infections in Ukraine, it is necessary to introduce such a verification as compulsory, and mandatory registration of relevant cases in the national system of epidemiological surveillance and biosecurity is required.

ESPID19-0886
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Acute appendicitis with pneumococcal bacteremia in a child patient

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Background

Streptococcus pneumoniae colonizes the mucosal surfaces of the human upper respiratory tract. It's known as a major bacterial cause of community-acquired pneumonia, sepsis, and meningitis. Pneumococcal intraabdominal infection is uncommon. We report the case of an 11-year-old boy with acute appendicitis associated with pneumococcus bacteremia.

Case Presentation Summary

An 11-year-old boy presented with a 2-day history of abdominal pain. On admission, he was afebrile and clinical examination was positive for abdominal right lower quadrant tenderness. CT showed a little ascites at right paracolic gutter. On the next day, the temperature was 39.2℃and abdominal tenderness became worse. Ultrasonography demonstrated a dilated, non-compressible appendix measuring 6.4mm in diameter, surrounded by thickening and hyperechoic inflamed fat. Blood examination revealed WBC count of 10570/μL with 82.5% neutrophils, CRP level of 1.3mg/dL. After blood cultures were obtained, Cefmetazole was started. Penicillin-susceptible *S.pneumoniae* was detected in a blood culture. Cefmetazole was changed to sulbactam/ampicillin and continued for 10 days. Ultrasonography showed appendix diameter less than 5mm after treatment. The patient improved without any complication.

Learning Points/Discussion

Pneumococcal intra-abdominal infections are rare and the mechanism is unclear. S. pneumoniae is not a common cause of appendicitis. However, there are some reports of Pneumococcal appendicitis. Pneumococcus were isolated from the peritoneal swab, pus, or appendix in their cases, and there were very few cases where pneumococcus is isolated in blood cultures. Indeed, blood cultures are not routinely obtained when acute appendicitis is suspected. Appendix cultures are also not routinely performed when undergoing an appendectomy. Therefore the number of pneumococcal appendicitis or pneumococcal bacteremia cases mimicking appendicitis might be underestimated.

ESPID19-0857
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Relapsing hepatitis in children: an atypical presentation of hepatitis a virus (hav) infection in children

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Background

There are different clinical presentations of HAV infection in children from asymptomatic to fulminant hepatitis but we faced here the case of a relapsing HAV infection. After remission, lasting between 1 and 3 months, a relapse of the infection is characterized by a reappearance of clinical, biochemical and viral markers of the disease.

Case Presentation Summary

A 14 years-old girl was admitted for an acute jaundice, associated with pale stools diarrhea, vomiting and high fever. Abdominal pain was present for the last 2 weeks, with anorexia, asthenia; she does not take any medications and she visited relatives in Morocco one month ago. Her previous medical history is marked by a congenital hepatosplenomegaly and G6PD deficiency. She was vaccinated according to the Belgian schedule (no HAV vaccination).

Clinical exam revealed mild dehydration, important jaundice, enlargement of spleen and liver and diffuse abdominal pain. Biology showed a cytolysis (ALT 2204UI/l, bilirubinemia 22mg/dl) and serology revealed HAV infection (IgM anti-HAV positive). Symptomatic treatment was given and she was discharged from the department one week later when cytolysis decreased moderately (ALT 264 UI/l, bilirubinemia 16mg/dl) and general status improved. She was closely followed and 4 weeks later she presented with diarrhoea and jaundice again. The diagnosis was a relapsing HAV infection with worsened cytolysis again (up to ALT 1330UI/µl and bilirubinemia 19mg/dl) that spontaneously slowly diminished.

Learning Points/Discussion

Hepatitis A infection in children is usually a benign and auto-limited disease but the clinical presentation of relapsing hepatitis can be tricky. Remember it can avoid unnecessary invasive procedures as liver biopsy, with close follow-up of the patient until recovery.

ESPID19-0759
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Community acquired clostridium difficile infection in children

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Background and Aims:

Currently, Clostridium difficile infection (CDI) is one of the main factors of nosocomial infections that cause colitis. But, it is now increasingly clear that a significantly high percentage of CDI cases are acquired from the community especially in younger patients without a history of antibiotic exposure. This study was conducted to survey of the extent of CDI among children hospitalized with community acquired diarrhea, to assess the prevalence of community acquired CDI, potential risk factors of CDI.

Methods:

The study was conducted among children (<18 years of age) with CDI who were admitted to Dongtan Sacred Heart Hospital, South Korea from September 1, 2015 to August 31, 2018. CDI cases were defined as patients with diarrhea and a positive PCR test (multiplex PCR, Seegene and Xpert C. difficile® PCR test). We performed a retrospective analysis of the clinical case records of children.

Results:

CDIs are founded in 52 cases of 3,742 child admitted with diarrhea(1.39%). All cases were community acquired. Antibacterial use preceded CDI in 50 patients (96 %). 11 cases had co-morbid viral infection. 8 cases had norovirus group II, 3 cases had rotavirus. 3 cases had severe CDI infection and they are less than 3 months old. 39 patients were treated with metronidazole and 13 patients were treated with vancomycin. We had no cases of recurrent infection.

Conclusions:

In CDI should be considered in the differential diagnosis in children with diarrhea. An omission of community-acquired cases could result in an underestimation of disease incidence and overestimation of disease severity in children with CDI. In children presenting with diarrhea, CDI should be considered in the differential diagnosis, even in outpatients with an absence of recent hospitalization and antibiotic exposure.

Systematic Review Registration:

N/A

ESPID19-0714
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Norovirus activity and genotypes in sporadic acute diarrhea in children during jan 2014-july 2018 in shanghai: multiple genotypes and recombinant polymerase/capsid genotypes co-circulated

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Background and Aims:

Based on the impact public health of norovirus and the current progress in norovirus vaccine development, it is necessary to continuously monitor the epidemiology of norovirus-associated diarrhea, especially in children who are more susceptible to norovirus. This study aim t**o monitor the activity and genotypes of norovirus infection in sporadic diarrhea in Shanghainese children during Jan 2014-July 2018.**

Methods:

Acute diarrheal cases were prospectively enrolled in the outpatient setting. Real-time RT-PCR was used for screening norovirus GI and GII genogroups. Dual norovirus genotypes were identified based on the partial capsid and polymerase gene sequences.

Results:

Of the 2757 diarrheal children, 430 (15.6%) were positive for norovirus with 10 (2.3%) being GI and 420 (97.7%) being GII.2. The increased activity of norovirus-associated diarrhea was usually observed from autumn to winter. Seven distinct capsid genotypes were identified, including GII.4-Sydney_2012 (51.03%), GII.3 (9.66%), GII.17 (5.75%), GII.2 (4.60%), GII.6 (0.69%), GII.8 (0.23%) and GI.3 (0.23%). Ten polymerase genotypes were identified, including GII.Pe (53.80%), GII.P17 (9.66%), GII.17 (7.59%), GII.P12 (7.13%), GII.P16 (3.68%), GII.P7 (0.69%), GI.Pd (0.46%), and GII.P8, GII.P4, GII.P2, and GI.Pb in each (0.23%). GII.17 strains were detected since September 2014. Recombinant GII.16/GII.2 strains were detected from December 2016 to September 2017.

Conclusions:

Norovirus is a major causative pathogen responsible for diarrhea in Shanghainese children. GII.Pe/GII.4-Sydney_2012 strains remained the predominant genotype circulating in Shanghainese children. The emergence of GII.17 and GII.16/GII.2 strains in sporadic diarrhea was almost in line with norovirus-associated outbreaks attributable to these two novel variants in China. Continuous monitoring norovirus genotypes circulating in pediatric population is needed for current vaccine development and future vaccine intervention.

Systematic Review Registration:

N

ESPID19-0485
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Impact of the national rotavirus immunisation programme on hospitalisation of children with all-cause and rotaviral gastroenteritis

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Background and Aims:

Universal rotavirus vaccination program was implemented in Estonia in 01.07.2014 and the vaccine coverage rate increased from 65.6% in 2015 to 88.7% in 2017. The aim of the study was to determine the change of all-cause gastroenteritis (AGE) and rotaviral gastroenteritis (RGE) hospitalisation 3 years before and 3 years after the introduction of rotavirus vaccination into the Estonian national immunisation programme (NIP).

Methods:

A retrospective review of hospital records of children aged <19 years admitted with AGE (ICD-10 A0-A9) and RGE (ICD-10 A08.0) to the Tartu University Hospital from 2011-2013 (pre-NIP) and 2015-2017 (post-NIP) was conducted. The reported cases of RGE were confirmed with commercially available immunochromatographic tests. The coverage area of the hospital has a population of about 400,000 people of which about 70,000 are children of <18 years.

Results:

There was 26% and 57% reduction in AGE and RGE cases respectively in post-NIP compared with pre-NIP period (Figure 1). The proportion of RGE cases of AGE cases declined from 32% (343 of 1064 cases) in pre-NIP period to 19% (147 of 792 cases) in post-NIP period (OR=2.1, 95% CI: 1.7-2.6, p<0.0001), while RGE cases in children <1 year old were reduced from 18.4% pre-NIP to 7.5% post-NIP (OR 2.8, 95%CI: 1.4-5.4, p=0.002). Median age of RGE hospitalisations increased from 1.7 years to 2.9 years (p<0.0001). There were 12 cases of RGE hospitalisations in immunised children in post-NIP period. No deaths were reported.

Conclusions:

Rotavirus vaccination in the Estonian NIP has resulted in a significant reduction in hospital admissions due to AGE and RGE in the 3 years following vaccine introduction. This reduction was more pronounced in the target age group.

Systematic Review Registration:

N/A

ESPID19-0477
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Why we still don't vaccinate our children against rotavirus infection

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Background

The Aim of this article is to investigate the presentation and characteristics of Rotavirus infection and need for vaccination

Methods

We used the hospital records of 46 hospitalized patients at the Department of Intestinal Infections at the Clinic of Infectious Disease and Febrile Conditions in Skopje, Republic of Macedonia in 2018, from the first of November to 31. of December. The exclusion criteria were age over 14 and confirmed other enteral pathogen. The main inclusion criteria was confirmed Rota virus in stool.

Results

The median age of the patients was 4.00 with Interquartile Range of 4.00 years (mean ± standard deviation 4.27±6.99). 43.5% of the patients had epidemiological information of the possible origin of the infection, whereas 60.9% were male. The patients were on average 5.87±2.39 days hospitalized at the Department of Intestinal Infections. 13% had complications from the infection, whereas 39.1% were treated with antibiotics. There was significant drop in Hemoglobin, Erythrocytes count, Leukocytes count, Hematocrit and Neutrophils while increase in Lymphocytes between admission and discharge of the patients. There was a significant correlation between the duration of hospitalization and intrahospital complications, number of days with fever and hospital threatment with antibiotics.. Positive epidemiological survey was associated with living in the city of Skopje, lower Sodium level and erythrocytes count at admission, higher level of CRP at discharge and higher decrease in Base excess.

Conclusions

Rotavirus infection is significant health problem in our country, with many cases that need hospital treatment. Immunization is the only effective preventive measure against this disease and we must break down the barriers among the population for acceptance and implementation of vaccination.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0476
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Protein – losing enteropathy in the course of intestinal viral infections of children

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Background

Protein – losing enteropathy (PLE) is a rare complication of various disorders characterized by excessive loss of proteins from the gastrointestinal tract due to impaired integrity of mucous membrane. One of the most common causes of PLE in children are intestinal infections, including viral infections, which cause degenerative changes and gastrointestinal epithelial necrosis.

Case Presentation Summary

Paper presents cases of three boys (3 years old boy with rotavirus infection and 9 and 2.5 months old boys with adenoviral infection) with protein – losing enteropathy in the course of intestinal infection with severe course, electrolyte disturbances and metabolic acidosis (high concentration of alpha-1 antitrypsin in faeces). Clinical picture was dominated by features of dehydration, edema and exudates to the body cavities. In laboratory tests, low levels of immunoglobulin G were observed, in addition to hypoproteinemia and hypoalbuminemia. In addition, in 9 months old child a significantly reduced percentage of CD4 and CD8 T cell subpopulations was observed and which was also observed, but to a lesser extent, in a 2.5-month-old boy. All children were treated with parenteral nutrition and steroid therapy for 7 to 10 days, improving the general condition and laboratory parameters, and in the following weeks a gradual improvement of the immune system parameters was observed. Children are under the care of a gastroenterological clinic.

Learning Points/Discussion

Protein – losing enteropathy (PLE) is a complication of acute viral diarrhea in infants that may lead to secondary, severe disorders of the immune system requiring intensive treatment.

ESPID19-0450
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Clostridium difficile infection in children; epidemiology and trend in a swedish tertiary care hospital

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Background and Aims:

Several studies have shown an increasing trend in pediatric CDI (Clostridium *difficile* infection) and presumptive risk factors for infection. However, the Public Health Agency in Sweden reports a decreasing incidence of CDI in the Swedish population since 2007. The main aim of this study is to analyse the trend of CDI in children.

Methods:

Retrospective study of patients 1- <19 years, positive for Clostridium *difficile* toxin B, tested at Karolinska University Hospital Units, over the time period July 1, 2010- June 30, 2018. Potential risk factors, comorbidities, treatment for CDI and the number of episodes of CDI was collected through chart-review. Episodes were classified as recurrences (>2 weeks, < 8 weeks from previous episode) or new episodes (>8 weeks from previous episode). New episodes were classified as hospital- (HA-CDI) or community-associated (CA-CDI). Annual infection rates/ 100 000 children in the catchment area was calculated.

Results:

328 tests in 206 patients were included of which 259 (79%) tests were defined as new episodes and 69 (21%) as recurrences. Many children (31%) experienced more than one episode of CDI. The mean infection rate was 8,5/100 000 children. There was an increasing trend in CDI-rate July 2014- June 2017 but no significant variability (p=0,061) over the study period. Factors associated with CDI were recent exposure to antibiotics and PPIs. Underlying medical conditions were present in 87% of the new episodes of which the most common was malignancy. Of the new episodes, 73% were HA-CDI and 18% were CA-CDI.

Conclusions:

There was an increasing trend in CDI in children in Sweden from 2014-2017, although not significant. Repeated episodes were common. CDI was associated with comorbid conditions and medications commonly prescribed to children.

Systematic Review Registration:

N/A

ESPID19-0364
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Clostridium difficile infection as a causing factor of severe cholestasis and haemolytic crisis in the patient with hereditary spherocytosis

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Background

Clostridium difficile (CD) is the most common pathogen causing nosocomial diarrhoea. The clinical presentation ranges from mild diarrhoea to severe complications, including pseudomembranous colitis, toxic megacolon, sepsis and/or multi-organ failure.

Case Presentation Summary

Case report. We present a case of 10-year old boy diagnosed with congenital spherocytosis at the 1st year of life, who was admitted to the Gastroenterology Unit of the Medical University of Silesia in Katowice due to severe jaundice. The boy was in good general condition, weakened on the day of admission. The physical examination revealed intense yellowing of the skin and eyes, severe itching and hepatosplenomegaly. The laboratory tests demonstrated very high concentration of bilirubin (total bilirubin 1040umol/l) with a predominance of the direct fraction (751.0 umol/L), increased activity of aminotransferases (ALT-272.0 U/L, AST- 119.0 U/L) and increased activity of gamma-glutamyltranspeptidase (GGTP-174.0 U/L). We didn`t observe anemisation or coagulation abnormalities. We found Clostridium difficile antigens and toxins in the bacteriological stool culture (in medical history, the boy had diarrhoea 3 days before hospitalization).

Ultrasound examination demonstrated hepatosplenomegaly and enlarged gall bladder with gall stones. Metronidazole, ursodeoxycholic acid and parenteral rehydration were used in treatment. We observed improvement of the general condition, normalization of the stools and decreased laboratory results. The patient was qualified to splenectomy and cholecystectomy.

Learning Points/Discussion

Summary. We would like to present the patient with hereditary spherocytosis, in whom the Clostridium difficile infection was a factor inducing severe cholestasis.

ESPID19-0281
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Differential diagnosis of secondary mesenteric adenitis: a case report

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Background

Secondary mesenteric adenitis is defined as lymphadenopathy associated with a detectable inflammatory process. Different causes have been described, infections are the most common.

Case Presentation Summary

An 11-year-old Latin-American boy presented at our hospital with abdominal pain and fever that had lasted 22 days. He had a medical history of drepanocytic trait and recurrent oropharyngeal aphthas from the age of 4. He was otherwise healthy.

Laboratory findings showed hemoglobin 11.6 g/dL, leukocytes 10600/uL (neutrophils 61.8 %, lymphocytes 23.8 %), PCR 7.46 mg/dL, LDH 533 U/L, VSG 56 m/h and prothrombin time 55%. Abdominal ultrasound and CT scan revealed multiple pathological mesenteric adenitis in right lower quadrant with major diameter 4 cm and no hepatosplenomegaly, so different causes were studied. Chest X-Ray was normal. Mantoux was negative. Serological studies which included HIV, CMV, EBV, *Rickettsia*, *Bartonella henselae* and *Coxiella burnetii* were all negative except for *Mycoplasma pneumoniae*, which was positive. Blood, urine and stool cultures were negative.

Initially, different empiric intravenous antibiotics were started (amoxicillin-clavulanic, cefotaxima and metronidazol, meropenem) with no improvement of clinical symptoms. After 15 days of hospitalization, he presented recurrent thrombophlebitis in two different veins (basilic vein and peripheral vein in upper limbs), new oral aphthas and inguinal adenopathy. Autoimmune tests only showed positive antiphospholipid antibodies, however these results were not confirmed after 12 weeks. Excision biopsy of inguinal lymph node was performed and results revealed necrotizing lymphadenitis consistent with Kikuchi disease. Steroid therapy was started with a very good initial response.**Learning Points/Discussion**

This case illustrates that differential diagnosis of secondary mesenteric adenitis could be challenging. It is fundamental to remember that autoimmune diseases could mimic infections, and in that way establish a correct diagnosis and early treatment.

ESPID19-0156
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Rhabdomyolysis in a child with norovirus gastroenteritis

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Background

A child with a background of global developmental delay, microcephaly, arthrogryposis and chronic lung disease was admitted with severe gastroenteritis and shock. The child developed AKI with rhadmomyolysis which was managed with fluid resuscitation. Stool PCR was positive for Norovirus.

Case Presentation Summary

A six year old child was admitted with a two day history of diarrhoea, vomiting and fever. She had severe dehydration with metabolic acidosis. She was managed in ICU with fluid resuscitation, high flow nasal cannula oxygen and IV antibiotics.

Investigations revealed Acute Kidney Injury (AKI) with a peak serum creatinine of 147 umol/L and creatinine kinase(CK) rose to a maximum of 166,000 iU/L suggesting rhabdomyolysis. There was evidence of transaminitis with a maximum ALT of 1053 iU/L. She also received broad spectrum IV antibiotics. CK and AKI resolved with appropriate fluid management. The only significant investigation was a positive stool PCR which confirmed Norovirus Genotype GII Genotype 4; Prototype strain was Sydney 2012 variant. Blood culture, sputum virology and culture were negative.

Learning Points/Discussion

In children, the most significant cause of rhabdomyolysis is viral infection. However, there is paucity of data on norovirus induced rhabdomyolysis. There is a published case report which describes such association with Norovirus Genotype II.

Our patient recovered without any renal failure and the transaminitis resolved as well.

Rhabdomyolysis has a broad etiology and there is a need for early detection and treatment. Management is supportive with intravenous fluids and treating any underlying infection.

Conclusion:
In children with gastroenteritis, rhabdomyolysis should be considered if there is any evidence of muscle weakness or clonus.

Urine analysis and serum CK are helpful tests in diagnosis.

Early detection and management helps to reduce morbidity and mortality.

ESPID19-0014
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Histologic parameters of h. Pylori-associated gastritis in extrahepatic portal vein obstruction

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Background

Basic histopathological finding in gastric mucosa is chronic gastritis patients with *Helicobacter pylori*-infection is known. Pattern of gastric mucosal lesion in children with *H. pylori*-infection and extrahepatic portal venous obstruction (EHPVO) is not known. We aimed to assess pattern of gastric mucosal lesion with *H. pylori*-infection and EHPVO, and to determine whether EHPVO contributed to the severity of gastritis.

Methods

We enrolled 158 patients, consisted of 30 with *H. pylori*-positive EHPVO (Group A: 18 male; 12 female; mean age, 10.38+0.64 years), and 40 with *H. pylori*-negative EHPVO (Group B: 27 male; 13 female; mean age, 11.43+0.66 years) and 88 *H. pylori*-positive without EHPVO (Group C: 49 male; 39 female; mean age, 8.89+0.39 years), who made up the control groups. In all esophagoduodenoscopy was performed, and gastric biopsies were taken. The gastric damage was classified according to the modified Sydney System.

Results

H. pylori were not found in gastric mucosa without histological changes. The prevalence of chronic superficial gastritis (13.33% versus 35%, p= 0.04) was significantly low in group A than group B. The prevalence of follicular gastritis and lymphocytic gastritis was similar in all the three groups. There was a significant increase in grade of inflammation, activity and *H. pylori* density on histologic examination in group A than group B and group C. The number of intraepithelial lymphocytes, degree of atrophy, intestinal metaplasia, microvessel congestion and edema was similar in all the three groups.

Conclusions

The gastric histological pattern appears to be independent of EHPVO. *H. pylori*-infection in children with EHPVO may identify cases of severe gastritis and marked bacterial colonization. The role of *H. pylori*-infection in the pathogenesis of congestive gastropathy seems to be unlikely.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0013
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Endoscopic nodular gastritis with h. Pylori infection: an indicator of highgrade bacterial colonization and severe gastritis in children

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Background

Endoscopic findings of antral nodularity can be seen in children much more frequently than in adults and believed that this gross change may suggest *H. pylori* infection and histologic gastritis. Aim was to assess significance of *Helicobacter pylori* infection associated with endoscopic nodular gastritis (NG).

Methods

This prospective study carried out over two years period and included 468 children in whom upper digestive endoscopy was performed for gastrointestinal symptoms and gastric antral mucosal biopsy was taken. Sixty seven children were diagnosed as having NG and were included in the study. Demographics, clinical characteristics, endoscopic and pathologic findings were recorded. *H pylori* were recognized in gastric biopsy on H&E sections; a modified Giemsa stain was performed in biopsy suspicious for *H pylori*.

Results

The prevalence of NG in children was 14.3% (67/468) and consisted of 46.3% male and 53.7% female. Children age ranged from 3 - 18 years (mean age, 9.2 ± 0.4 years). The prevalence of NG increased gradually with age. *H pylori* infection was identified in 68/468 (14.5%) children. Nodular gastritis had a poor accuracy rate to determine *H. pylori* infection (sensitivity, 40.3%; positive predictive value, 39.7%) and was observed in 27/68 (39.7%) *H pylori* positive patients and in 40/400 (10%) *H pylori* negative patients. There was a significant increase in grade of inflammation, activity, atrophy, number of lymphoid follicles and *H pylori* density on histologic evaluation in *H pylori* positive patients with NG than other groups.

Conclusions

Nodular gastritis has a poor prediction for H pylori infection in children. Gastric biopsies should always be obtained during endoscopy in children to establish the H pylori infection. *H. pylori* infection in children with NG identifies cases with severe gastritis and marked bacterial colonization.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0007
E-Poster Viewing - May 7-10 - E-Poster Hours

Gastrointestinal infections

Molecular epidemiology of the genus entamoeba (amibiasis) in children

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Background and Aims:

The organisms that are grouped in the genus *Entamoeba* are unicellular eukaryotes, life cycles, consists of an infecting stage, called a cyst and a multiplicative stage known as the trophozoite. The transmission of the infection occurs via the ingestion of cysts. The human can be the host of 6 species, only one is the cause of clinical pathology of amoebiasis in humans, *Entamoeba histolytica*. Two species have identical morphology to the pathogen, the nonpathogenic species are *E. dispar* and *E. moshkovskii*.

Methods:

Children under 15 years-old were studied with coproparasitoscopic techniques by flotation and sedimentation, and faecal stains of Kinyoun and Ziehl-Neelsen modified. From positive samples DNA were extracted by means of the QIAamp DNA Stool Mini kit from QIAGEN and the identification of the *Entamoeba* was performed by the PCR technique.

Results:

351 were studied with coproparasitoscopic techniques. From the total of studies, 117 (33%) children parasitized with *Entamoeba* were found by microscopy. DNA from 117 samples were extracted. The analysis of the molecular data revealed that 40.2% (n = 47) of the samples were positive for *E. histolytica*, 5.1% (n = 6) were positive for E. *dispar* and 54.7% (n = 64) were co-infections of *E. histolytica* and *E. dispar*. With respect, to the identification of *E. moshkovskii* no sample were positive.

Conclusions:

The results showed that the pathogenic *E. histolytica* is the prevalent species, unlike what is known in most publications, which implies that these children are more likely to suffer from the disease and its complications.

Systematic Review Registration:

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ESPID19-1090
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Changes in biochemical and immunological profile of greek hiv-infected children receiving lopinavir/ritonavir-containing art during a 6-year period

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Background

The most used protease-inhibitor in children is Lopinavir/ritonavir (LPV/r) which provides sustain suppression of viral load. However, serious side effects such as lipid abnormalities have been well recognized. Our aim was to evaluate changes in biochemical and immunological profile in Greek HIV-infected children treated with LPV/r-containing ART.

Methods

A cohort study of 12 Greek HIV-infected children receiving LPV/r-containing ART at Department of Infectious Diseases in “Aghia Sophia Children’s Hospital” in Athens, Greece was performed. Medical records were reviewed for a 6-year period after treatment initiation.

Results

The study population consisted of 5 boys and 7 girls perinatally infected with HIV. ART included zidovudine, lamivudine and LPV/r and was well tolerated from all children. The median baseline levels of cholesterol were 2.55 mmol/L, increased during the first 3 years after treatment initiation and remained high during the rest follow-up period. In details, the median levels were significantly higher during the last 3 years than those of the first 3 years (*P*-value 0.036). Regarding the immunological profile, the median baseline plasma HIV RNA concentrations were 1.12 $x10^5$ copies/mL and the median baseline $CD4^+$ lymphocyte count was 2160 cells/mm^3. The median $CD4^+$ lymphocyte count increased during the first 3 years after treatment initiation. However, the $CD4^+$ lymphocyte count were significantly lower during the last 3 years of study period despite the undetectable viral load during the same period (*P*-values 0.011 and 0.018 respectively).

Conclusions

LPV/r-containing ART seems to be safe and well-tolerated from patients of our Department. However, prospective studies as well as close monitoring are necessary in order to evaluate the significant reduction in median $CD4^+$ lymphocyte count and the increase in cholesterol levels that were detected.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0720
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Bcg vaccination in hiv-positive children

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Background and Aims:

According to the Ukrainian national vaccination schedule the live attenuated bacilli Calmette -Guerin (BCG) vaccine is to be done on 3rd day after birth(1,2). The WHO did not recommend BCG for HIV-positive children since 2007 till 2018(3). Although, HIV positive children have happened to get BCG vaccination. Aims of this retrospective study was to find out the frequency of BCG vaccination and the reasons why BCG was given to HIV- positive children, to compare TB frequency, severity of process, mortality in BCG vaccinated and non-vaccinated group of HIV- positive children.

Methods:

The medical records of 67 HIV-positive patients 0-18 years old who first came to the Center «Clinic for treatment children with HIV/AIDS» since June 2016 till June 2017 were revised. There were collected the following data: demographical, BCG vaccination status, level of CD4 cells before ART prescribing and TB status with localization and information about TB contact.

Results:

In this cohort n=27(40%) patients received BCG(group 1), n= 30(45%) were not BCG vaccinated (group 2) and the BCG status was unknown in n= 10 (15%). in 59% cases BCG was done after 2007 year and in 77% on the 3 day after birth. In 2 cases vaccine was not done because of it absence in the maternity hospital. The incidence of TB cases in group 1 and 2 were identified as 38% and 36%. Mortality level was the same in both group - 3%.

Conclusions:

- BCG vaccination frequency in the HIV-positive children is quite high- 40%, that is indirect evidence of late diagnostic of HIV in children.
- There were no significant differences in TB frequency and negative outcomes in BCG vaccinated and non-vaccinated groups.

Systematic Review Registration:

N/a

ESPID19-1181
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Second generation hiv exposed by vertical transmission: a case control study

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Background and Aims:

Second generation HIV exposed by vertical transmission: a case control study

Dra Denise Lopes Santos

Prof Dr Daisy Maria Machado

Dra Suenia Vasconcelos Beltrão

Dra Aída de Fátima Barbosa Gouvêa

Dra Fabiana Bononi do Carmo

Professor Regina Célia de Menezes Succi, succi@picture.com.br - Escola Paulista de Medicina / Universidade Federal de São Paulo

Introduction: The number of pregnancies among young people HIV infected HIV is increasing. Our goal was describe the development of young children born from mothers HIV infected (vertical or horizontal transmission).

Methods:

Observational epidemiological study of a retrospective cohort nested case-control type. Follow - up of 32 infants born from mothers vertical HIV infected women (TV) and 74 born from mothers horizontal HIV infected women (controls- TH) were evaluated, the gestations were matched by controls 6 months (forward or behind) . Anthropometric development, and immunization were evaluated. Approved by Institutional Ethics Committee.

Results:

TV:birth w. 2922/ -0.85, h. 46.50/-1.58, BMI 13.43/-0.03; 6 m w. 7515/0.13, h. 65.52(z -0.48),BMI17.43/0.19;12 m w. 9693/0.28, h.74.22/-0.35, BMI 17.60/ 0.64; TH birth w. 2938/-0.83,h. 43.51/-1.30,BMI 13.39/-0.05;6 m w 7784/0.13,height 65.57/-0.50, BMI 18.06/0.56; 12 m w. 9877/0.61, h. 74.61/ -0.15, BMI 18.11/0.96. Loss vaccines, TV 1/32 BCG, 12/32hep B, 6/32 penta, 6/32 polio, 8/31 Rota, 8/31 Pneumo, 4/31 Meningo, 8/32 SCR, 12/28 Varicella, 14/28 hep.A; TH 1/74 BCG, 1/74 hep.B,1/74 penta, 3/74 polio,4/71 Rota,9/71 Pneumo, 1/71Meningo,12/74 SCR, 16/68 Chickenpox, 15/65 hep. A. Pre term TV 2/32 ,TH 9/74

Conclusions:

Conclusions: We found greater vaccine delay among children born from TV compared to those born from TH . Growth was similar in both groups.

Systematic Review Registration:

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ESPID19-1042
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Cachexia due food allergy as a cause of false-positive hiv serology

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Background

The symptoms of HIV infection in children are very diverse and may affect various organs. According to WHO Clinical Staging “Stage 3” include unexplained persistent diarrhea and “Stage 4” unexplained severe wasting.

Case Presentation Summary

Male born at 40 weeks gestation, birth weight was 3470 grams. In neonatal period he was breastfed and he gain weight correctly. In the second month of life parents started to bottle-fed him with formula milk. Thereafter he began to lose weight and he suffered from watery diarrhea (without blood) for 1 month. At the age of 2 months he was admitted to hospital because of cachexia, his body mass was 3450 grams. Laboratory investigations revealed: high IgG and IgE titer, leucocytosis, thrombocythemia, decreased prothrombin activity, positive faecal occult blood test. Diagnostics for HIV infection was conducted, because the child's symptoms could indicate a HIV infection. Despite mother of the patient had a negative HIV screening test result, fourth-generation HIV Ag/Ab test in our patient was positive in two consecutive blood samples. HIV Western Blot in another blood sample was also positive. CD4+ T cells count was in normal range and HIV viral load was negative - HIV infection was excluded. Severe food allergy was recognized. Nutrition with an amino acid-based infant formula was introduced and patient gradually improved. In this case, the positive HIV serology turned negative two weeks after changing diet.

To our knowledge, this is the first case of false-positive HIV serology that is associated with food allergy.

Learning Points/Discussion

Cachexia due to severe food allergy can be a cause of false-positive HIV serology – both ELISA and Western-Blot.

ESPID19-1036
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Hiv-infected infant born by a mother with negative anti-hiv testing during pregnancy - a case report

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Background

Mother-to-child transmission (MTCT) of HIV is the most common source of HIV infection in children. In Poland, all pregnant women should be screened towards HIV infection twice, in the first and the third trimester. In this case report we aimed to present an HIV-infected infant born by a woman with negative results of HIV-testing during pregnancy.

Case Presentation Summary

A male neonate was delivered at 39-week of gestation by natural labour with a birth weight 3365 g. He received 10 points in Apgar-score. His mother was tested towards HIV infection twice during pregnancy, in 1st trimester and at 36. week of gestation. Both results were negative. Short before delivery, the woman underwent a mononucleosis-like illness. At the age of 2 months, the infant was hospitalized due to gastroenteritis accompanied by dehydration, metabolic acidosis, and severe anaemia, requiring blood transfusion. At the age of 3 months, he was hospitalized with pneumonia, persistent anaemia, hepatitis, and maculopapular rash. Due to increasing cardiorespiratory failure, the infant required hospitalization in ICU. HIV-testing was performed as the child was 4 months old and it was positive. HIV viral load was >10.000.000 copies/mL. AIDS was diagnosed. Combined antiretroviral treatment (cART) was administered (ABC, 3TC, LPV/r regimen). The patient improved clinically after starting cART. His cardiorespiratory functions stabilized. After 8. months of therapy HIV viral load was 10.428 copies/mL. Patients physical and neurological development was normal**.** HIV infection was confirmed in the mother and her sexual partner.

Learning Points/Discussion

Woman acquired HIV in late pregnancy (mononucleosis-like illness). The second test towards HIV was wrought in window period. Thus, HIV infection should be considered in all infants with remittent or severe infections.

ESPID19-0978
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Factors associated to late presentation of hiv newly diagnosed adolescents in spain

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Background and Aims:

Adolescents represent a growing share of new HIV diagnoses. Late presenters (LP) is a universal challenge that also affects adolescents. Nevertheless, data are scarce.

Methods:

Retrospective study of LP(<350 CD4/ul or AIDS-defining events at diagnosis) in HIV newly diagnosed adolescents(12-<20years-old) included in CoRIS and CoRISpe Spanish cohorts until end of 2017. CoRIS enrols HIV-naïve patients from adult units and CoRISpe from pediatric units. Demographic, clinical data and way of transmission were analysed.

Results:

From 357 HIV newly diagnosed adolescents, 123 (34.5%) were late presenters with a median CD4 rate of 235/ul at diagnosis. LP were mainly male (69.9%) and median age was 18.7 years, similar to general cohort. The main way of infection in LP was sexual (64.2%; 35.8% men who have sex with men (MSM) and 28.4% by heterosexual contact), 21.1% were injection drug users, 7.3% vertical transmission, 3.3% hemoderivates receivers. LP was significantly more frequent for heterosexual transmission (41.7%) than for MSM (23%), p=0.0023. Regarding the origin, 30.4% of MSM born outside Spain were LP vs 18.4% of Spanish MSM (p=0.07). Foreign women with heterosexual transmission was a vulnerable group with 50% of LP vs 18.4% in Spanish MSM(p=0.0006). Despite mainly behaviourally transmission and younger age, LP rate for middle adolescents (15-17.9 years-old) was as high as for late adolescence (18-19.9 years-old): 34.6% vs 32%; p= 0.684. LP among adolescents decreased over time but not in the last 15 years: 34.3% in 2003-2007 vs 28.8% in 2013-2017 (p=0.504).

Conclusions:

More than one third of HIV newly diagnosed adolescents were late presenters, with no decline in the past 15 years. Adolescents with heterosexual transmission, foreign MSM and heterosexual foreign women presented higher LP rates. Specific approaches are needed to tackle this situation.

Systematic Review Registration:

ESPID19-0942
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Kawasaki disease like syndrome in a hiv infected adolescent

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Background

Kawasaki disease (KD) is a medium vessel vasculitis that predominantly, but not exclusively, affects children below 5 years. It is unusual to see KD in adolescents and adults. 'KD like syndrome' however, can occur in adults with human immunodeficiency virus (HIV) infection.

Case Presentation Summary

A 13 year old boy was diagnosed to be HIV seropositive and initiated on anti-retroviral therapy (zidovudine, lamivudine and nevirapine).He remained clinically well for next 3 years.He presented at 16 years of age with fever and cough for 1 month.He was diagnosed to have disseminated tuberculosis and initiated on isoniazid, rifampicin, pyrazinamide and ethambutol.He became afebrile in next 3 days.However, 7 days later he had recurrence of fever associated with erythematous non-itchy rash, jaundice and lethargy.On examination,he had maculopapular erythematous rash all over the body,icterus and lip cracking.Laboratory investigations showed anemia,neutrophilic leukocytosis, thrombocytosis,raised inflammatory markers(erythrocyte sedimentation rate [ESR] and C-reactive protein, transaminitis and hyperbilirubinemia.Work-up for all other infectious causes was normal. The clinical possibilities included anti-tubercular therapy (ATT)induced hepatitis and drug rash.He was given modified ATT (levofloxacin, streptomycin and ethambutol).On day 30 of hospital stay(i.e. on day 10 of re-appearance of fever), he developed periungual peeling of skin from fingers and toes.A clinical possibility of incomplete KD was considered. Serum pro-brain natriuretic peptide (pro-BNP) level was elevated (365 pg/ml; N: <125pg/ml). 2-Dimensional echocardiography revealed normal coronary arteries. He was given intravenous immunoglobulin infusion (2 gm/kg) and aspirin.He showed prompt clinical recovery.On follow up at 6 weeks, 2-Dimensional echocardiography revealed normal coronary arteries.Aspirin was stopped

at this time.

	At admission	Day 20	Day 30*	Day 40	At discharge
Hemoglobin(gm/l)	87	97	93	90	96
White blood cell counts ($\times 10^9$ cells/L)	5.6	11.1	5.5	10.8	7.5
Differential counts	$N_{56}L_{33}M_{10}E_1$	$N_{67}L_{21}M_{10}E_1$	$N_{35}L_{37}M_{19}E_6$	$N_{46}L_{37}M_{14}E_1$	$N_{52}L_{31}M_{12}E_3$
Platelets ($\times 10^9$/L)	360	468	557	677	801
ESR (mm in 1st hour)	120	100	102	-	-
CRP (mg/L)	81	39	10	-	-
AST (IU/L) ALT (IU/L)	82 61	866 585	43 65	50 52	-
Bilirubin Total (mg/dl) Direct (mg/dl)	 0.32 0.19	 5.3 3.3	 1.65 0.78	 1.64 0.61	-

Abbreviations: ALT- Alanine aminotransferase; AST- Aspartate aminotransferase; ALP-Alkaline phosphatase; CRP- C-reactive protein; E- eosinophils; ESR- erythrocyte sedimentation rate; L- lymphocytes; M- monocytes; N- neutrophils.

*IVIg was given on day 30 of hospital stay

Learning Points/Discussion

'KD like syndrome' is uncommon in HIV infected children, adolescents and adults. It should be considered in the presence of prolonged fever when other common causes have been ruled out.

ESPID19-0918
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Hiv: a rare case of mother-to-child transmission of an hiv negative mother in the third trimester

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Background

The identification of all pregnant women, through the offer and recommendation of HIV testing, is an essential first step in the intervention pathway, reducing the rate of mother-to-child HIV transmission (MTCT) to less than 1%.

Case Presentation Summary

We present the case of a 2-month-old Caucasian female, previously healthy and asymptomatic. She was born at 39 weeks by spontaneous vaginal delivery from a 33-year-old mother who was reportedly in a monogamous relationship with the infant's father, her sexual partner. The mother received adequate prenatal care, had no known illnesses during the pregnancy and denied any risk behaviours. The pre-natal serologies, including HIV (Elisa fourth generation test), were negative. After birth, she was breastfeeding exclusively. When she was 2 months old, her father was diagnosed with HIV 1 infection, after presenting with oral candidiasis and weight loss. The mother and the infant were both tested positive for HIV 1 (confirmed by PCR DNA and RNA). Her HIV viral load at the time of diagnosis was greater than 10 600 000 (log 7) and the CD4% was 36.4%. She immediately started triple antiretroviral therapy with Lamivudine, Zidovudine, Lopinavir and co-trimoxazole (prophylaxis), obtaining undetectable viral load after 4 months.

Learning Points/Discussion

Pregnant women have an elevated risk of HIV acquisition in comparison to with non-pregnant women. This case report highlights that the screening for HIV infection during pregnancy may be not enough to prevent MTCT. Further studies are required in order to evaluate the efficacy of other HIV tests, the necessity of testing partners of pregnant women or repeating HIV testing during labour and delivery.

ESPID19-0917
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Hiv microvasculopathy of retina in children: a clinical oddity. Our experience at chandigarh, north india

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Background and Aims:

Retinal microvasculopathy associated with Human Immunodeficiency Virus (HIV) infection has been infrequently reported in children. These lesions are usually asymptomatic and resolve after initiation of anti-retroviral therapy (ART).

Methods:

A retrospective review of 1420 retroviral infected children with HIV infection registered in Pediatric Immunodeficiency Clinic was carried out and records of children with retinal involvement were reviewed. Of these, 4 children had findings consistent with HIV microvasculopathy of retina.

Results:

While 3 of the 4 affected children had bilateral retinal changes, 1 had unilateral lesion of left eye. Mean CD4+ T cell count was 644 cells/µl (355-1215 cells/ µl). While 2 children presented with decreased visual acuity, the other 2 were asymptomatic and the lesions were picked up on routine ophthalmological screening before initiation of ART. Serology for cytomegalovirus (CMV) and toxoplasma was negative in all 4 children. All 4 were treatment naïve prior to detection of retinal changes. After detection of these changes, ART (zidovudine, lamivudine and efavirenz) was initiated. At a mean follow-up of 1 year, all 4

patients showed improvement in visual acuity and retinal changes gradually regressed.

Case	Age of onset of sympto-ms of HIV infection	Sympto-ms at presentat-ion	Visual symptoms/first detection of retinal changes	Type of visual sympt-oms	Parental status for HIV infection	CD4 coun-ts at start of ART	CD4 coun-ts on follow-up	CMV and Toxopl-asma serolo-gy	Age of initiation of ART	Retinal changes on follow-up
1	7 years	Fever,co-ugh	+/7 years	Blurri-ng of vision	Negative	660	184	Negati ve	7 years	Recovered
2	2.5 years	Fever, diarrhea, rash	2.5 years	None	Positive	355	704	Negati ve	2.5years	Recovered
3	14 months	Diarrhoea, Otitis media	+/13 years	Decre-ased vision in left eye	Positive	1215	467	Negati ve	13 years	Recovered
4	1 ½ years	Diarrhoea	10 years	None	Positive	348	1008	Negati ve	10 years	Recovered

Conclusions:

HIV related microvasculopathy of retina is a distinctly unusual finding in children with HIV infection and needs to be differentiated from other common causes of retinitis like CMV and toxoplasma. This microvasculopathy can develop even in patients with preserved CD4 counts and resolves after initiation of ART.

Systematic Review Registration:

N/A

ESPID19-0888
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Multi-drug resistant human immunodeficiency virus infection in an 8 year old boy: a heroic struggle against multiple odds

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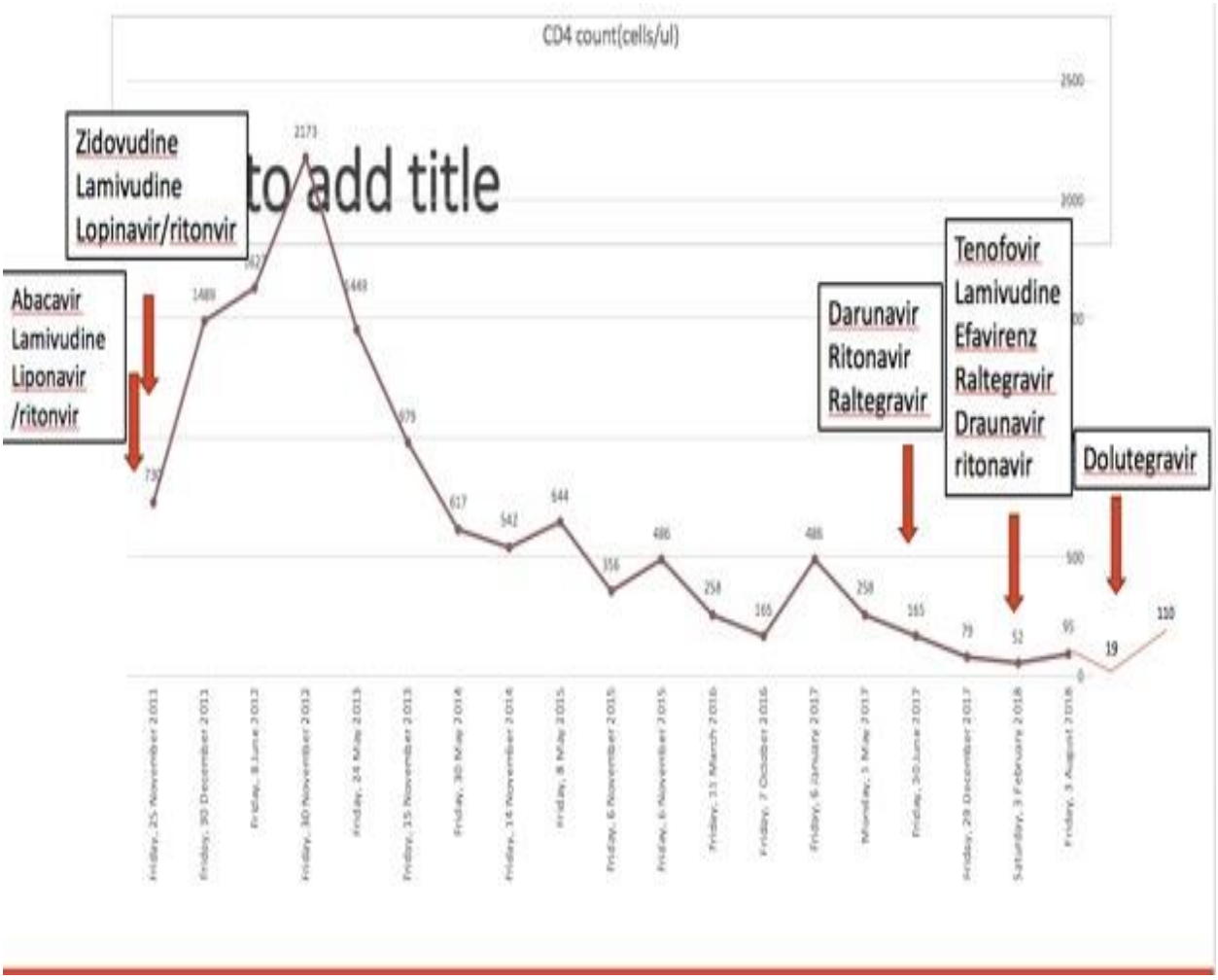
Background

ART has scaled up but there is an emergence of drug resistance.Knowing the drug resistance pattern becomes essential in a child developing clinical,immunological or virological failure.

Case Presentation Summary

A.was born to a mother with HIV and received zidovudine and was given cotrimoxazole prophylaxis.While DNA PCR at 8 weeks and whole blood PCR at 4 months of age were both positive,retroviral serology continued to be non-reactive.He was lost to follow-up for 8 months.At 1 year,he presented with fever,oral thrush,lymphadenopathy,hepatosplenomegaly.He was initiated on ART-abacavir,lamivudine,liponavir,ritonavir.As he developed rash following abacavir,this was replaced with zidovudine.He received zidovudine based regimen till 6 years of age when he presented with fever,lymphadenopathy and was diagnosed to have Hodgkin lymphoma(Stage III)and attained remission with chemotherapy.As he had low CD4 counts,high viral loads,ART was changed to darunavir,ritonavir,raltegravir.He persisted to have virological and immunological failure even after 6 months of therapy.During this time,he had recurrent episodes of febrile illness.Drug resistance analysis revealed resistance to both NRTIs and protease inhibitors and none with NNRTIs.Hence, third line ART(tenofovir,lamivudine,efavirenz,raltegravir,darunavir,ritonavir)was initiated.Six months later,his CD4 counts had risen from 52/ml to 95/ml,but there was no significant clinical improvement.At 7½ years,he developed high grade fever spikes,lymphadenopathy.Excision biopsy of the inguinal node showed a relapse of Hodgkin lymphoma.A repeat drug resistance analysis revealed sensitivity to maraviroc and dolutegravir,hence dolutegravir was added to the regimen along with tenofovir, lamivudine, darunavir and ritonavir.A week later,he developed high grade fever,cytopenias and bleeding.Clinical possibilities included worsening of HIV disease,opportunistic infections and secondary hemophagolymphohistiocytosis(HLH).Investigations confirmed HLH and he was treated with steroids.After 3 months of initiation of dolutegravir,his CD 4 started to improve and is presently

110/ml.



Learning Points/Discussion

Children with HIV infection may present multiple challenges.These include drug reactions,drug resistance and malignancy.

ESPID19-0756
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Art-therapy may improve attitude and compliance in hiv-positive adolescents, initial experience at the st. Camille hospital in ouagadougou, burkina faso

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Background

Since 2004 the University of Brescia, Italy has an ongoing paediatric-HIV collaboration with the Hospital of the Camillian Fathers in Ouagadougou, capital of Burkina Faso.

Case Presentation Summary

After an initial pilot-phase in 2014, from December 2016 to December 2018 biweekly sessions of 2 hours duration under the supervision of a trained art-therapist were scheduled for selected adolescents followed at the paediatric HIV-outpatient-clinic.
Among the 61 HIV+ teenagers, only 7 (age 14-17 years, 2 females) fulfilled the initial inclusion criteria: disclosure process initiated, living close to the hospital, French speaking, consent of caregiver.
During the initial three months the participants were invited to explore the artistic materials under the supervision and with the explanation of the therapist. Thereafter each decided for an individual technique and theme, based on personal preference.

Learning Points/Discussion

Over time trust in the art-therapist and themselves developed and self-confidence improved, allowing to express personal thoughts and feelings. A real need to communicate through unrestricted artistic expression emerged showing, fear of the future, frustration due to illness, cultural restraints and family bonds, but also the desire to be like the uninfected, and finally courage to change. Interestingly, with time compliance improved and overall a more positive attitude was noted by the medical team.
Financial and logistic constraints allowed for only half of the sessions to be held, threatening the whole project. However, the patients themselves were determined to continue the project and finally were able to achieve continuity.
We are trying now to find a stable financial and logistic basis which will allow to better integrate this approach with other educative measures and offer this therapy systematically to more children of different ages and verify the effect on compliance and coping.

ESPID19-0706
E-Poster Viewing - May 7-10 - E-Poster Hours

HIV - AIDS

Adverse treatment reaction in perinatal hiv exposed children in the western romania

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Background and Aims:

In our country, rate of HIV vertical transmission is 6 cases in 2017 and 3 cases between January-June 2018 according to data of the HIV/AIDS Monitoring and Evaluation Department in Romania, published by the Institute of Infectious Diseases “Prof. Dr. Matei Bals”, Bucharest. The aim is to discuss the adverse effect of prophylactic treatment in perinatal HIV exposed children

Methods:

Thirty-eight newborns from HIV-infected mothers, from the Western Romania, admitted in our Department between January 2017 and December were analyzed. Prophylactic treatment for HIV vertical transmission, with Zidovudine associated with Lamivudine was administered to all these newborns. A single dose of Nevirapine was added in eighteen patients. This study data is making reference to the first six weeks of life.

Results:

Ten mothers were detected HIV positive during pregnancy. One newborn was detected with viral load over 1 million copies/ml at birth, the rest presented undetectable values and after 6 weeks of treatment. Anemia was noticed in 34 from 38 patients as sole adverse effect. Folic acid supplementation was initiated with good response increasing hemoglobin values. Hemoglobin values ranging between 7.3 – 8.2 g/dL , was corrected by packed red blood cells. 14 patients required transfusion within 4-6 weeks from the treatment onset. One case was positive for HIV vertical transmission.

Conclusions:

89.47% from newborns in our Department had anemia, 36.8% required packed red blood cells, especially premature newborns with a LBW (in spite Zidovudine was administered at 8 hours).

Systematic Review Registration:

N/A

ESPID19-1061
E-Poster Viewing - May 7-10 - E-Poster Hours

Host-pathogen interaction

Kikuchi fujimoto's disease. Fever of unknown origin and lymphadenitis

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Background

Kikuchi Fujimoto's disease (KFD) or histiocytic lymphadenitis is especially rare in paediatrics. Although it is a self-limited and benign disease, its differential diagnose is vast including lymphoma, various infections and autoimmune diseases.

Case Presentation Summary

Previously healthy**,** 15 year-old male admitted with fever for 18 days, weight loss of 2.7kg and painful cervical, axillar and inguinal lymphadenopathies for the last four weeks. He lived in a rural area and had contact with rabbits. Etiologic investigation revealed leukopenia with neutropenia (0,84x10^9/L), thrombocytopenia (128x10^9/L), CRP 0,75mg/L, ESR 74mm/h, ferritin 958ng/mL and high lactic dehydrogenase (726U/L). The serum was positive for *Francisella tularensis* antibodies by agglutination test (titre of 40) and the *Brucella sp.* was negative. However, a real-time multitarget TaqMan PCR, using tul4 and ISFtu2 assays were negative. He was started on doxycycline and ciprofloxacin. Other infections and autoimmune diseases were excluded. Chest X-ray, echocardiogram and bone marrow aspiration revealed no alterations. Abdominal ultrasound showed a mildly enlarged liver. Lymph node excisional biopsy showed histiocytic lymphadenitis with paracortical expansion by foamy histiocytes, highlighted with CD68 immunohistochemistry, containing phagocyted cell debris, which is compatible with KFD on the xanthomatous phase (recovery phase). The patient had resolution of fever and lymph node enlargement and *F. tularensis* antibodies decreased after 3 weeks (titre of 2).

Learning Points/Discussion

KFD causes remain unknown, although it is considered to be the result of a self-limited autoimmune process triggered by an infectious agent. In some patients it is possible to find false-positive results against several agents. It is important to be aware of KFD in the presence of FUO and lymphadenopathies. Clinical features are not specific, therefore the histological findings after excisional lymph node biopsy are essential to have a definitive diagnosis.

ESPID19-1044
E-Poster Viewing - May 7-10 - E-Poster Hours

Host-pathogen interaction

Nmdar encephalitis. Infection-triggered autoimmunity

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Background and Aims:

Anti-NMDA receptor encephalitis is the most common autoimmune encephalitis. Self-antibodies against NMDA receptors in the brain can be created after trigger mechanisms such as infectious agents and tumours.

Methods:

A retrospective study between 2012 and 2018 was conducted. Demographic, clinical, complications data, treatment and outcome were analysed

Results:

We report 9 cases, six females and three males, with a median age of 14,5 years (min-15days, max-15years). Most common manifestations were behaviour changes (8/9), psychiatric disorders (7/9), movement disorders (7/9), insomnia (5/9) and seizures (4/9). NMDA antibody was positive in CSF (9) and in serum (5). An infectious agent was identified in four cases: HSV1 (1), HSV2 (1), *Mycoplasma pneumoniae* and HHV7 (1) and adenovirus (1). In one patient ovarian teratoma was identified and the other four cases were considered cryptogenic. All cryptogenic cases were female between 14-15 years old and infections were investigated only in two. MRI and CSF were normal in most patients (6), the abnormal MRIs had changes related to the infectious disease. Electroencephalography was abnormal in six patients, most of them showing slow activity. Treatment included immunoglobulin in all patients, intravenous methylprednisolone (6), rituximab (7) and plasmapheresis (3). Cyclophosphamide (2) was used in patients refractory to previous treatments. Sequelae were reported more frequently in post-infectious cases (4/6): spastic tetraplegia, behavioural disorders and learning disability.

Conclusions:

Infectious agents, such as HSV and *Mycoplasma*, should be investigated in all patients with NMDAR encephalitis. It is important an early suspicion and recognition of this disease. Presenting this case review, the authors intend to raise the discussion about infection as a trigger to autoimmunity against NMDA receptors in predisposed patients.

Systematic Review Registration:

N/A

ESPID19-1024
E-Poster Viewing - May 7-10 - E-Poster Hours

Host-pathogen interaction

Still unknown infectious disease that caused facial and limb tissue destruction: case report

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Background

Demonstration of patient with unknown aetiology skin and subcutaneous tissue disease with extensive necrosis and the following tissue defects. No pathogen that matched the clinical scene was found, but it could be unknown immune system impairment with a possible infection as a trigger factor.

Case Presentation Summary

A 11-year-old boy was admitted to hospital with complaints about pronounced oedema spreading from left nostril to the left cheek and eyes; covered with yellowish scabs and temperature till 39℃. Wide spectrum antibacterial therapy was started, but no positive dynamics was achieved. Therapy with Acyclovir and anti-fungal therapy was added, 2 incisions and drainage were performed. There was a temporary improvement, but the course of the disease was progressing, because new necrosis appeared. Child was investigated to fungal, more frequent and very rare bacterial infections, viral infections, however, no pathogen was found. Therefore, immunological and genetical investigation was started. For further examination patient was transported to Finland. There child undergone whole exome sequencing **–** no mutation which would be associated with immune deficiency was found. Skin lesion and biopsy staining (Giemsa positivity) could fit with mucocutaneous leishmaniosis diagnosis, but antibodies and PCR were negative. The treatment with biological therapy was started, but no effect was reached. After 2 weeks overall condition was compensated, temperature was normal. There was cavity at the nasal root, filled with detritic mass; wing of nose was undergoing epithelization process and left cheek was covered with granulation tissue.

Learning Points/Discussion

In severe patient cases the multidisciplinary investigation and treatment approach is needed, but despite that the cause of local tissue change was not found. The potential infection was thought to be a trigger factor for such a severe local tissue change.

ESPID19-0700
E-Poster Viewing - May 7-10 - E-Poster Hours

Host-pathogen interaction

Influenza virus exploits an interferon-independent lncrna to warrant viral rna synthesis by suppression of rig-i mediated immune response

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Background

Long noncoding RNAs (lncRNAs) participate in host antiviral defense by modulating immune responses. However, it remains largely unexplored whether viruses can exploit interferon (IFN)-independent host lncRNAs to evade innate immunity.

Methods

We performed functional lncRNAs screening using an esiRNAs library targeting human lncRNAs, to identify lncRNAs involved in IAV replication. The role and molecular mechanism of lncRNA in IAV infection were studied in lncRNA overexpression or knockdown cells by reporter activity assay, RNA-FISH, qRT-PCR and other techniques.

Results

We have identified a group of human lncRNAs that modulate influenza A virus (IAV) replication in a high-throughput loss-of-function screen. GO and KEGG pathway analysis suggested that these lncRNAs might modulate IAV infection by regulating the host immune and inflammation responses. Importantly, we found that an IFN-independent lncRNA IPAN is hijacked by IAV to suppress RIG-I mediated immune responses. The expression levels of IPAN are correlated with viral replication levels. IPAN is specifically induced by IAV infection independent of interferon, and IAV infection causes IPAN translocation into the nucleus. We identified that IPAN associates with viral RNA dependent RNA polymerase PB1 and promotes its stability, warranting efficient viral RNA synthesis. Silencing IPAN results in RIG-I dependent PB1 degradation triggered by viral RNA synthesis, severely impairs viral infection.

Conclusions

Our data unveil a new role of host lncRNAs, which is the hijack of a host lncRNA by viruses to counter host restriction, which will advance our understanding of IAV pathogenesis and may open new avenues to the development of novel antiviral therapeutics.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0031
E-Poster Viewing - May 7-10 - E-Poster Hours

Host-pathogen interaction

Diagnosis improvement of marshall syndrome (pfapa)

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Background

Marshall Syndrome (PFAPA) is a recurrent condition including fever episodes, aphthous stomatitis, pharyngitis and adenitis. Clinical distinction from infectious mononucleosis and Streptococcal pharyngitis is difficult. Authors emphasize clinical and investigational peculiarities regarding PFAPA-patients and propose a diagnosis algorithm.

Methods

Authors studied 3 patient-groups during 3 years period: 62 patients with PFAPA (Marshall syndrome group, MSG), 29 children with infectious mononucleosis (IMG) and 28 patients with streptococcal pharyngitis (SPG). 1.Regarding MSG, authors analyzed symptoms onset age and period between disease onset and diagnosis. Inclusion criteria: patients with fulfilled PFAPA-diagnostic criteria. 2.Considering IMG, inclusion criteria were: positive serology for Epstein-Barr Virus (EBV-serology) correlated with negative Streptococcal-A test. 3.For the patients that belong to SPG, inclusion criterion was the positive Streptococcal-A test. Authors analyzed for all groups “C” reactive protein (CRP). The statistical analysis used independent sample „t” test.

Results

1.Regarding MSG: mean age of symptoms onset was 26.09 months; period between disease-onset and diagnosis was 19.92 months; CRP mean values was 68.06 mg/dl (normal <10). 2.For IMG: mean CRP-value was 10.37 mg/l. 3.The analysis of patients diagnosed with streptococcal pharyngitis has shown a mean CRP-value 30.14 mg/l. Authors noticed statistical difference regarding CRP-value between MSG and the other 2 groups.

Conclusions

1.PFAPA diagnosis is late (low suspicion index). 2.CRP remains a sensitive marker for MSG as compare to IMG ($p<0,05$). 3.Algorithm diagnosis regarding patients with recurrent fever, cervical adenitis and pharyngitis: firstly Strep-test evaluation. When positive - confirmation of streptococcal pharyngitis. By Strep-test negative, recommendation for CRP test. When normal CRP, attempt EBV-serology. When CRP-value ist high, think about PFAPA. When PFAPA possible – try single dose oral corticotherapy. A good and quickly response confirm PFAPA.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-1175
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

A neglected enemy of hematopoietic stem cell transplant patients: tuberculosis

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Background

Bone marrow transplantation plays an important role in childhood hematological diseases, malignancies, and immunodeficiencies. Treatment regimens before or during hematopoietic stem cell transplantation (HSCT), other immune suppressive therapies and graft versus host disease can impair cell-mediated immunity. This situation increases the development of viral infections, fungal infections in patients. Also, cellular immunodeficiency increases the susceptibility of these patients to mycobacterial infections. This study aims to summarize the characteristic features, diagnostic approach, management and treatment responses of our patients with tuberculosis (TB) infection which is a rare condition after HSCT.

Case Presentation Summary

	Case 1	Case 2	Case 3	Case 4
Age (month)/ gender	43 / M	29 / F	25 / F	39 / M
Primary diagnosis	SCID	SCID	SCID	JMML
Diagnosis age	6	8	8	4
Type of HSCT	Allogeneic	Allogeneic	Allogeneic	Haploidentical
BCG vaccination	+	+	+	+
TB prophylaxis before HSCT	-	+	+	-
TB disease development time (after HSCT)	66	138	31	141
Mycobacteria isolated	-	M. tuberculosis	M. tuberculosis	M. bovis
Site of ınfection	Lymph node + Liver	Lymph node + Bone + Liver	Lymph node + Bone	Skin + Bone
Treatment regime	HRZE	HRZE	HRZE	HRE + Quinolone + Clarithrmyc.
Treatment duration	14	14	12	12
Outcome	Cure	Refractory	Cure	Refractory

Patients who underwent HSCT in Erciyes University Medical Faculty Pediatric Hematology / Oncology and Bone Marrow Transplantation Centre were evaluated retrospectively between 2011-2018. Two hundred and ninety-seven patients with HSCT evaluated. Primary diagnosis of these patients was; primary immunodeficiency (53/297), solitary malignancy (71/297), malign hematological diseases (96/297), other hematological diseases (63/297), and other diseases like metabolic diseases, epidermolysis bullosa, osteopetrosis (7/297). Four patients with TB evaluated further. In our HSCT patients, tuberculosis incidence in malign hematological disease and immunodeficiency groups were 1.04% and 5.6% respectively. Demographic and clinical features of patients with TB after transplantation are given in Table 1.

Learning Points/Discussion

In developing countries, with an increasing rate of HSCT, TB is getting more important in these patients. Especially in patients with immunodeficiency, HSCT is of vital importance. Therefore, early diagnosis of immunodeficiency and prevention of BCG vaccination of these patients are very important in preventing TB after transplantation. Also, it should be taken into consideration whether patients have tuberculosis exposure and TB infection before transplantation. Close monitoring is required to identify early reactivation of TB.

ESPID19-1126
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Disseminated cryptococcal infection in a patient with autoimmune disease

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Background

Cryptococci disease is a potentially fatal fungal disease caused by *Cryptococcus neoformans*, which is common in immunocompromised hosts. An important determinant of outcomes in patients with cryptococcosis is the presence of disseminated disease, defined as cryptococcemia and/or meningitis. Cryptococcal disease occurs less frequently in children than in adults. Besides AIDS, cryptococcosis has been reported in children with a variety of underlying conditions.

Case Presentation Summary

Female, 15 years, with autoimmune hepatitis, waiting for a liver transplant; in use of cyclosporine 100mg/day and prednisone 20mg/day.

Sought emergency on 10/10/18 due to respiratory distress. Three days before started fever, anasarca, increased abdominal volume, cough. Cyclosporine was switched to mycophenolate 20mg/kg/day.

Physical examination showed regular general condition, jaundiced, dehydrated, dyspneic, with anasarca and oxygen desaturation. Ultrasound revealed free fluid in the cavity, performed diagnostic puncture, without peritonitis. Antimicrobial therapy was initiated with piperacillin tazobactam, vancomycin and micafungin.

In 15/10, she presented worsening of respiratory discomfort and anasarca. Chest x-ray evidenced consolidation and signs of congestion.

Cryptococcus neoformans was isolated on 10 and 12/10/18 blood cultures, as well as in ascitic fluid on 11/10/18. Lumbar punction and CNS CT scan were not performed due to clinical instability. Treatment with liposomal amphotericin B 5mg/kg/day was initiated on 15/10, but still, the patient died within 48 hours.

Learning Points/Discussion

Cryptococcus infection is relatively common in immunocompromised patients, like HIV-infected, malignant diseases and transplantation. However, there are few reports of cryptococcosis associated with autoimmune diseases and pour data on disseminated disease in pediatric population. This population normally presents whit unspecific clinical manifestation representing a diagnostic and therapeutic challenge for physician. Early diagnosis and introduction of appropriate antifungal therapy may improve clinical outcomes.

ESPID19-0939
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Fatal progressive herpes simplex virus primary disseminated infection transmitted through solid organ transplantation

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Background

Infectious diseases are the first cause of mortality in children with kidney transplantation. In these patients, infections by cytomegalovirus (CMV), Epstein-Barr virus (EBV) or BK virus, are systematically investigated; but other agents must be recognized and promptly treated because of its life-threatening potential.

Case Presentation Summary

A 16 years-old male with stage 4 chronic kidney disease due to cystinosis, undergone renal transplantation (deceased donor; recipient and donor CMV IgG-positive) and immunosuppressive therapy was initiated (basiliximab, methylprednisolone, mycophenolate mofetil and tacrolimus). The patient presented with fever on day fifth after transplantation and cefotaxime was initiated. On the following three days, he presented progressive clinical worsening, persisting fever, pancytopenia with coagulopathy, upper gastrointestinal bleeding, hypotension, renal failure and marked elevation of liver enzymes, requiring admission in the pediatric intensive care unit (PICU). Meropenem, vancomycin and ganciclovir were initiated, immunosuppressive therapy was reduced. Vasoactive support, blood and platelet transfusion, mechanical ventilation, and continuous veno-venous hemodiafiltration were also warranted. Serum and urine CMV, EBV and BKV PCR and viral hepatitis (A, B and C) serologies were all negative. The donor was from Venezuela and the recipient of the other kidney had the same clinical evolution, thus tropical infections were investigated (plasmodium, trypanosome, endemic mycoses, strongyloidiasis, toxocara) and ivermectin plus amphotericin-B were initiated. The patient died one day after PICU admission. All microbiological tests were negative, necropsy and donor serum investigation showed herpes simplex virus (HSV)-1 disseminated primary infection being transmitted through the transplanted organ.

Learning Points/Discussion

Systemic HSV infection is a potentially life-threatening disease in immunosuppressed patients and it is not easily recognized nor systematically investigated in all kidney transplantation recipients. High clinical suspicion and promptly antiviral and supportive therapy are necessary.

ESPID19-0907
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

When bruise is not a bruise

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Background

Mucormycosis is a rare life threatening fungal disease, primarily affecting severely immunocompromised patients.

Case Presentation Summary

We report a case of a 2-year-old girl with hyperdiploid B-cell precursor acute lymphoblastic leukaemia (ALL). She was profoundly neutropenic on diagnosis and just 3 weeks into her induction chemotherapy developed a small (2cm) contusion below her left elbow after a minor fall. Three days later she reported low grade temperatures and was admitted for broad spectrum antimicrobials in view of her immunosuppressed status. The contusion evolved into a purple induration 2x2cm without coliquation or discharge. Inflammatory markers remained negative. The lesion was biopsied on day 4 of admission. *Rhizopus oryzae* was identified by fungal culture and panfungal PCR.

No other sites of infection were identified. The lesion was surgically debrided. Our patient received G-CSF to reverse her neutropenia, and was treated with dual antifungal therapy of posaconazole and amphotericin B for 4 weeks. She then continued with posaconazole monotherapy maintenance. She made a full recovery and continues with her haematological treatment and posaconazole.

Learning Points/Discussion

This case highlights the need for close monitoring and early diagnosis of mucomycosis, and for timely treatment with antifungal therapy, surgical debridement, and reversal of neutropenia. It also emphasises the necessity of maintenance antifungal treatment in high risk immunosuppressed patients.

ESPID19-0748
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Cryptococcal meningitis in a patient with x-linked hyper igm syndrome – cd40l deficiency: a case report

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Background

Cryptococcal meningoencephalitis (CM) is an opportunistic infection that predominantly affects immunocompromised patients. Hyper IgM syndrome (HIGM) is a primary immunodeficiency that increases susceptibility to several opportunistic infections. It is caused by a gene defects of CD40 ligand required for activation of B-lymphocytes and a normal production of immunoglobulins.

Case Presentation Summary

A 22 years-old-boy affected by HIGM syndrome was admitted because of severe headache started in the previous two weeks. He denied fever or focal neurological sign. On physical examination, a bilateral mild papillary border elevation was perceived by fundoscopy. Brain CT scan and MRI were negative. Blood tests were normal. A lumbar puncture (LP) was performed, analysis of CSF showed 78 leucocytes/mmc, glucose level <50% (35 mg/dl) of seric value and 84 mg/dl of proteins. The cryptococcal antigen test was positive on blood (titer 1:10) and liquor (titer 1:100), the liquor culture confirmed the diagnosis of CM. A therapy with Ambisome and Fluconazole iv was started, then replaced with Flucytosine iv. Because of persistent headache and diplopia appearance, an external ventricular derivation was used in order to reduce the high cerebrospinal pressure. After 10 days of combination therapy, a LP was repeated yielding negative culture. Because of persistent diplopia the administration of steroids was widely discussed, we found high levels of inflammatory cytokines on CSF therefore treatment with prednisone was started. During the hospitalization, the patient maintained his usual antibiotic prophylaxis the weekly administration of Ig sc.

Learning Points/Discussion

Our case emphasized that Cryptococcus neoformans should be included among aetiological agents in patient with X-linked HIGM syndrome presenting with signs of meningitis. More frequent description of similar cases would support a univocal approach to similar situation where the use of steroids is still debated.

ESPID19-0615
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Effectiveness of ivig in the prevention of infections in children with hypogammaglobulinaemia secondary to chylothorax: a systematic review

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Background

Intravenous immunoglobulin (IVIG) is recommended for children with primary and secondary antibody deficiencies. Chylothorax (CL) has been associated with T-lymphocyte loss and hypogammaglobulinemia. Aim of our systematic review was to summarize the evidence on the potential protective role of IVIG in children with clylothorax.

Methods

Medline was systematically reviewed using relevant keywords and articles were retrieved for full-text review. Data were summarized in a qualitative analysis in order to examine the evidence of IVIG use in children with CL.

Results

A total of five retrospective, descriptive cohort studies and case series were retrieved; no prospective randomized control trial was identified. Use of IVIG as adjunct to conservative treatment was reported in 29 patients aged 5 days to 5 years. All cases were diagnosed with CL after cardiac surgery. Hypogammaglobulinemia, lymphopenia and septicaemia were the most common indications for IVIG treatment (13/29). IVIG doses varied from 0.1 to 1 gr/kg/day. Administration of IVIG did not prevent recurrent infections or serious complications in the majority of patients (51.7%, 15/29). Blood stream infections were seen after IVIG therapy in 13 cases (44.8%). Mortality was high and affected 24.1% of the treated patients (7/29). Only one study (N: 37) provided comparative data between treated and untreated patients and did not manage to show significant differences in outcome.

Conclusions

Limited evidence exists to support the treatment with IVIG in preventing infections in children with CL or improve long term survival. Large, well designed prospective studies on IVIG administration would help guide new treatment strategies and improve outcomes.

Systematic Review Registration (Please input N/A if not registered)

n/a

ESPID19-0572
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

My child is always sick, and sadly there is a reason for it.

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Background

Specific antibody deficiency (SAD) it's a type of immunodeficiency where patients can't produce antibodies against the polysaccharide coating of bacteria like *S.pneumoniae, M.catarrhalis* or *H.influenzae*. This results in recurrent upper and lower respiratory tract infections. There is not specific treatment for it at the moment.

Case Presentation Summary

Three children between 2 and 3 years old were referred to our Immunology Unit for recurrent upper tract respiratory and lower respiratory tract infections. In the two first cases, the great number of infections became a nuisance for the families but the third child had mastoiditis caused by S. pneumoniae (serotype 19F), had to be admitted in the hospital and received a long course of intravenous antibiotics. Immunological tests such as antibody levels and lymphocyte B, T and NK count were normal. The diagnosis was made administering the 23-valent pneumococcal polysaccharide vaccine and determining the specific antibody titers to it one month late. No response to the vaccine was detected. Families were informed about the results, and annual influenza vaccine was recommended together with routine immunizations (including conjugate 13-valent pneumococcal vaccine).

Learning Points/Discussion

In a children older than 2 years with recurrent upper and lower respiratory tract infections, SAD must be considered. The diagnosis is made testing the response to the 23-valent pneumococcal polysaccharide vaccine. Although there isn't a specific treatment for it, families benefit from having a diagnosis. New pneumococcal conjugate vaccines will probably play a key role in the future.

ESPID19-0463
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Recurrent pneumonias and bronchiectasis revealing c2 deficiency in a child

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Background

Children commonly have airway infections, and they usually recover uneventfully. There are classic warning signs reported to suspect Primary Immunodeficiency (PID), like 2 or more pneumonias within a year. We present the case of a child with recurrent pneumonias in different locations that developed bronchiectasis.

Case Presentation Summary

A boy of 3 years and 6 months of age was followed up at paediatric respiratory clinic due to recurrent pneumonias: since he was 18 months-old he presented with 5 pneumonias in different locations (hospitalized twice of them), but no other past medical history of interest, born from Spanish Caucasian unrelated parents, older brother healthy, nothing else remarkable. During last pneumonia, chest X-ray revealed bronchiectasis, checked by CT-scan, and then the patient was referred for further studies.

Full blood count, renal and liver functional test and immunoglobulins were within normal limits; tuberculin skin test was 0 mm, bronchoscopy and sweat test were normal. Complement studies showed a decrease in CH50 test of <14 U/mL (normal limits 25-95), with normal C3 (134 mg/dL) and C4 (22 mg/dL), and low C2 0.5 mg/dL (1.4-2.4). These results were checked a second time, and then the patient started on prophylactic penicillin PO and he was transferred to a PID unit. At this unit, the patient received the genetic confirmation diagnosis of type I C2 deficiency due to homozygous 28 base-pair deletion at exon 6, carried by the parents.

Learning Points/Discussion

In patients with recurrent airway infections and bronchiectasis immunological tests should be performed. When evaluating complement functioning we should not forget CH50 test, because just the study of C3 and C4 could miss an underlying complement deficiency.

ESPID19-1160
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Recurrent life-threatening influenza a (h1n1) infection in a 9-year-old boy with systemic capillary leak syndrome

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Background

Idiopathic systemic capillary leak syndrome is, especially in childhood, a rare disorder, characterised by episodic microvascular leak of fluids into peripheral tissues with life-threatening hypotension, hypoalbuminaemia and haemoconcentration. We present a child with two episodes of capillary leak syndrome caused by influenza infection.

Case Presentation Summary

An almost 9-year-old, otherwise healthy boy presented to the primary care paediatrician with moderate vomiting, facial oedema, polydipsia and polyuria, all of which occurred two days after the onset of an acute respiratory infection. Due to the history and the clinical appearance (Glasgow coma scale 15), serious hypotension, which developed subsequently, was unexpected; however, it was reversed entirely by the first bolus of fluids. A few hours later, the ongoing shock was treated in an intensive care unit. Acute plasmapheresis and haemodialysis were indicated after massive rhabdomyolysis, myoglobinuria and acute renal failure as a result of influenza A infection. Neurological complications, including tetraparesis, epilepsy and psychological problems, required long term rehabilitation. In three months, he returned to school. The forthcoming season the child again suffered from influenza A infection. After a few hours of moderate signs of respiratory infection, the patient again developed life-threatening hypotension and shock. Systemic capillary leak syndrome (Clarkson’s disease) was diagnosed. After second episode yearly influenza vaccination was introduced, which successfully prevented further attacks of capillary leak syndrome in the last 7 years.

Learning Points/Discussion

Systemic capillary leak syndrome is a rare condition in childhood, which should be considered in the event of a life-threatening illness of unknown cause. Only influenza infection was identified as a cause of two episodes of severe capillary leak in our patient.

Yearly influenza vaccination has prevented further attacks so far.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Invasive pulmonary aspergillosis in 15-months old child with mixed-phenotype acute leukemia and rapid metabolism of voriconazole

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Background

Invasive pulmonary aspergillosis (IPA) is one of the most common and serious complications occurring in immunocompromised children. Fast recognition, diagnostics and sufficient therapy are crucial. We report a case of IPA in a child with mixed-phenotype acute leukemia (MPAL) and genetic variant of *CYP2C19*17,* responsible for rapid voriconazole metabolism.

Case Presentation Summary

A 15-months old girl with MPAL, who was initially refractory to induction chemotherapy (ALL-BFM protocol) and then received AML-oriented intensification, was admitted to PICU due to respiratory failure. Laboratory results showed pancitopenia: leukocytes $0{,}1 \times 10^9$/L, platelets 43×10^9/L, hemoglobin 87 g/L and CRP 243 mg/L. Bone marrow aspiration revealed hypoplastic sample and discrete hemophagocytosis. High-resolution CT revealed bilateral difuse nodular (>1 cm) consolidations with necrotic components, massive pleural effusion (L<R) and small atelectasis in left apical region. Despite prophylaxis with Ambisome, PCR from BAL and pleural fluid confirmed *Aspergillus* spp infection. Broad antimicrobial coverage was initiated before ICU admission. We initiated treatment with voriconazole. Despite ascending voriconazole doses (max. 24 mg/kg/8 hours), we failed to reach terapeutic serum levels. We found that she is heterozygote for polymorphism of *CYP2C19*17* and consequentially a rapid metabolizer of voriconazole. We added fluconazole, a competitive inhibitor of CYP2C19. To overcome hyperinflammation due to hemphagocytosis we added anti IL-1 therapy with anakinra. During prolonged period of severe neutropenia she received 30 granulocyte transfusions. The child was discharged from ICU after 67 days. She was breathing with support of non-invasive mode of ventilation (CPAP/PS) through traheostomy.

Learning Points/Discussion

We present a child with refractory leukemia and pulmonary aspergillosis where genetic variant of *CYP2C19*17* was responsible for low serum concentrations of voriconazole. We successfuly overcame it with fluconazole as competitive inhibitor and granulocyte transfusions.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Fibrous dysplasia: an uncommon cause of frontal lobe abscess in pediatric age

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Background

Cerebral abscesses could be caused by infections of structures adjacent to the brain (sinusitis, otitis, cranial osteomyelitis); however, they may also be associated with systemic infections, especially lung abscesses, and less commonly dental infections. Sinus infection has been reported as a result of obstruction of the sinus by tumour.

Case Presentation Summary

We describe the case of a 12-year-old female patient visited at the Pediatric Emergency Unit of the Bambino Gesù Children Hospital for asthenia and right front-orbital headache without vomiting. Neurological examination and blood tests were normal. Cerebral CT scan and MRI showed images suggesting of right frontal abscess with diffuse perilesional edema and a surprising finding of suspected osteoid osteoma in fronto-ethmoid region. Suddenly intermittent exophoria and diplopia appeared. Thus, intravenous therapy with Ceftriaxone, Meropenem, Metronidazole, Dexamethasone, Mannitol was started. After multidisciplinary consultation, the patient underwent a bifrontal craniotomy with evacuation of the cerebral abscess and partial excision of ovoidal formation from frontal sinus. Culture tests from bioptic material and drained purulent material were negative for bacteria and fungi. The bone histological examination showed a probably secondary acute osteomyelitis, associated with fibrous bone dysplasia (FD). Four weeks of antibiotic treatment was completed and the control MRI highlighted the improvement of peri-lesional edema and disappearance of abscess. A bone scintigraphy and a hole body MRI were performed and both demonstrated multiple lesions of the tibial bones, right fibula and left radius characteristics compatible with the diagnosis of polyostotic FD.

Learning Points/Discussion

Probably FD could cause a collection of infected mucous by obstruction of the frontal sinus determining an unusual clinical presentation and a rare complication as cerebral abscess. Clinicians should be aware of the association between these two conditions.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Type-b haemophilus influenzae meningitis: two recent french paediatric cases

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Background

We report two cases of bacterial meningitis due to type-B *Haemophilus influenzae*, in correctly vaccinated children, in 2018, in the Alpes-Maritimes department (French Riviera, France).

Case Presentation Summary

The first child was a 4-year-old boy, referred to the paediatric emergency for one-day fever, general alteration, prostration and vomiting. Blood test showed 126 mg/L C reactive protein, 30 ng/ml pro-calcitonine, 14 400 leucocyts (88 per cent neutrophils), and lumbar puncture highlighted 10 000 elements/mm3 (93 per cent neutrophils), hyperproteinorachia and hypoglycorachia, Gram-negative-bacillus in direct examination.

The second one was a 4-years-old girl, referred to the paediatric emergency for fever, general alteration and vomiting since 3 days. Blood test showed 500 mg/L C reactive protein, 122 ng/ml pro-calcitonine, 11 000 leucocyts (84 per cent neutrophils), and lumbar puncture highlighted 2495 elements/mm3 (92 per cent neutrophils), hyperproteinorachia and hypoglycorachia, Gram-negative-bacillus in direct examination.

Both of all, antibiotherapy by cefotaxim 300mg/kg/day and dexamethason 2mg/kg/day were rapidly started and children were closed to paediatric intensive care unit. Cerebro-spinal fluid culture and serotype identification showed type-B *Haemophilus influenzae* (antibiotic sensitivity's wild profile). Their evolution were favorable without any sequellae after 14 days-treatment, and normal immune checkup.

Learning Points/Discussion

In industrialized countries, the prevalence of type-B *Haemophilus influenzae* meningitis is very weak in childhood due to generalization of vaccination. In literature, we don't observe an increase of recent cases of type-B Haemophilus influenzae meningitis. In our report, Haemophilus sensitivity doesn't show particular antibiotic resistance, and bacterial serotype show us the same profile as in the childhood vaccine. We are surprised to the presence of these situations in correctly vaccinated children. This is important to follow up this pediatric resurgence.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Rare cause of cervical osteoarthritis

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Background

Acquired torticollis is a common presentation of various paediatric diseases, including muscle contraction, trauma, infection or malignancy. Cervical osteoarthritis is rare and difficult to diagnose. So this is interesting to know the clinical presentation of *Kingella kingae's* infection.

Case Presentation Summary

We report a rare cause of osteoarthritis due to *Kingella kingae* in a two year's old child concomitant with a primary Epstein-Barr Virus infection. The diagnosis was suspected on the cervical scanner, confirmed by the Magnetic Resonance Imaging (MRI) in front of a persistent torticollis. Biopsies formally eliminate differential diagnoses by reporting a positive Polymerase Chain Reaction (PCR) to *Kingella kingae* in the joint fluid. The child was cured without sequela thanks to an empiric antibiotic therapy adapted to the type of germs.

Learning Points/Discussion

We recall the importance of imaging in front of any persistent torticollis in a child. Cervical arthritis may be under diagnosed due to the localization hardly accessible to bacteriological samples. Moreover *Kingella kingae* specific PCR provides high specificity and sensitivity.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Gram – vs gram + blood stream infections in children with cancer

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Background and Aims:

Identifying possible predictive factors for the type of bacteremia (Gram- vs Gram+) may be crucial for the selection of the appropriate empiric antibiotic treatment.

Methods:

Patients' characteristics and clinical/laboratory findings of children with cancer who developed a bacterial Blood Stream Infection (BSI) (1/2/2011-28/2/2018) were recorded retrospectively and were correlated with the type of infection (monomicrobial or polymicrobial) as well as with the type of isolated bacteria (Gram- vs Gram+).

Results:

Of the two hundred and fifty-two bacterial BSI episodes, 28 polymicrobial (P) episodes (11%) were observed in 26 patients (24 with one episode and 2 with two). No demographic or clinical/laboratory variables were found to be predictive of polymicrobial BSI. Of the 224 monomicrobial bacterial BSI episodes, Gram- were detected in 110 episodes whereas Gram+ were isolated in the rest. Gram- vs Gram+ were isolated significantly more frequently in girls (1.7:1) vs boys (0.72:1) (***p=0.002*****)** in patients with previous BSI episodes (1.4:1) vs those without (0.8:1) (***p=0.042***) and in children who suffered from haematologic malignancy (1.3:1) vs those treated for solid tumors (0.52:1) (***p=0.003)***. Gram- were detected significantly later after relapse (median 79 vs 36 days, ***p=0.030***). Moreover, in Gram- BSI episodes leucocyte count (WBC) (***p=0.009***), neutrophil count (ANC) (***p=0.009***) and platelet count (PLT), (***p=0.002***) were significantly lower, whereas CRP levels were significantly higher (***p=0.049***). Gender, cancer type and CRP remained independent risk factors for Gram- vs Gram+ BSI in the multivariate analysis.

Conclusions:

1.Gram- and Gram+ BSIs occur at the same frequency among children with cancer. 2.Gram- bacteremia is more common among girls, children with haematologic malignancies and patients with higher CRP. 3. Bone marrow involvement related factors such as neutropenia and PLTs did not remain statistically significant in the multivariate analysis.

Systematic Review Registration:

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Headaches in a guinean adolescent

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Background

The HIV prevalence rate in the sub-Saharan Africa is 7%, almost 3/4 of the world's HIV-infected population. Toxoplasmosis is the most common central nervous system infection in patients with the acquired immunodeficiency syndrome (AIDS).
Toxoplasma encephalitis can manifest like a cerebral mass mimicking CNS tumor, with headache, confusion, fever or motor weakness.

Case Presentation Summary

A 14-years-old male patient, evacuated to Portugal from Guiné-Bissau with aortic valvular disease (on captopril and diuretic therapy), presented to a Pediatric Emergency Department with headache and nausea. The physical examination showed oral candidiasis and a systolic heart murmur.
Cranioencephalic CT scan revealed 3 oval lesions in the putamen, frontal and subcortical occipital lobe with 6mm, 14mm and 5mm of diameter, suggestive of toxoplasmosis; HIV-1 antibody and antigen (p24) positive, HBsAg and HBeAg positive, HBcAg and HBsAc negative, anti-toxoplasma immunoglobulin (Ig) G antibodies positive, IgM antibodies negative, RT- PCR detection of Toxoplasma gondii DNA positive in CSF and negative in blood, CD4 count 9 cells/µL, HIV-1 viral load 582311copies/mLand a IGRA positive. His mother was HIV negative.
He started on pyrimethamine, sulfadiazine and leucovorin, and then antiretroviral therapy with emtricitabine, tenofovir and dolutegravir.

Learning Points/Discussion

This case represents a late manifestation of HIV infection since we didn't find mother-to-child transmission. It was also a challenge to coordinate multiple therapies in a pediatric patient.
HIV test should be offered to anyone coming from countries with high prevalence of HIV infection irrespective of their health status. A severe disease with a protracted course would have been avoided in this case. It is recommended that clinicians have a high index of suspicion for those who could be identified as being at risk.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Prolonged vaccine strain viremia and bilateral sensorineural hearing loss following mmrv vaccination in a child with stat2 deficiency

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Background

Live viral vaccines are contraindicated in patients with serious immunodeficiences of T-cells, B-cells or phagocytes. However, serious complications following routine measles mumps rubella varicella (MMRV) vaccinations are rare - due to the rarity of (combined) monogenetic immunodeficiencies and the fact that most of those severe defects manifest before scheduled live viral vaccinations. We here report on a 13 months old girl where severe complications following routine MMRV vaccinations were the initial manifestation of an interferon signaling defect caused by STAT2 deficiency.

Case Presentation Summary

A 13 months old girl presented with the clinical picture of viral sepsis including high-grade fever, encephalopathy and rash following routine MMRV vaccination. Prolonged viremia with all four vaccine-strain viruses could be detected one month following post-vaccination, and measles viremia persisted over more than two months. The patient ultimately cleared all vaccine viruses and recovered from the acute illness, but audiometric tests revealed a complete bilateral sensorineural hearing loss as residual defect. Of note, the infection history before the MMRV vaccination infancy was uneventful. Immunological workup was initiated and strongly suggested a defective interferon signaling axis in the peripheral blood mononuclear cells of the patient. Subsequent whole-exome-sequencing trio confirmed the functional immunological data by identification of a compound heterozygous STAT2 loss-of-function defect.

Learning Points/Discussion

Live attenuated viral vaccines are readily cleared by an immunocompetent host but can pose a significant threat when exposed to immunodeficient patients. This case illustrates the importance of an intact type I interferon signaling axis for the clearance of vaccine strain viruses and underscores the importance of immunological and genetic testing in patients with complications following routine vaccination.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Sepsis caused by kytococcus schroeteri in an infant with acute myeloid leukemia

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Background

Kytococcus schroeteri is a skin commensal discovered in 2002 and rarely reported to cause invasive infection. There are only a few case reports of adult acute myeloid leukemia (AML) patients with *K.schroeteri* sepsis and pneumonia, but none of children. We present first successfully treated pediatric *K.schroeteri* bacteremia and invasive lung injury.

Case Presentation Summary

A 9-month-old infant with AML had completed the first induction chemotherapy (NOPHO-DBH AML 2012) and was in her first bone marrow aplasia, when she developed fever. Blood cultures were drawn and antibacterial regimen with ceftazidime and amikacin and antifungal therapy with fluconazole was started, however her status worsened, and she was transferred to intensive care unit due to septic shock. No improvement was seen after 48h and ceftazidime was changed to meropenem. Blood cultures from Port-a-cath and peripheral blood were positive for *Kytococcus schroeteri* (detected my MALDI-TOF MS). On day 4 of febrility antibacterial regiment was narrowed to vancomycin and amikacin based on *in vitro* sensitivity data. On day 9 Port-a-cath was evacuated due to local infiltration. The patient developed maculopapular rash, was still febrile and severely neutropenic, so meropenem was added. Repeated blood cultures were negative, however desaturations were observed, so lung CT on day 16 showed bilateral infiltrates. As in literature *K.schroeteri* infection has been described to cause maculopapular rash, bacteremia and pneumonia, suspicion of untreated *K.schroeteri* infection causing pneumonia was raised, so amikacin was changed to rifampicin and voriconazole was added and clinical improvement was noted. On day 23 the patient was afebrile.

Learning Points/Discussion

Invasive *Kytococcus schroeteri* infection manifests with maculopapular rash, pneumonia and bacteremia and responds to combined therapy with rifampicin. Unusual microbial causes for sepsis in oncological patients pose difficulties in choosing antimicrobial therapy.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Cytokines profile in children with cancer, fever and neutropenia with demonstrated infections and with fever of unknown origin

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Background and Aims:

Fever and neutropenia (FN) is a common complication of cancer treatment, mainly caused by bacterial, viral and fungal infections. The aim of this study was to determine serum concentration of 38 cytokines at day four of treatment in children with cancer and FN with demonstrated bacterial, viral and fungal infections compared to children with FN with fever of unknown origin (FUO)

Methods:

A prospective, multicenter study was conducted in six hospitals, in Santiago, Chile. Children < 18 years of age with cancer and FN were enrolled after their parents signed the informed consent. Clinical, laboratory, microbiological and molecular evaluation was made in each child at admission. At day 4 of evolution, serum levels of 38 cytokines were measured using Luminex 200, and were compared between children with FN and a demonstrated pathogen versus children with FUO.

Results:

A total of 112 children were evaluated. Median age was 8 years (pc 25-75, 4-12 years), 50% were male, 83% had a hematological malignancy. Sixteen of 38 cytokines evaluated were significantly higher in children with a detected pathogen compared to children with FUO: G-CSF, GM-CSF, IFN-γ, IL-1α, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-15, IL-17A, IP-10, MCP-1, MIP-1α, Flt-3L. We did not observe any cytokine whose values were higher in children with FUO compared to children with a detected pathogen.

Conclusions:

Our study shows cytokine's levels significantly higher in children with a detected pathogen compared to children with FUO. Our traditional approach for understanding infections based exclusively on the characterization of the pathogens is insufficient and leaves out the other key player, the host. The knowledge of host immune response could be an essential tool to optimize the management of FN in children with cancer

Systematic Review Registration:

no

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Transplacental maternal engraftment (tme) in a child with severe combined deficiency (scid) receiving mmr vaccine: a potential protective effect?

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Background

Severe combined immunodeficiency (SCID) is a potential fatal disease, typically presenting with failure to thrive (FTT) and severe/opportunistic infections in the first months of life. Early diagnosis (new born screening, positive family history) allows initiation of supportive and subsequent curative therapy (hematopoietic stem cell transplantation (HSCT) or gene therapy) thereby improving survival from 0% to >95%. We present a case with SCID, who received live vaccine MMR without inducing disseminated disease possibly due to the “protective effect” of transplacental maternal engraftment (TME) of CD8 T lymphocyte

Case Presentation Summary

A 15 months-old patient, born to non-consanguineous parents, was admitted with fever, respiratory distress, vomiting, diarrhoea and FTT. Since birth, he suffered from recurrent oral thrush and “skin atopy”. Empiric broad-spectrum empirical antibiotic therapy was started and he was transferred to our centre. A FBC was normal, however lymphocyte subsets revealed 9/ul CD4 T cells, 642/ul CD 8 T T cells, 54/ul NK cells and 4521/ul, B cells. Blood PCR for HIV was 0 and for CMV 14000copies/ml. Clinical suspicion of T-B+NK- SCID with TME was confirmed using next generation sequencing (JAK3-deficient SCID. Homozygous mutation c.2892G>C). TME was likely responsible for mild skin graft-versus-host-disease (“skin atopy") but it might have also conferred partial immunity to opportunistic pathogens and vaccine live antigens. He received supportive therapy and urgent donor research was initiated to perform HSCT, however he sadly died due to disseminated CMV infection.

Learning Points/Discussion

This case highlights the importance of global implementation of NBS for SCID. Furthermore TME may delay the onset of severe viral infections as well as having a protective effect to live attenuated vaccines such as MMR.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Viral infections after kidney transplantation in children in the republic of belarus

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Background and Aims:

Viral infections are frequent complications after kidney transplantation. To prevent their development pre-emptive therapy is used. And for the latter exploration of the spectrum of viral infections in children after kidney transplantation is essential.

Methods:

Laboratory diagnosis of viral reactivation was carried out in 105 children after kidney transplantation. In the early postoperative period 35 children were observed, in the late one - 70. All recipients took immunosuppressive therapy with glucocorticosteroids (GC), mycophenolate mofetil (MMF), and tacrolimus, as well as induction therapy with basiliximab and prevention of CMV infection with valganciclovir. The selection of an organ by class I and II HLA antigens was carried out only in 13 of the examined patients (18.6%).

The detection of BKV, JCV, CMV, EBV, HHV-6, HHV-7, VZV, AdV and HSV-1,2 DNA was performed by real time PCR.

Results:

In the early postoperative period, polyomaviruses (BKV and / or JCV) were detected in urine in 40.0% of the recipients, whereas DNA of HSV-1,2, CMV, VZV, EBV and AdV in serum were absent. The frequency of virus reactivation in the late post-transplant period was 51.7% (45 positive), including EBV infection in 1.2%, HHV-6 infection in 3.6%, HHV-7 in 2.4%, AdV in 2.3%, BKV in 14.9% and JCV in 36.9% of patients. DNA of CMV, HSV-1,2 and VZV were not detected in this group of recipients.

Conclusions:

Polyomaviruses were predominant in children in both early (40.0%) and late (47.1%) postoperative periods. In the early post-transplant period BKV prevailed (22.9%), in the late one - JCV (36.8%) with persistence in 5.7% of patients.

Systematic Review Registration:

n/a

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Infections in immunocompromised patients

Immunosuppressed patients as a target for leishmania species.

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Background

Leishmaniasis is a disease caused by protozoan parasites of the genus Leishmania. Visceral leishmaniasis is characterized by irregular bouts of fever, substantial weight loss, enlargement of the spleen and liver, and anemia. Armenia is an endemic region for this disease. Immunosuppressed patients are prone to develop visceral leishmaniasis. Our goal is to introduce a case of patient with acute lymphoblastic leukemia who developed visceral leishmaniasis.

Case Presentation Summary

A 3-year-old boy was admitted to haematologic center with pallor, pancytopenia (RBC=2.33x10^6/ml, PLT=23/ml, WBC=5/ml). His temperature was 37.5-37.8^{0}C. As the patient's family was from an endemic region for visceral leishmaniasis, thus laboratory studies were done (rK-39 negative, serology negative, microscopy of bone marrow aspirate negative). Bone marrow biopsy showed T-cell acute lymphoblastic leukemia. Treatment was started according to ALL IC-BFM 2009 protocol I. Although clinical symptoms were improved, but the spleen enlargement was going on and HGB level was decreasing. Following the guidelines, the treatment was changed to HR I protocol, however the same symptoms were maintained. Spleen solid tumor was suspected and spleen biopsy was done, which proved visceral leishmaniasis. The above-mentioned analyses for visceral leishmaniasis were repeated which revealed positive results. The treatment with Liposomal Amphotericin B 40mg/kg (as indicated for immunosuppressed patients) was started. Meanwhile the treatment of ALL was continuing based on ALL IC-BFM 2009.

During the therapy aforementioned symptoms were disappeared.

Learning Points/Discussion

Living in endemic region for leishmaniasis we have to check immunosuppressed patients for visceral leishmaniasis as they are in risk group for developing the disease, even if it was excluded previously.

ESPID19-0949
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Infection profile in children with chronic granulomatous disease in a tertiary care centre in mumbai

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Background and Aims:

Background- Chronic Granulomatous disease (CGD) is an inherited disorder due to inability to kill catalase-positive microorganisms because of a defect in the generation of microbicidal oxygen metabolites.

Aims -We retrospectively analysed 52 patients with CGD seen at our centre over a period of 14 years.

Methods:

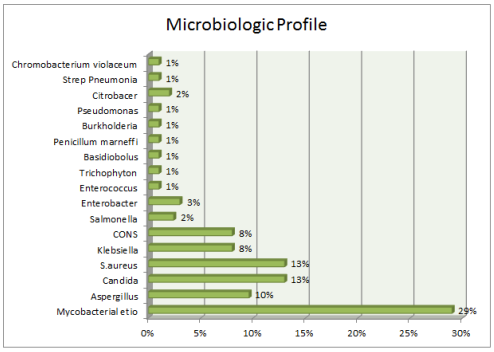
All patients had confirmed CGD and genotype was determined where possible. Microbiological spectrum of infection isolated from blood or soft tissue was analysed. For fungal infections: fungal culture, galactomannan and radiology findings were used to aid diagnosis. Clinical course and treatment profiles of patients was evaluated.

Results:

Results- Mean age of presentation was 1.3 years (birth to 10 years) and mean age at diagnosis was 2.3 years (birth to 10 years) with a delay in diagnosis of 1 year. Male to female ratio was 3.2:1. Consanguinity was present in 43% cases with a previous history of sibling death in 13% cases(7 out of 52 patients). 92% had failure to thrive. Average number of infective episodes was 1.7 in the cohort. Infections seen were pneumonia (90%), abscess(32%), otitis media (3%), urinary tract infections (19%), osteomyelitis (11%) and one case of hepatitis. One child presented with Kawasaki disease with family history of CGD.

Organism isolated are attached in figure. Fungal infections include aspergillus (15%), Candida (21%), one case each of Basidobolus, Trichophyoton rubrum and Penicillium species each.

34(65%) children are well on follow up, 9(17%) expired and 9(17%) lost to follow up.



Conclusions:

The infection profile in CGD can vary in developing countries, the commonest organisms seen were Mycobacterium tuberculosis, Candida and Aspergillus. Early diagnosis and prophylaxis can improve morbidity and mortality.

Systematic Review Registration:

Not applicable

ESPID19-0937
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Combined immunodeficiency in 3 children in a family: when whole exome sequencing remained inconclusive

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Background

We report a non-consanguineous family from Central India wherein 3 children succumbed to a combined immunodeficiency. All three had similar clinical and immunological profiles. However, the youngest child also went on to develop non-Hodgkin lymphoma in infancy.

Case Presentation Summary

The proband (A) was a 9 year old boy who had been symptomatic with recurrent lower respiratory infections and multiple warts since the age of 3 months. On examination he had pallor, clubbing, generalized lymphadenopathy, hepatomegaly and bilateral coarse crepitations. He succumbed to these complications at 11 years.

His younger sister (B) was 8 years had similar symptomatology. Computerized tomography (CT) of lung showed bilateral bronchiectasis and pulmonary nodules. Fine needle aspiration cytology (FNAC) of these nodules revealed small and large lymphoid cells that were difficult to characterize further. She eventually expired due to pulmonary complications.

The youngest child (C)- a girl aged 11 months who had been having recurrent episodes of pneumonia and 1 episode of left ear discharge since infancy. She had developed fever, swelling of left eyelid and abdominal distention for last 2 months. There was no response to broad spectrum antimicrobials. On examination she had pallor, swelling and induration of left lower eye lid, hepatomegaly and splenomegaly. CT abdomen and lung revealed multiple space occupying lesions (SOLs) in liver and spleen and pulmonary nodules. FNAC of liver SOLs and flowcytometric analysis of aspirate revealed mature B cell lymphoma. Epstein-Barr virus (EBV) IgM was positive and EBV DNA PCR was also positive. However whole exome sequencing carried out in the proband (A) and one of the affected sisters (B) was inconclusive. We now intend doing whole genome sequencing to unravel the underlying

immunodeficiency.

Table depicting immunological investigations of 3 children

	Proband (A)	Affected sister (B)	Affected sister (C)
Ig A (g/L)	4.56 (0.35-3.50)	5.68 (0.70-2.50)	1.45 (0.20-0.70)
Ig G (g/L)	21.09(6.50-16.00)	16.07 (5.40-16.10)	10.94 (3.00-10.90)
Ig E (IU/ml)	>6000	4392 (3.6 – 81.0)	1844
Ig M (g/L)	0.90 (0.4-2.4)	1.36 (0.50-1.80)	
Lymphocyte subsets: CD3 CD19 CD56 CD3+CD56+	 45.1% 3.9% 7.2%	 43% 8.1% 9.4%	 52.40 (54- 76%) 36.87 (15-39%) 03.55 (2-14%) 03.9%
TCR α/β on CD3+ cells TCR γ/δ on CD3+ cells TCR α/β on CD4+ cells TCR γ/δ beta on CD4+ cells	 46%	0.2% 53%	0.73% (control-93.3%) 84.43%(control 3.25%) 3.14% (control 98.12%) 8.86% (control 0.1%)
HLA DR expression			Increased on gated CD3+ T cells

Learning Points/Discussion

This family highlights a rare EBV related combined immunodeficiency.

ESPID19-0904
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Infective endocarditis, osteomyelitis of skull and invasive aspergillosis in a child with chronic granulomatous disease

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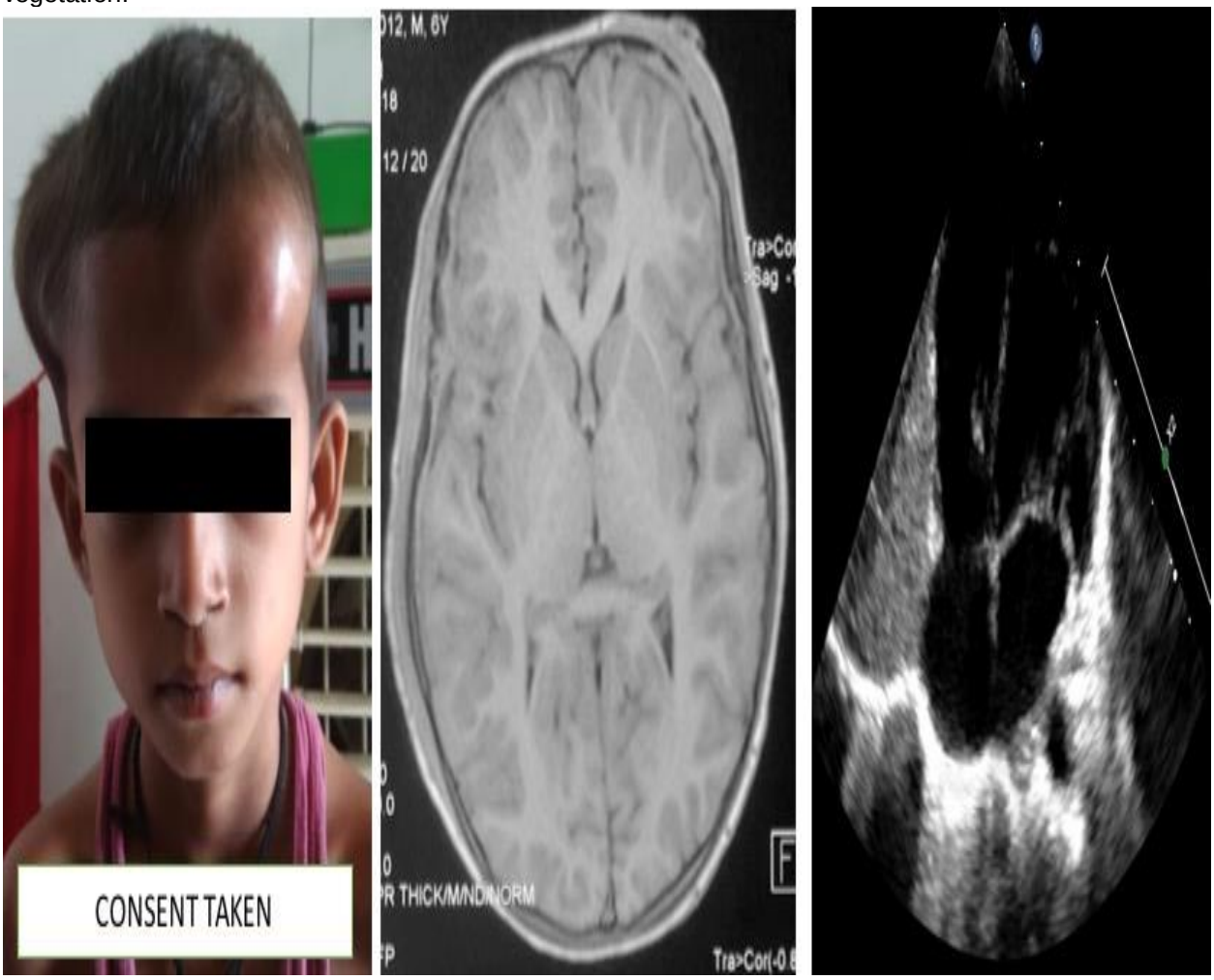
Background

Children with chronic granulomatous disease(CGD) are at high risk for fungal infections(especially with Aspergillus species).Infective endocarditis and fungal osteomyelitis of skull are distinctly unusual.

Case Presentation Summary

A 6-year-old boy,born out of a non-consanguineous marriage,presented with soft tissue swellings of skull for 2 months.His past history was significant with an episode of pneumonia at 1 year and recurrent soft tissue swellings.On examination he had cervical lymphadenopathy and two abscesses,12x4 cm on right temporo-parietal region and 4x3 cm over left frontal region.He was also found to have an ejection systolic murmur.Investigations revealed total leukocyte count $13x10^9$/L(N_{60}/L_{23}/M_{13}/E_1);elevated CRP(244mg/L) and ESR(104 mm1^{st}hr).Chest x ray revealed cardiomegaly (cardiothoracic ratio 67%) and 2D echocardiography showed vegetation of 6x3 mm over the anterior mitral leaflet suggestive of infective endocarditis.Blood and urine cultures were sterile.Culture from pus over the temporo-parietal abscess showed growth of *Aspergillus fumigatus*.Human immunodeficiency virus serology was non-reactive.Immunoglobulin profile revealed elevated IgG 21.20g/L and IgA 5.66 g/L;IgM was 1.63 g/L.In view of strong suspicion of CGD,nitroblue tetrazolium dye reduction test(NBT) was carried out-it revealed no reduction and Dihydrorhodamine(DHR) assay showed a low stimulation index(4.34).Flow cytometry for gp 47 phox and gp 67 phox was normal and DHR of mother did not reveal X linked carrier state.CEMRI brain showed heterogeneously enchancing soft tissue lesion in the scalp at right fronto-parietal region and left frontal region with underlying bony destruction suggestive of osteomyelitis.He was given intravenous antimicrobials(ceftriaxone,gentamycin,cloxacillin,voriconazole).After 6 weeks of therapy,he showed resolution of findings on MRI brain and a repeat 2Dechocardiography showed significant decrease in size of mitral leaflet

vegetation.



Learning Points/Discussion

This case highlights a rare presentation of CGD with infective endocarditis and skull osteomyelitis due to *Aspergillus fumigatus*.To the best of our knowledge,this has not been reported previously.

ESPID19-0897
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Extensive warts in a young boy with novel mutation in dock8

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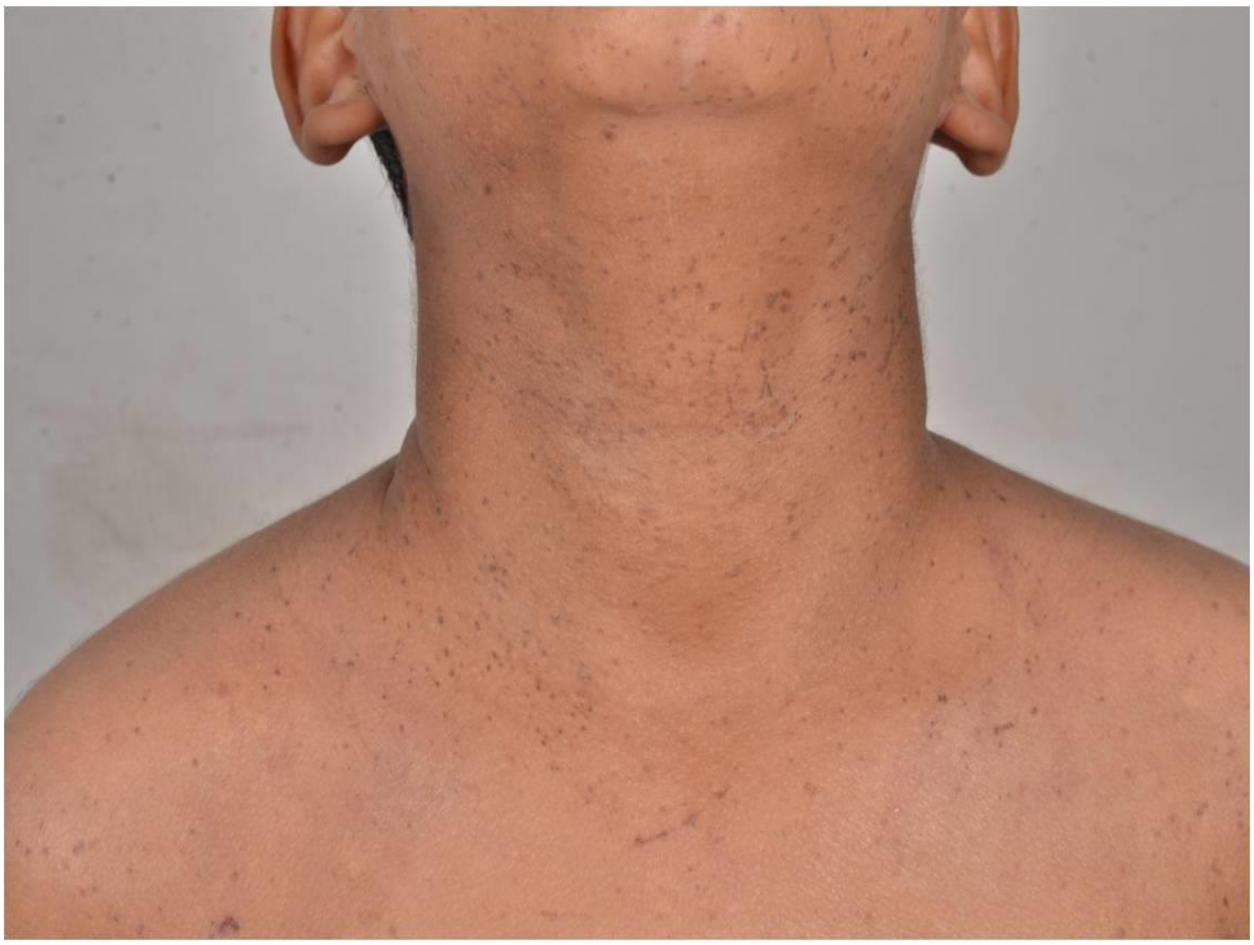
Background

Warts associated with human papilloma virus (HPV) infection when extensive, recurrent and disfiguring often signal an underlying combined immunodeficiency like DOCK 8 deficiency. We describe a young boy who had persistent warts for many years and was found to have a novel mutation in DOCK8 gene.

Case Presentation Summary

An 11-year-old boy, born to non-consanguineous parents, presented with atopic eczema and multiple flat warts over whole body including face. He also had history of recurrent pustular lesions over body since the age of 3 months. This was accompanied by recurrent respiratory infections. He developed varicella at 5 years but recovery was uneventful. At presentation to our hospital he had eczema and multiple wart-like papules. Examination of nails, mucosae, and hair was unremarkable. Systemic examination was normal. In view of clinical history of recurring infections, an immunodeficiency disease was suspected. Serology for Human Immunodeficiency Virus (HIV) was non-reactive. Immunological investigations showed normal levels of IgG, IgA and IgM; serum IgE was 1449 kU/L; absolute eosinophil count: 1.2 $X10^6$/L, mild decrease in CD3+ T cells (48%) with normal CD4/CD8 ratio (1.95; normal: 0.9-3.4); increased expression of HLA-DR on CD3+T lymphocytes. Serology for cytomegalovirus, Epstein–Barr virus, and Parvovirus was negative. Skin biopsy revealed epidermodysplasia verruciformis. These clinical findings were consistent with a phenotype of DOCK8 deficiency. Next generation sequencing confirmed (a novel) mutation in DOCK 8 gene (exon 23, c.2843c>g; p.ser948ter). He was initiated on monthly immunoglobulin replacement therapy (400 mg/kg/month) and trimethoprim-sulphamethoxazole prophylaxis and is awaiting investigations for hematopoietic stem cell transplantation.



Learning Points/Discussion

Warts associated with viral infections are usually benign and self-limiting. However, when these are extensive and associated with other infections an underlying primary immunodeficiency disorder should be looked for.

ESPID19-0874
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Valley fever in an immunocompromised host

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Background

The differential for pulmonary nodules in an immunocompromised host is broad and dependent on a detailed exposure and travel history. Coccidioidomycosis, or Valley Fever, is endemic to the southwestern US and parts of Central/South America. Endemic mycoses are increasingly recognized in those receiving anti-TNF therapy, due the critical role TNF-alpha plays in immunity against intracellular pathogens including fungi. Here, we describe the case of pulmonary coccidioidomycosis in a patient with remote history of travel to an endemic region, who presented 3 years later with pulmonary disease.

Case Presentation Summary

An 18-year-old male with anti-phospholipid antibody syndrome and ulcerative colitis on infliximab therapy presented with 2-day history of dyspnea, chest pain, and dry cough. He denied fevers, weight loss, night sweats or hemoptysis. Chest CT was obtained to exclude pulmonary embolism which instead revealed pulmonary nodules in the left lower lobe. He had traveled to San Diego, CA 3 years prior, and lived in Argentina in early childhood. A BAL revealed 94 WBC: 67% lymphocytes, 7% monocytes, 17% eosinophils. Cytology was negative, including silver stain for PJP. Histoplasma,IGRA, HIV and Paracoccidioides testing was negative. Coccidioides IgG returned positive by ELISA, confirmed with complement fixation. Due to ongoing immunosuppressive therapy, treatment was started with fluconazole for 6-months, without recurrence to date.

Learning Points/Discussion

- This case highlights the need for a detailed exposure history in an immunocompromised patient with pulmonary nodules, particularly those receiving TNF-alpha inhibitors like infliximab.
- Optimal diagnosis of Coccidioidomycosisis is by a combination of ELISA and complement fixation.
- Due to the dissemination risk, treatment is indicated for any symptomatic patient with need for ongoing immunosuppression; including oral azoles for mild-moderate infection with IV amphotericin or higher dose fluconazole indicated for more severe cases.

ESPID19-0862
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Respiratory microbiota, local cytokine response and respiratory viral infections in children with cancer undergoing hematopoietic stem cell transplantation

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Background

There are few data related to clinical outcome of respiratory viral infections(RVI) in children undergoing hematopoietic stem-cell transplantation(HSCT) and no information regarding the role of the respiratory microbiota as a possible factor of severity. We compared respiratory microbiota composition and local cytokine response among children with HSCT during a febrile episode with and without RVI.

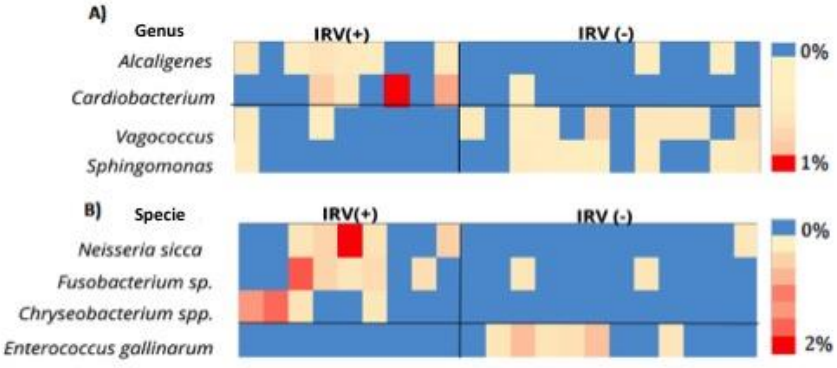
Methods

Prospective study, children with cancer and HSCT admitted for fever at Hospital Calvo-Mackenna (September 2017-August 2018). Children were evaluated clinically, with laboratory tests, microbiological cultures, nasal lavage (study of 38 cytokines by Luminex®), nasopharyngeal swab (20 respiratory pathogens by Filmarray-Respiratory-Panel®) and pharyngeal swab (respiratory microbiota by 16S-rRNA-sequencing, PacBio-MrDNA®-USA). Pharyngeal samples were obtained from a control healthy group. Clinical variables from admission to discharge were obtained, being classified into two groups (RVI(+);RVI(-)). Study was approved by the IRB.

Results

Twenty-one febrile episodes were enrolled, 12 RVI(+)(57%) and 9 RVI(-). Median-age was 7.6 years, 11(52%) male. Virus detected were: rhinovirus(7),coronavirus(3),RSV(1) and parainfluenza(1). The median hours of fever on admission was 1hr. At discharge,11/12 RVI(+) children had diagnosis of respiratory infection (50% were lower-tract infection) and only one case in RVI(-) group($p < 0.0001$). There were no differences in the days of fever, days of hospitalization, days of antibiotic and cytokines between both groups. Significant differences were observed in respiratory microbiota; *Vagococcus* and *Sphingomonas* were indicative of RVI(+), as same as *Neisseria sicca*, *Fusobacterium sp* and species associated with *Chryseobacterium*, at species

level.



Conclusions

Unlike local cytokines, respiratory microbiota did allow to find significant differences in its composition, with indicative species for RVI(+) and RVI(-) groups. This first report could help for a better characterization of the risk and severity of RVI in children with cancer and HSCT (FONDECYT#1171795).

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0773
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Complicated osteomyelitis caused by salmonella species in children with sickle cell disease

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[7]Evelina London Children's Hospital- Guy's & St. Thomas NHS Foundation Trust- London- United Kingdom, Department of Cardiac Surgery, London, United Kingdom
[8]UCL Great Ormond Street Institute of Child Health- University College London, Department of Infection- Immunity & Inflammation, London, United Kingdom

Background

Osteomyelitis is an uncommon but important disease in childhood. Unlike in the general paediatric population, non-typhoid salmonella (NTS) species are major causative pathogens of osteomyelitis in children with sickle cell disease (SCD). The high susceptibility of SCD patients for NTS osteomyelitis is poorly understood, but asplenia, impaired blood circulation and excess iron are thought to contribute. Early diagnosis and appropriate management are key, particularly as distinguishing between bone infarction and infection is often a major challenge in this vulnerable patient group.

Case Presentation Summary

We report 3 cases of NTS osteomyelitis in children with SCD we encountered over the last 6 months. Patient 1, an 8-year-old boy with osteomyelitis of the sternal manubrium and a left anterior chest wall collection. Patient 2, a 14-year-old girl with extensive osteomyelitis of the right femur. Patient 3, a 7-year-old girl with multifocal osteomyelitis affecting the right scapula, both tibiae and tali bones. All patients presented with high-grade temperatures and markedly elevated CRP levels (> 150 mg/L). Only patient 2 had a recent travel history (Uganda). Salmonella species were detected by pan-bacterial 16s PCR (patient 1), and isolated from pus (patient 2 [*S. enteritidis*] and 3 [*S. typhimurium*]) and blood cultures (patient 3). All patients required 2 or more surgical interventions and antibiotic treatment for longer than 6 weeks, guided by inflammatory markers and clinical improvement.

Learning Points/Discussion

All 3 cases showed delayed response to antibiotic treatment and required multiple surgical interventions, highlighting the severity of NTS osteomyelitis in young SCD patients. Early diagnosis, multidisciplinary management and aggressive treatment are key to improving disease outcomes. Treatment duration and tools for disease monitoring are poorly-defined in this patient group, and require further research.

ESPID19-0744
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Immunoglobulin substitution in paediatric patients with haematologic malignacies and solid tumors

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Background and Aims:

In paediatric haemato-/oncologic patients, underlying diseases and cytotoxic chemotherapy may lead to B-cell-deficiency with consecutive low immunoglobulin (IG) levels. While substitution of IG (if necessary) is commonly recommended for patients with haematologic malignancies, risk of hypoimmunoglobulinaemia in patients treated for solid tumors remains unclear.

Methods:

IG-serum-levels were routinely measured in all children receiving cytotoxic chemotherapy for haemato-/oncologic diseases and IG were administered intravenously (IVIG, 0.4-0.5g/kg) if levels were below age-dependent normal range. We retrospectively analysed IG-levels and IVIG-substitutions in patients treated with cytotoxic chemotherapy from 2006 to 2017 and compared IG-levels and rate of IVIG-substitutions between patients treated either for haematologic malignancies (HAEM-group) or for solid tumors (SOLID-group) using Mann-Whitney-U-Test and Fisher-Exact-Test.
Patients with primary immune deficiency or secondary malignancies as well as recipients of autologous and allogeneic stem cell transplantation were excluded.

Results:

Between HAEM-group (n=181, age at initial measurement: 0.0-26.9, median 9.4a, 43.1% female) and SOLID-group (n=218, 0.2-32.5, median 10.3a, 47.5% female), there were no statistically significant differences in initial IG-levels.
While 142/181 (78.5%) patients in the HAEM-group received IVIG, only 78/218 (35.8%) received IVIG in the SOLID-group ($p<0.00001$). Additionally, numbers of administered IVIG-substitutions per patient were significantly higher in the HAEM-group (0-22, median 3) compared to the SOLID-group (0-10, median 0, $p<0.0001$).
Minimal measured IG-levels (which had partly been affected by prior IVIG-substitutions) were significantly lower in patients of the HAEM-group (2.3-19.4, median 9.2 vs. 0.7-16.8, median 6.5 g/l, $p<0.0001$).

Conclusions:

Our retrospective study clearly underlines the frequency of hypoimmunoglobulinaemia in patients with haematologic malignancies, while in contrast only one third of patients treated for solid tumors showed IG levels below the normal range.

Systematic Review Registration:

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ESPID19-0694
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Invasive renal fungal infections in preterm- report on 3 cases

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"Louis Turcanu" Emergency Hospital for Children, Pediatrics, Timisoara, Romania
[2]University of Medicine and Pharmacy "V. Babes" Timisoara-
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Background

Preterm newborns have immature immune systems; there is a reduced production of cytokines which limits T cell activation that explain the increased risk of infection. Invasive fungal infections in preterm is more common and can lead to sever multiorgan affection with poor outcome. Aim: We present 3 cases with atypical urinary fungal infections.

Case Presentation Summary

Case 1: Triplet II born at 28 weeks referred from the Neonatal unit with clinical picture of acute abdomen at the age of 2 weeks. Imaging was inconclusive therefore he proceeded to an exploratory laparotomy, where a diagnosis of urinary ascites was made. Candida albicans infection was confirmed on urine culture. He was treated with antifungals and made a full recovery. Case 2: Triplet I presented to ED one month later with symptoms of respiratory infection. Commenced on empirical antibiotic medications but clinically deteriorated. Urine culture was positive for fungal infection so antifungal medication was commenced as well. Ultrasound scan demonstrated a right perinephric urinoma. This was drained percutaneously. Case 3: Preterm who received antibiotherapy for 3 weeks and developed fungal pyelonephritis with typical image on ultrasound, urine culture was negative but also with a good response after antifungal therapy.

Learning Points/Discussion

Fungal ball formation in urinary tract can cause obstruction leading to extravasation. Extravasation of urine and formation of urinoma is rare. Conclusions: Invasive fungal infections in preterm are common and extremely difficult to diagnose.Empirical treatment with antifungal therapy should be considered in high-risk, low-birth-weight infants who fail to quickly respond to empirical antibacterial treatment. Risk factors to consider when deciding to administer empirical antifungal therapy include: prior exposure to antibiotics, extreme prematurity, long term hospitalisation.

ESPID19-0664
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Invasive sinusitis caused by tropicoporus tropicalis in a patient with acute lymphoblastic leukaemia

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Background

Tropicoporus tropicalis, a filamentous basidomycete is a common environmental organism and a rare human pathogen, seen predominantly in patients with Chronic Granulomatous Disease. Species identification and susceptibility testing of basidiomycetes can be difficult and may delay appropriate management. Here we report a case of invasive sinus disease from *Tropicoporus tropicalis* identified via molecular diagnostic techniques in a patient with Acute Lymphoblastic Leukaemia (ALL).

Case Presentation Summary

A 16-year-old girl with medullary relapsed ALL developed headache, eyelid oedema and erythema while receiving piperacillin-tazobactam and caspofungin for prolonged febrile neutropenia. CT-orbits showed left sided sinus disease with pre-septal and anterior orbital cellulitis. Antimicrobials were escalated to amphotericin, voriconazole, meropenem and vancomycin. Urgent debridement revealed extensive invasive disease. Abundant septated hyphae with angioinvasion were seen at frozen section. Due to invasion into the skull base, complete debridement was unattainable. She was treated with granulocyte infusion, voriconazole and amphotericin. Mould grew on culture at 72 hours. Phenotypic characterization combined with DNA sequencing identified *Tropicoporus tropicalis* (formerly *Inonotus tropicalis*). The patient underwent three additional surgical debridements until the first negative culture was obtained after 7 weeks of amphotericin and voriconazole. She showed marked clinical improvement and was discharged home on therapy.

Learning Points/Discussion

To our knowledge, this is the first case of invasive sinus disease caused by *Tropicoporus tropicalis* in a patient with a haematological malignancy. The timely diagnosis via molecular methods was critical in preventing a possibly fatal outcome. Disease control was ultimately achieved through aggressive surgical debridement and targeted antifungal therapy.

ESPID19-0662
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Analysis of a protocol of febrile neutropenia in a referral center for pediatric oncology in latin america

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[1]Federal University of Sao Paulo, Pediatric Department, Sao Paulo, Brazil
[2]Institute of Pediatric Oncology - Federal University of Sao Paulo/GRAACC, Hospital Infection Control Center, Sao Paulo, Brazil

Background and Aims:

Fever during chemotherapy-induced neutropenia may be the only indication of a severe underlying infection, because signs and symptoms of inflammation typically are attenuated. In this context, several institutions adopt risk stratification to guide conduct. So, our aim was to check the protocol adopted in our institution regarding risk stratification and patient outcomes.

Methods:

We conducted a prospective study using data of medical records of patients between 0 to 21 years with febrile neutropenia (FN) treated at a referral center of pediatric oncology in Brazil, from January 2017 to June 2018. Patients classified as low risk (LR) were treated as outpatients with oral or intravenous therapy and those at high risk (HR) were hospitalized and performed intravenous therapy.

Results:

In this period, there were 553 patients with 575 FN episodes, with 384/575 episodes classified as HR (66.8%) and 191/575 LR (33.2%). Of those classified as HR, 205/384 were fever of unknown origin (FUO) (53.4%), 89/384 microbiologically documented infections (MDI) (23.2%), 74/384 clinically documented infections (CDI) (19.3%) and 16/384 were MDI and CDI (4.2%). Of those LR, 141/191 were FUO (73.8%), 28/191 MDI (14.6%), 21/191 CDI (11.0%) and 1/191 MDI and CDI (0.5%). When comparing the groups, FUO were most observed in the LR group and MDI, CDI and MDI/CDI in the HR group ($p<0.001$). There were 15/575 deaths (2.6%), being that 14 were HR (93.3%) ($p=0.034$).

Conclusions:

In conclusion, HR group evolved more to documented infections and death than LR group and the mortality found was in accordance with that reported in the literature. These findings make us think that the risk stratification protocol adopted in our institution is in good assessment of the main risk factors for unfavorable outcomes in these patients.

Systematic Review Registration:

N/A

ESPID19-0635
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Brain abscess due to e. Coli in a very preterm infant

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Background

Immature immune system exposes preterm infants to infections. *E. coli* is one of the two predominant pathogens, causing several neonate affections (congenital pneumonia, necrotizing enterocolitis, meningitis and sepsis). We here report a *E. coli* brain abscess in a preterm infant - an unusual complication for which only three other cases are described in literature. Moreover, *E. coli* resistance to Ampicillin and Gentamicin is increasing, and we observed a resistance to Amikacin which is exceptional and must alarm us.

Case Presentation Summary

A 24 week old preterm infant presented a sepsis and intestinal perforation on day 5 of life. Abdominal surgery and antimicrobial therapies were provided (Vancomycin from day 5 to 6, Cefotaxime and Metronidazole from day 5, Amikacin from day 6 and Diflucan from day 9). Despitefully he developed a brain abscess on day 9 of life. Cultures of three samples (blood, intestine and brain abscess) revealed the presence of an *E.coli*. However, there was no sign of meningitis - the cerebrospinal fluid was negative. Antimicrobial susceptibility was marked by an intermediate resistance to Amukin (I 16.00) and a resistance to Ampicillin (R>32.00) and Gentamicin (R 8.00). Support cares were stopped the same day because of clinical signs of coma.

Learning Points/Discussion

First, *E. coli* is a major pathogen during the neonate period causing death of up to 33% of infected preterm infants. Second, brain abscess can complicate *E. coli* sepsis. Third, antibiotic resistance should always be considered during cares to the patient.

ESPID19-0563
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Outcome and infectious complications of t-cell depleted haploidentical hematopoietic stem cell transplantation in patients with familial hemophagocytic lymphohistiocytosis in oman

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Background and Aims:

Familial hemophagocytic lymphohistiocytosis (HLH) is a fatal disorder of immune regulation, that is curable by allogeneic hematopoietic stem cell transplantation (HSCT). T-cell depleted (TCD)-haploidentical HSCT could be a viable option when matching sibling donor is not available. Unfortunately, serious infections and disease relapse resulting from delayed immune reconstitution remain the 2 most frequent causes of mortality and morbidity. We report on the outcome of TCD- haploidentical HSCT for HLH in Oman.

Methods:

This is a retrospective report of 12 HLH pediatric patients transplanted in Sultan Qaboos University Hospital between Aug 2010- Dec 2018. Data were collected from electronic patient records, and included epidemiological, clinical characteristics, transplantation details and outcome. Detailed data on different infectious complications (bacterial, viral, fungal) were collected, focusing on CMV infection.

Results:

Out of the twelve patients included, seven patients (58.3%) were cured, four patients expired, and one patient had primary graft failure

Three patients died due to Gram negative sepsis ± candidemia/ invasive aspergillosis. Adenoviremia was detected in two patients, and viral gastroenteritis in four (adenovirus, norovirus, and astrovirus). CMV viremia was detected in 9/12 patients (75%), their viral load ranged 72-296370 copies/ml, starting from day 2 post transplantation. Two patients developed CMV end organ disease (enteritis and retinitis), while the rest had asymptomatic viremia. Successful treatment with Foscarnet/ganciclovir was achieved.**Conclusions:**

TCD- haploidentical HSCT for HLH had survival rate comparable to other transplantation types. Gram negative sepsis accounted for most deaths. Although CMV viremia was frequently encountered, monitoring and preemptive treatment resulted in no CMV related mortality.

Systematic Review Registration:

N/A

ESPID19-0559
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

A frequently sick child – when should we consider a primary immunodeficiency?

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Background and Aims:

Recurrent infections are main features of primary immunodeficiencies (PID). Early diagnosis can decrease frequency of infections and improve quality of life.

Methods:

Retrospective prospective study had been carried out at Ternopil Regional Children's Hospital, Ukraine during 2016-2017. Clinical and laboratory profiles of children up to 18 years diagnosed with PID were investigated.

Results:

The study includes 30 PID cases: 16 males, 14 females. PID with syndromic features were most common (15 cases/50%), including: Nijmegen breakage syndrome; Di George syndrome (6 cases of each); ataxia-teleangiectasia (2 cases); hyper IgE syndrome (1 case). Antibody deficiencies were diagnosed in 4 patients (13.3%): X-linked agammaglobulinaemia, selective IgA deficiency, common variable immunodeficiency, IgG subclasses deficiency. PFAPA syndrome was diagnosed in 8 patients. Leukocyte adhesion deficiency syndrome type I, congenital neutropenia, and chronic granulomatisis disease were diagnosed in 1 case each.

In half of the patients, the infectious syndrome presented as recurrent sinopulmonary infections: pneumonia (10/33.3%), bronchitis (8/26.7%), sinusitis (5/16.7%). Recurrent otitis was observed in 3 cases; and pharyngitis in 9 cases, mostly in the patients with PFAPA syndrome. Skin infections occurred in 4, lymphadenitis in 3 cases. Aphtous stomatitis was observed in 7 cases. Urinary tract infections were reported in 3 cases, intestinal infections in 2 cases. Deep-seated infections (septicemia, encephalitis, osteomyelitis) occurred in 3 cases. Recurrent respiratory viral infections we observed in 5 cases. In 12 cases recurrent infections were associated with recurrent fever, in 7 cases with chronic anemia, and in 7 cases with delayed physical development.

Conclusions:

Recurrent sinopulmonary infections are the most common type in patients with PID with syndromic features and antibody deficiencies. Cases of recurrent infections associated with chronic anemia and/or delayed physical development should also suggest PID.

Systematic Review Registration:

5jpKtIb8fY2hSAzGMA2EbQfOQUWb

ESPID19-0522
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Paradoxical reaction in an immunocompetent child with tuberculous meningitis

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Background

Paradoxical reactions in tuberculosis are defined by a clinical and/or radiological worsening pre-existing tuberculous lesions or by the development of new lesions during appropriate treatment. In some series, such paradoxical reactions may happen in up to 23% of cases in immunocompetent patients.

Case Presentation Summary

A 3-year and 10-month old girl, HIV seronegative was admitted for tuberculous meningitis with pulmonary and cerebral lesions. The diagnosis was made by PCR detection of M tuberculosis in the cerebrospinal fluid. M tuberculosis cultures were negative. Therefore, no antibiotic susceptibility testing was obtained. Antituberculous therapy consisting of 5 drugs (Induction therapy: pyrazinamid, isoniazid, levofloxacin, rifampicin and ethambutol), as well as corticosteroids (methylprednisolone) during the first 8 weeks of treatment. Her physical and neurological exams improved during the first weeks of therapy.On the 46th day of treatment, a routine ophthalmologic exam revealed visual acuity loss of the right eye. The cerebral MRI demonstrated a new lesion on the optic chiasma whereas the preexisting lesions were improved. High doses of corticosteroids were re-administered and a surgical excision was performed. The biopsy of the lesion was compatible with a tuberculom and the PCR was poorly positive for M tuberculosis. The culture was again negative. After 4 months of the initial treatment, it was switched to isoniazid and rifampicin for a total duration of one year. Currently, 5 months after the diagnosis of tuberculous meningitis, the patient has excellent general state but has not recovered right eye vision.

Learning Points/Discussion

This case emphasizes that tuberculosis paradoxical reaction can occur under a well carried out treatment. However, given the relative rarity of this phenomenon, paradoxical reaction remains an exclusion diagnosis with no consensus on its management.

ESPID19-0413
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Opsonophagocytic activity of commercially available intravenous immunoglobulin preparations against group b streptococcus

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Background

Group B Streptococcus (GBS) is a major cause of sepsis and meningitis. In the immunocompromised, invasive diseases could be developed by infrequent serotypes such as IV, VI to IX; however, opsonophagocytic activities against these serotypes are unknown. Intravenous immunoglobulin G (IVIG) therapy is used to prevent invasive infections in patients with primary antibody deficiency (PAD). This study aimed to evaluate opsonophagocytic activity against GBS in IVIG preparations.

Methods

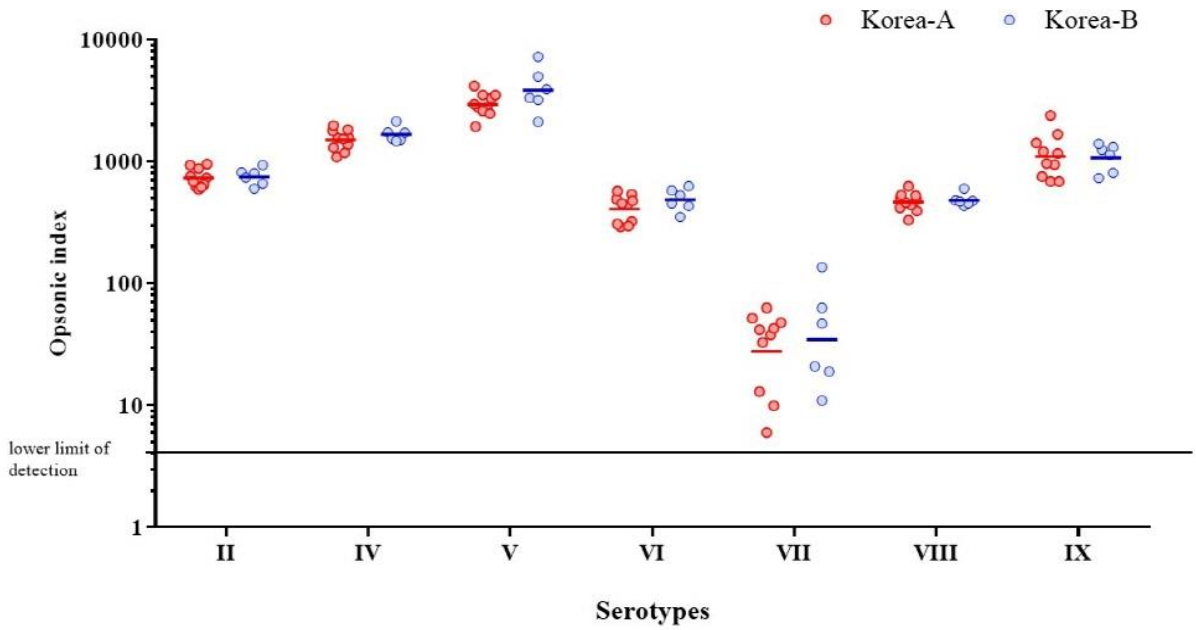
Sixteen lots of IVIG, collected from two manufacturers in Republic of Korea, were evaluated. Opsonophagocytic activity (opsonic index [OI]) against seven GBS serotypes (II and IV to IX) was evaluated via the opsonophagocytic assay using HL-60 cells and baby rabbit complement (UAB GBS OPA, at http://www.vaccine.uab.edu).

Results

Opsonophagocytic activity against GBS in various IVIG preparations are shown in Figure 1. The estimated trough levels of OIs against GBS exceeded the limit of detection in most IVIG preparations, except for serotype VII. Upon estimating trough levels of IVIG, the usual IVIG dose (400 mg/kg) was

appropriate for immunocompromised individuals to prevent severe GBS infections.

Figure 1. Opsonic indices against group B streptococcus in various intravenous immunoglobulin products



Conclusions

Opsonophagocytic activity against GBS in various IVIG preparations are shown in Figure 1. The estimated trough levels of OIs against GBS exceeded the limit of detection in most IVIG preparations, except for serotype VII. Upon estimating trough levels of IVIG, the usual IVIG dose (400 mg/kg) was appropriate for immunocompromised individuals to prevent severe GBS infections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0394
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Fatal pasteurella multocida in a patient with cirrhosis

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Background

Pasteurella multocida is a commensal of the upper respiratory tracts of mammals and birds. Although usually causing skin/soft tissue or bone/joint infections, *P. multocida* has been described to cause serious invasive infections in immunocompromised hosts even without a known bite or scratch from an animal. We report a patient who presented with septic shock as a result of *P. multocida* bacteremia, presumably from close contact with pet dogs' saliva.

Case Presentation Summary

A 23-month-old male with Transaldolase Deficiency and associated cirrhosis, coagulopathy, hepatosplenomegaly and thrombocytopenia presented with increased work of breathing, non-bloody, non-bilious emesis, and fever to 101.4°F. Sick contacts included mother with a runny nose. No exposure to farms or petting zoos, and no recent travel. He had two dogs and a fish at home. Liver function tests were at baseline. WBC was 3.9 $x10^3$/mcL [4.86-13.18] with 69% neutrophils. CXR was notable for an enlarged heart and hazy opacities throughout. Viral respiratory panel was positive for coronavirus and rhinovirus. Echocardiogram was within normal limits. He was started on piperacillin-tazobactam given concern for cholangitis. Liver ultrasound was at baseline. Blood cultures grew *P. multocida* and the patient was narrowed to ampicillin-sulbactam. Given impaired liver synthetic function, complement studies were sent: CH50 was 0 units/mL [150-250], C3 was 48 mg/dL [83-174], C4 was 12.5 mg/dL [16-45]. He developed worsening respiratory distress with multisystem organ failure. He ultimately died of recurrent pulmonary hemorrhage 1-month after admission.

Learning Points/Discussion

Pasteurella multocida serves as an opportunistic pathogen in humans, especially in patients with depressed immune systems. *P. multocida* should be included in the microbiologic differential diagnosis in patients with underlying chronic liver diseases as an important and potentially lethal pathogen, even without a history of significant exposure to animals.

ESPID19-0304
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Role of caspofungin therapy in candida haemulonii/auris candidemia in immunocompromised neonates

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Background

The incidence of hematogenous infections due to Candida specially non-albicans species among immunocompromised neonates has increased significantly in recent decade. The emerging fungal pathogens comprising the Candida haemulonii complex are notable for their antifungal resistance with higher mortality and morbidity. Caspofungin is effective, safe and well-tolerated as an alternative therapy for persistent and progressive candidiasis in these group of patients.

Case Presentation Summary

Material and methods
We here report our experience of caspofungin therapy in four cases of neonatal fungemia caused by C haemulonii. All the isolates were recovered in BACTEC Peds plus/F culture vials. Species identification was done in VITEK 2 yeast ID system followed by PCR based molecular methods and MALDI-ToF mass spectrometry-based assay. All of these isolates of C.haemulonii were resistant to amphotericin B and azoles but sensitive to caspofungin.

Results

In all the 4 cases clinical and microbiological cure were possible.

The dosage of caspofungin was 2 mg/kg/day, and the mean treatment duration was 14 days and the mean duration of antifungal therapy was 21 days.

2 out of the 4 patients had multifocal multidrug resistant (MDR) colonization and had history of azole exposure.

	Gender	Birth Weight (Kg)	Total Leukocyte Count & CRP	Total Platelet Count ($*10^9$)	Previous Bacteria isolated& Antibiotic Administered	Organism Isolated
Patient 1	**Female**	**1.8**	**16000/42.3**	**170**	**K.Pneumonnia inj Meropenam**	**C.haemulonii**
Patient 2	**Female**	**2.3**	**12500/16.3**	**220**	**E.Faecalis Inj. Tiecoplanin**	**C.auris**

Patient 3	**Male**	**0.94**	**26000/88.6**	**43**	**K.Pnemonnia Inj Polymixin E**	**C.haemolinii**
Patient 4	**Female**	**1.3**	**13800/74.4**	**193**	**Stenotrophomonas Maltophilia Inj. Minocycline**	**C. haemulonii**

Learning Points/Discussion

The resistance of C. haemulonii represents therapeutic challenge in treatment of invasive candidiasis in neonatal patients.Caspofungin therapy is well tolerated, safe and effective in neonatal resistant C. haemulonii infections.This drug should be further investigated amongst selected population.

ESPID19-0228
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Late onset group b streptococcal sepsis in a neonate with intra-uterine rituximab exposure in the second trimester of pregnancy

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Background

Rituximab is a chimeric monoclonal antibody that binds to anti-CD20 antibody, causing sustained depletion of peripherally circulating $CD20^+$ B cells[1]. There is limited data on its use in pregnancy. Late Onset Group B Streptococcal (GBS) infection is a known, but rare, complication in preterm infants, with a reported incidence of 1.4 per 1000 live births [2].

Case Presentation Summary

Infant B was born at 30+2 weeks gestation, weighing 1.59kg. Maternal history was significant for scleroderma, with cardiac and renal involvement, necessitating rituximab infusions. Most recent dose given at 18 weeks gestation. Maternal testing did not identify GBS carriage.

The infant was in good condition on delivery and initial neonatal course was uneventful, respiratory support was rapidly weaned, and he began to tolerate full enteral feeds. On DOL 30 lymphocyte subsets demonstrated normal B cell subsets, however, immunoglobulin levels found a low IgG level, at 1.88 g/l (2.4-8.8).

The infant became unwell on DOL 35 with an acute clinical de-compensation requiring cardio-pulmonary resuscitation. Respiratory support was initiated and intravenous antibiotics were administered. GBS was isolated from blood culture and a diagnosis of late onset GBS sepsis was made. He received 10 days of antibiotics and recovered well, and was discharged home on DOL 54.

Learning Points/Discussion

The estimated median terminal elimination half-life of rituximab is 18-22 days. Active drug has been detected in peripheral blood beyond 24 weeks after the last infusion in some patients, and has been known to deplete B cell numbers and cause hypoglobulinemia in infants[1]. While trans-placental transfer of rituximab at 18 weeks gestation is relatively low, and transient neonatal hypogammaglobulinemia is reasonably common, we cannot out-rule that hypogammaglobulinemia in this infant may have contributed to development of GBS sepsis[3].

ESPID19-0070
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in immunocompromised patients

Cytomegalovirus retinitis during maintenance chemotherapy for acute leukemia

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Background

Cytomegalovirus (CMV) disease in children who receive anticancer chemotherapy and have not undergone stem cell transplantation is not well recognized.

Case Presentation Summary

This case was a 7-year-old boy who was on maintenance chemotherapy for acute lymphoblastic leukemia with a chief complaint of fever and decreased visual acuity. About three months prior this presentation, persistent pancytopenia was found during the evaluation of neutropenic fever. Fever and pancytopenia did not improve despite empirical intravenous antibiotics. Bone marrow biopsy was done but there was no relapse. Two months prior, he started to complain about decreased visual acuity but his parents did not report it to his doctor. CMV antigen of 51/200,000 WBC was first detected and CMV antigenemia rose to 170/200,000 WBC 3 weeks later. On ophthalmological exam, multiple retinal infiltration and granular like lesion were found in both eyes. CMV retinitis was diagnosed and he was treated with intravenous ganciclovir for 4 weeks and intravitreal injection of ganciclovir three times, followed by oral administration of valganciclovir. CMV antigenemia became negative and retinal infiltration improved on follow-up fundoscopy.

Learning Points/Discussion

To our knowledge, CMV disease in children with hemato-oncologic diseases receiving chemotherapy is not well studied. Future studies should address the need of standardized screening and appropriate strategies for preemptive therapy in children at high risk.

ESPID19-0893
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in paediatric oncology and HSCT patients

Chemotherapy-induced febrile neutropenia. Germ isolation and experience in a tertiary hospital

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Background and Aims:

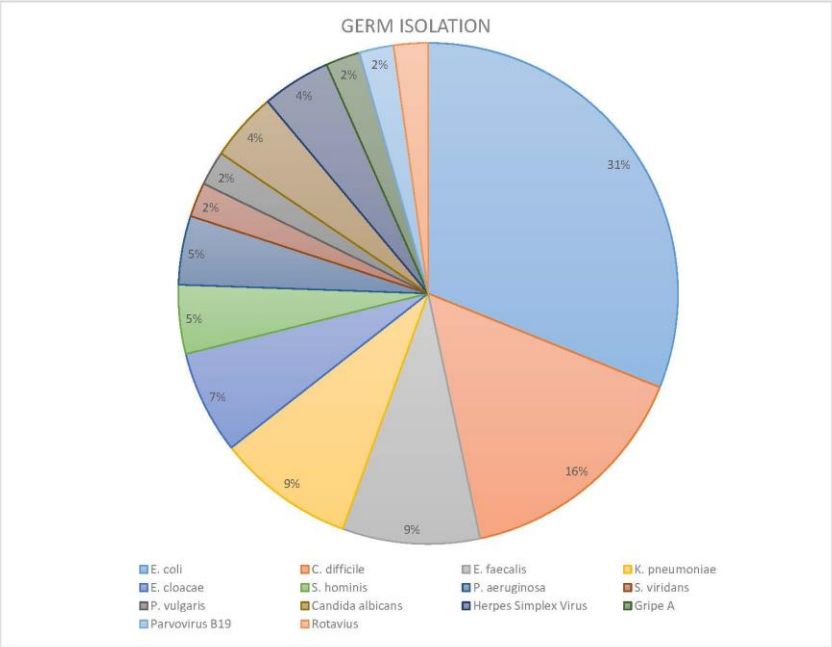
Infections are an important cause of morbidity and mortality in cancer patients (mortality is estimated around 3%). Febrile neutropenia often leads to hospitalization of cancer patients, increasing the risk of nosocomial infection as well as health costs.

Methods:

Retrospective(01/07/2015-31/12/2017) and prospective(01/01/2018-31/12/2018) observational study of all episodes of chemotherapy-induced febrile neutropenia in pediatric population. We collected age, gender, length of stay(days), temperature(ºC), germ isolation, infectious source, antibiotic or antifungal prophylaxis, hemoglobin(g/dl), platelets(/mm3), neutrophils(/mm3), lymphocytes(/mm3), monocytes(/mm3), CRP(mg/L) and procalcitonin(PCT)(ng/ml) on admission and days with neutropenia<500/mm3. Statistical analysis was made with the SPSSv.23 program.

Results:

Of 69 patients, 101 episodes were recorded. Germ isolation was found in 44,6% of the episodes, and no infectious source identified in 36% of them. The most common isolations were(in order) *E. coli, C. difficile, E. faecalis and K. pneumoniae.* 5 of the isolations(11,1%) were identified as Extended Spectrum Beta-Lactamase (ESBL) infection. There is not statistical difference between isolations in relation to gender or antibiotic prophylaxis. The length of stay was longer in those patients with known microorganism(9,6 vs 5,59 days,p0,004). It was also longer in those patients with ESBL isolation(12,6 vs 9,23 days,p0,029). The number of days with neutropenia<500/mm3 was higher in those children with E. faecalis isolation(9,25 vs 3,57,p0,008).



Conclusions:

The percentage of germ isolation in our study was slightly higher than the published data(10-40%). The infectious source was similar to the published data. All ESBL isolations were *E. coli*, and the proportion was higher than the average in our area(9,2%), which can be used to choose the empiric antibiotic therapy. In those patients with germ identification the average length of stay was longer, as in those with ESBL isolation, which increases the risk of nosocomial infection.

Systematic Review Registration:

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ESPID19-0724
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in paediatric oncology and HSCT patients

The primary infection and reactivation of hhv-6 and hhv-7 after hsct in children

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Background

The purpose of our study was to evaluate the frequency of primary infection or reactivation of HHV-6 and HHV-7 in children with leukemia following HSCT.

Methods

12 children (4 months -11 years) with leukemia were recruited in the study at Raisa Gorbacheva Memorial Research Institute of Children Oncology, Hematology and Transplantation, Saint-Petersburg, Russia. We used PCR of plasma and IgG before and on the days +14, +24 and +30 after HSCT.

Results

The PCR of plasma of all patients before HSCT was negative. Four patients had IgG to HHV-6 and four had IgG to HHV-7. Six patients were seronegative to both HHV-6 and HHV-7.

On day +14 we found seroconversion to HHV-6 in two patients (primary infection) and the reactivation of HHV-6 (PCR +, genotype B, Lg 5,0/ml).

On day +24 seroconversion to HHV-7 was found in one patient (primary infection) and one primary HHV-6 infection (PCR+, genotype B, Lg 4,6/ml).

On day +30 we found one primary HHV-6 infection (PCR+, genotype B, Lg 3,1/ml).

All patients with HHV-6 and HHV-7 infections had fever and neutropenia. No one of patients did not experience of encephalitis.

Conclusions

The examination on the HHV-6 and HHV-7 after HSCT is not routinely perform. Our small survey shows that the reactivation and primary infection of these viruses are very often after HSCT among pediatric patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0650
E-Poster Viewing - May 7-10 - E-Poster Hours

Infections in paediatric oncology and HSCT patients

Blood culture isolates considered as contaminants in immunocompromised children - a retrospective single centre study

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Background and Aims:

Blood culture (BC) isolates are the cornerstone of appropriate antibiotic treatment. However, BCs can become contaminated. There are no current guidelines to identify which organisms isolated in blood cultures, should be considered contaminants in immunocompromised children. The aim of this retrospective study was to review the management and clinical outcome of patients with BC isolates considered as contaminants.

Methods:

Positive blood cultures were identified from patients admitted to a London tertiary hospital, under the paediatric haematology, oncology and immunology/ID teams between 01/08/2013 and 01/08/2018. Clinical and microbiological data were collected for each episode. A contaminant was defined when; there was lack of correlation with clinical picture and ≥1 of: i) repeat BC was negative or ii) no targeted treatment was prescribed.

Results:

There were 371 positive cultures (102 patients), with 53 episodes (24 patients) presumed contaminants (14.4%). In 28% of contaminated BC, repeat BC grew a different isolate. Isolates are showed in Figure1.

Median age was 4 years, 51% males. Underlying conditions included: 29 acute leukaemia (26 ALL, 3 AML), 9 solid/CNS tumours, 10 relapsed malignancies, 2 aplastic anaemia. Central venous catheters were present in 93%.

Median number of antibiotic therapy days was 2 (0-7). No treatment was given for 38% episodes and no central lines were removed. There were no deaths.

Conclusions:

There is no consensus on which organisms are considered as contaminants amongst immunocompromised populations, who have additional risk factors including indwelling catheters and oral and gut microbial translocation. A total of 86% of positive BCs in immunocompromised children were considered pathogenic, and of the remaining 14%, no adverse outcomes occurred following our definition of contaminants.

Systematic Review Registration:

N/A

ESPID19-0789
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

Kawasaki disease shock syndrome - a case report

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Background

Kawasaki disease (DK) is a systemic acute-onset vasculitis of medium-sized vessels that primarily affects infants and young children. Today, DK is the most common form of primary vasculitis and the leading cause of heart disease acquired in children at risk for infarction and sudden death. Kawasaki Disease Shock Syndrome (KDSS) is defined as hemodynamic instability in the acute phase with sustained systolic hypotension and clinical signs of poor perfusion. We present a classic case of KDSS treated with criteria fulfilled associated with coronary dilatation in a paediatric patient.

Case Presentation Summary

A 5-month, previously healthy male patient was diagnosed with DK due to a 5-day fever, cutaneous rash, non-purulent bilateral conjunctivitis, oropharyngeal hyperemia, hand and foot edema and generalized lymphadenopathy with hepatomegaly. On the sixth day, the patient developed tachycardia, hypotension, flush perfusion and gemency, requiring volume expansion and orotracheal intubation. Acetyl salicylic acid and gammaglobulin were initiated, associated with intravenous antibiotic therapy due to the differential diagnosis of Toxic Shock Syndrome, which was discarded after evidence of coronary dilation at the first echocardiogram. He also presented resistance to the standard treatment with immunoglobulin presenting rash and maintenance of fever for 48 hours, being chosen by the second line treatment with good response (pulse therapy). The patient was discharged after 18 days of hospitalization, with echocardiogram maintaining coronary dilatation, but with improvement of mitral insufficiency.

Learning Points/Discussion

Patient presented a classic case and fulfilled criteria of KDSS associated with coronary dilation at an age lower than usual for this pathology. The main differential diagnosis (Toxic Shock Syndrome) was discarded during the evolution of the condition. He presented improvement to the treatment with Pulse therapy, after not having answer to the first line treatment (Immunoglobulina).

ESPID19-0636
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

Kawasaki disease shock syndrome: uncommon presentation of a not uncommon condition – a series of 3 cases

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Background

Kawasaki Disease Shock Syndrome (KDSS) is an unusually severe clinical presentation of KD. Its clinical characteristics include systolic hypotension and clinical signs of poor perfusion. We present 3 cases of children with KDSS.

Case Presentation Summary

Seventeen years old girl was admitted to hospital with fever and watery diarrhea. Her laboratory tests revealed high CRP, low platelets (PLT), anemia and prolonged INR. Her general condition deteriorated within 24 h with hypotension (70/25 mmHg) unresponsive to fluid resuscitation. She met all diagnostic criteria of KD and improved after intravenous immunoglobulin (IVIG) plus methylprednisolone administration, although she developed myocarditis subsequently.

Ten years old boy was admitted to hospital with fever, watery diarrhea, headache, meningeal signs, hypotension (86/39 mmHg) and all clinical signs of KD. Laboratory tests revealed high CRP, decreased PLT, prolonged INR and hypoalbuminemia. He received IVIG and methyprednisolone. In the convalescent phase we observed transient bradycardia and high troponin levels.

Eight years old girl was admitted to hospital with fever, watery diarrhea, vomiting and anuria. She had no clinical signs of KD. Her laboratory tests revealed high CRP, high creatinine (2.9 mg/dl), low PLT, high INR and leucocyturia. Initially she was suspected to have sepsis and treated with antibiotics, but her general condition deteriorated with persisting fever and severe general edema. She further presented „strawberry tongue." We diagnosed incomplete KD and started IVIG plus prednisone with prompt clinical improvement and no cardiologic complications.

Learning Points/Discussion

KDSS is a severe form of KD that can be easily confused with sepsis. The characteristic features of our patients with KDSS were: unusually „old age", hypotension, watery diarrhea and laboratory markers of coagulopathy. According to the newest guidelines by the SHARE initiative KDSS warrants initial co-administration of IVIG and glucocorticosteroid therapy.

ESPID19-1088
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

Refractory kawasaki disease: the slovenian experience

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Background

Children who fail initial immunoglobulin (IVIG) and corticosteroid therapy in Kawasaki disease (KD) have increased risk for coronary artery (CA) aneurysms.

We report 5 cases of IVIG and corticosteroid resistant KD treated at University Children's Hospital in Ljubljana between 2006 and 2018.

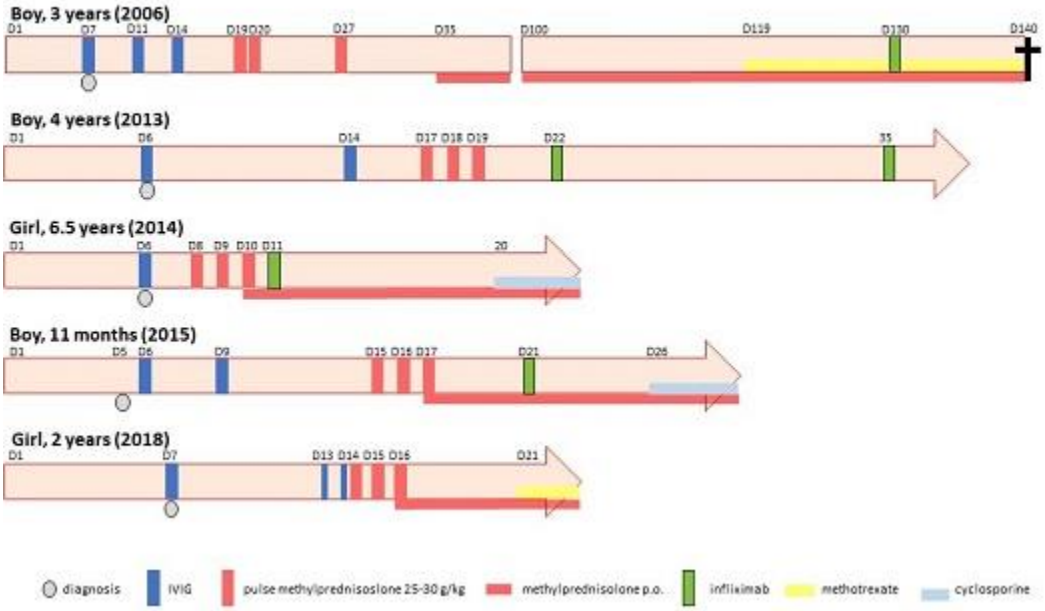
Case Presentation Summary

KD was diagnosed according to clinical criteria by the American Heart Association (AHA). All patients were initially treated according to AHA guidelines. Five children (2 female) with median age 3 years (0.9 – 6.5) and median 6 (5-7) days since the start of fever to diagnosis failed to respond to therapy with 1-3 doses of IVIG and pulse methylprednisolone.

Due to persistent inflammation 4 patients received infliximab 4-6 mg/kg, one needed a second dose after relapse. Two additionally received cyclosporine, first one with KD complicated by multiple organ failure and second one with changes on CA from D15. Two patients received methotrexate due to concomitant arthritis. One was a boy treated in 2006, who improved partially over weeks after IVIG and corticosteroid therapy. Low grade inflammation that persisted for weeks was attributed to arthritis. Echocardiography showed diffuse dilation of all CA. After exacerbation of inflammation he received infliximab on D130 with subsequent normalization of inflammatory parameters. However, due to complete CA fibrosis he died of cardiac arrest on D140.

Other patients recovered completely without cardiac or other sequelae. Detailed clinical courses of our patients are presented in Figure 1.

Figure 1. Clinical courses



Learning Points/Discussion

In refractory KD, timely aggressive immunomodulatory therapy is crucial to control the inflammation as early as possible. Anti-TNFα therapy had important influence on the outcome of disease in our patients. The only patient with prolonged disease and fatal outcome received anti-TNFα therapy late in the disease course.

ESPID19-0935
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

The diagnostic enigma of extensive lip excoriation: is it kawasaki disease?

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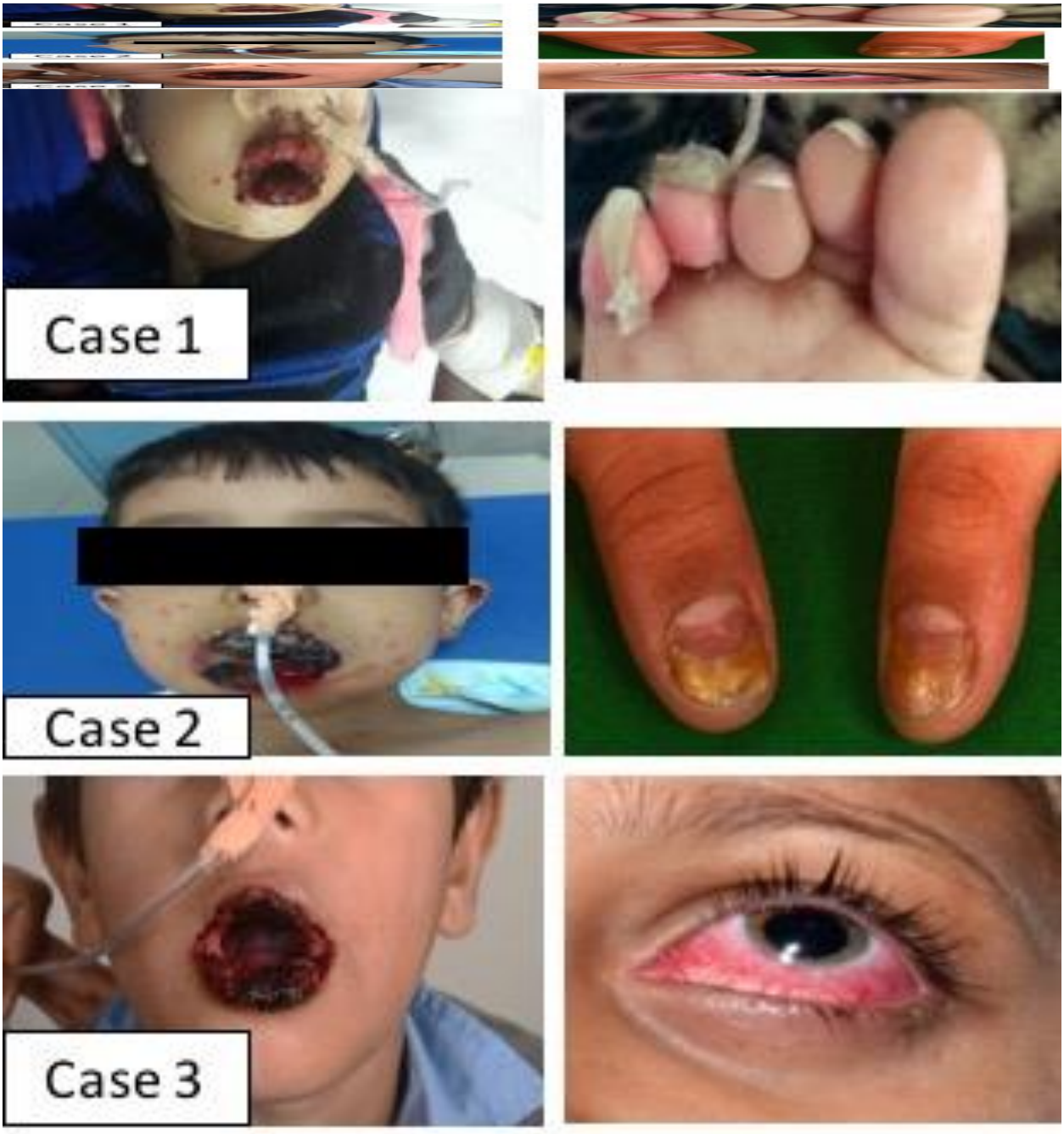
Background

Extensive lip excoriation is an unusual occurrence in Kawasaki disease(KD).We report 3 such cases.

Case Presentation Summary

Case 1:A 1year old girl presented with redness of lips,fever,rash for 5 days.She also had redness,discharge from eyes.She had unilateral cervical lymphadenopathy,diffuse maculopapular rash with bullae over palms and soles,swollen and cracked lips and bilateral exudative conjunctivitis.Initial clinical possibilities considered were atypical Hand-Foot-Mouth disease,Staphylococcal Scalded Skin syndrome and SJS.Laboratory investigations showed anemia,thrombocytosis(1,156X10^9/L, leukocytosis(14.7X10^9cells/L)and high CRP(50mg/dl) and serum proBNP 755 pg/ml.Enterovirus 71 PCR from fluid of bullous lesion was positive.2-D ECHO was normal.She was initiated on ceftriaxone and cloxacillin but continued to have symptoms.There was periungual peeling on day 7 of hospital stay and was given IVIg.At 6 weeks follow-up,she was noted to have Beau's lines in all finger nails.2-D echocardiography was normal.
Case2:A 5-year-old boy presented with 15 days history of fever,rash,red eyes.He had non-exudative conjunctival injection and maculopapular erythematous rash,lip excoriation.Investigations revealed thrombocytosis (632 X 10^9 /L),pleocytosis(39.8 X 10^9 /L;P_{72} L26) and high CRP(148 mg/l).2DECHO was normal.A diagnosis of KD was considered,IVIg was administered.The fever subsided,symptoms improved.He developed periungual peeling on day 5 of hospital stay.At 6 weeks follow-up,he was noticed to have chromonychia and Beau's lines in all finger nails.2-D echocardiography was normal.
Case3:A 9-years-old boy presented with history of fever for 6 days, redness and stickiness of eyes,swollen and cracked lips.He had non-exuduative conjunctival injection with typical perilimbal sparing and severe lip excoriation.However,Investigations showed normal inflammatory parameters including a normal proBNP and IVIg was not given.2D echocardiography was normal.



Learning Points/Discussion

Extensive lip excoriation has rarely been reported in KD.Case 1,2 developed periungual peeling,Beau's lines thereby confirming the diagnosis of KD.In Case 3,there was characteristic conjunctival injection with perilimbal sparing.KD is often a diagnostic dilemma.

ESPID19-0851
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

Kawasaki disease may closely mimic bacterial infections

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Background

Kawasaki disease (KD) is the commonest vasculitis in children. Clinical presentation of children with KD can be very heterogeneous and may mimic streptococcal and staphylococcal toxin mediated diseases. As a result physicians can face several diagnostic and therapeutic dilemmas. We report 2 such children with KD.

Case Presentation Summary

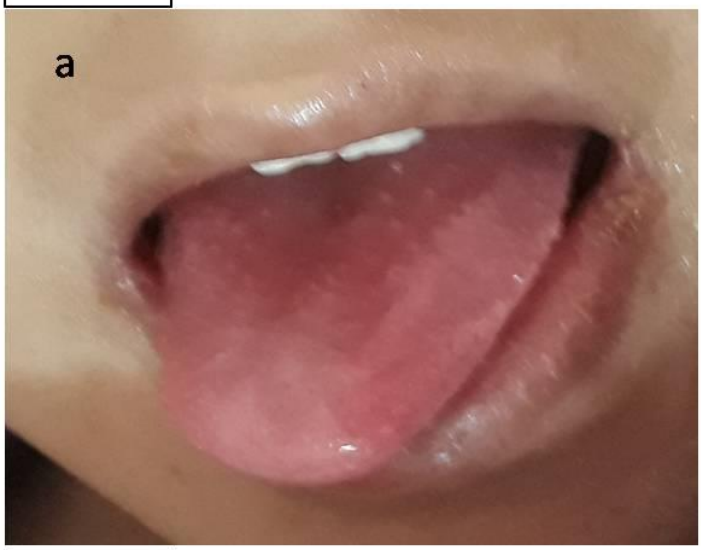
Case 1-

A 4-year-old boy presented with fever for 1 week, swelling in left thumb, generalized rash and redness of tongue for 6 days. He had paronychia in thumb requiring drainage and oral antimicrobials for 5 days. At presentation to our hospital he was febrile and in shock. He had diffuse rash over body, strawberry tongue, non-exudative conjunctivitis and edema of extremities. Differential diagnosis included KD and staphylococcal toxic shock syndrome. Investigations revealed elevated erythrocyte sedimentation rate 65 mm in 1st hour; C-reactive protein 141 mg/L and pro-brain natriuretic peptide (4994 pg/ml). Two dimensional (2D) echocardiography revealed mild pericardial effusion. He was administered intravenous immunoglobulin (IVIg; 2g/Kg) along with intravenous ceftriaxone and vancomycin. There was rapid recovery in clinical and hemodynamic parameters. At 2 week follow-up he had periungual peeling suggesting that he had had KD shock syndrome.

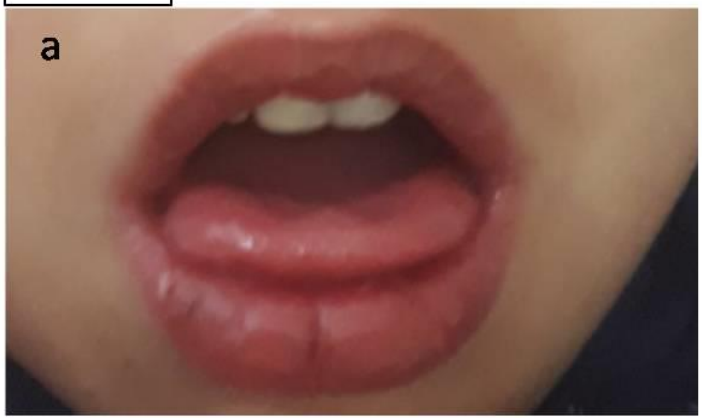
Case 2:

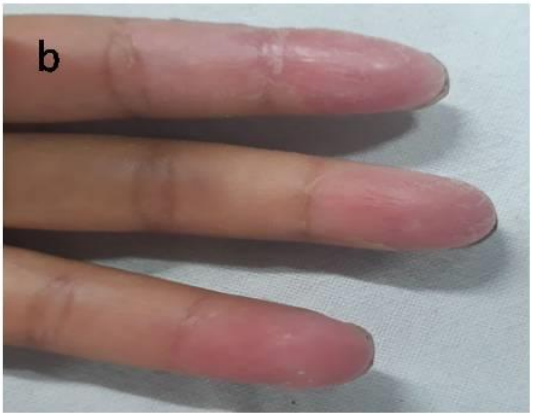
A 10-year-old presented with fever for 10 days with cracked and red lips, non-exudative conjunctivitis and periungual peeling. Investigations revealed thrombocytosis and elevated inflammatory parameters- erythrocyte sedimentation rate 69 mm in 1st hour; C-reactive protein: 14 mg/L. 2D-echocardiography was normal. A possibility of KD was considered. However, anti-streptolysin O antibody titers were 2863 IU/ml. There was dilemma between KD and streptococcal infection. He was given IVIG (2g/kg) along with intravenous ceftriaxone and he gradually recovered.

Case1



Case 2





Learning Points/Discussion

KD is often a diagnostic challenge and may test the clinical acumen of astute physicians. Bacterial infections can closely mimic KD.

ESPID19-0753
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

Giant aneurysms of the coronary arteries with thrombus formation in late diagnosed kawasaky disease - a dilemma for best treatment options and evolution

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Background

Objective: To present 3 cases of Kawasaki disease, from a series of 9, that developed severe coronary complications despite complex medication, one developing myocardial infarction.

Case Presentation Summary

Methods: Nine patients with Kawasaki disease were admitted into our clinic, 4 infants, 2 small children and one 7 yo child with disease recurrence. Only one patient was diagnosed within first 10 days of illness. All performed complex cardiology evaluation and selective Angio CT. Treatment was initiated with intravenous immunoglobuline IGIV and Aspirin.

Results: Three patients, all infants and males, lately diagnosed developed severe coronary complications, despite IGIV and Aspirin therapy. One developed giant LAD aneurysm with thrombus inside and medium aneurysm of RCA. Clopidogrel 0.2 mg/kg/day was added to Aspirin, with no results, aneurysm and thrombus increased. Clopidogrel was changed to Enoxaparin 0.1 mg/kg/day in addition to Aspirin. Enoxaparin was changed to Warfarin, due to the difficulty of administration. INR was monitored. Evolution was good, with slow reduction of both aneurisms and thrombus. In the other two patients, Enoxaparin was administered in addition to Aspirin, with anti-ATIII monitoring. Despite that, one infant developed myocardial infarction. Now he is 2 yo, continuing the anticoagulant therapy.

Learning Points/Discussion

Conclusions: It was a dilemma to choose the best treatment for lately diagnosed Kawasaki disease patients, to stop aneurysm and thrombus evolution, in order to prevent myocardial infarction. It is mandatory to have clear treatment indications in such severe cases. All patients are well, on medication and in close monitoring for the aneurysm evolution.

ESPID19-0703
E-Poster Viewing - May 7-10 - E-Poster Hours

Kawasaki disease

Clearing the cobweb- need for clarity in treatment of resistant kawasaki

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Background

Treatment of resistant kawasaki disease (KD)i is a diagnostic dilemma. Optimal management of resistant KD remains uncertain, the outcomes are potentially serious. They are at increased risk of developing coronary artery damage and associated sequelae. There is lack of high quality evidence on optimal management of these patients. Role of adjuvant additional therapy is always a matter of hot debate.

Case Presentation Summary

1. :A 2 year male got admitted with features of kawasaki disease.2D ECHO showed mildly dilated LMCA-3mm.Treated with IvIgand high dose aspirin .Fever persisted even after IVIg & repeat ECHO showed further dilatation of coronaries.Child was given second dose of IVIg. After 48 hours of 2nd dose ,child was given Infliximab in view of no clinical improvement & ECHO showing further dilated coronaries .ECHO showed further dilatation of coronaries after 48 hours and child was started on pulse methyl prednisolone for 3 days. ECHO findings remained same. Child was afebrile and was discharged ,on oral steroid & aspirin .

Child was readmitted as fever recurred 48 hours of stopping methylprednisolone . Considering ongoing vasculitis, CT angiogram, was done, showed no aneurysmal dilatation or narrowing .Non gated cardiac study showed dilated coronary arteries involving LAD,ramus &RCA,representing coronary artery ectasia. Child remained afebrile and discharged Follow up ECHO showed aneurysm of proximal right coronary with dilatation .treated with .Infliximab, cyclosporine and LMWH. Child is on warfarin,atorvastatin,carvedilol & aspirin. ECHO showed coronary artery ectasia with aneurysm.Child is on regular follow up.

Learning Points/Discussion

Failure to respond to 1st dose of IVIg ,should we give 2nd dose of IVIg or Infliximab or upfront steroids especially in a case where the coronaries show constant dilatation inspite of IVIg. There is no robust recommendations for management of resistant KD.

ESPID19-0815
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Treatment of recurrent respiratory papillomatosis with pulmonary involvement with bevacizumab: a report of two cases

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Background

Recurrent respiratory papillomatosis (RRP) is a rare disease caused by the low-risk human papillomavirus and represents the most common neoplasm of the pediatric larynx. The disease is characterized by recurrent exophytic papillomas in the respiratory tract.Recently, the monoclonal antibody Bevacizumab has been used in the treatment of RRP with pulmonary dissemination.
We present two cases of PRR treated with Bevacizumab with good clinical response.

Case Presentation Summary

Patient 1: A 5-year-old female patient with a RRP diagnosis at 6 months of age used tracheostomy for one year due to recurrent airway obstruction and respiratory failure. She received treatment with 4 complete cycles of intralesional Cidofovir and 30 doses of recombinant interferon, both with no clinical response. It was performed about 20 surgeries for removal of papillomas. Pulmonary lesions were identified on chest tomography, so we started the treatment with bevacizumab in April 2018, with 5mg/kg/day. After the third application the decannulation of the tracheostomy was performed. After the fifth application, the patient presented improvement of 95% of the lesions.

Patient 2: Male patient, 24 years old, diagnosed with RRP since childhood. He used tracheostomy for 10 years due to acute respiratory failure and recurrence of injury. About 80 surgical resections of the papillomas were performed and the patient developed pulmonary dissemination. The treatment with intravenous Cidofovir was chosen, with a stability of the pulmonary lesions. After a few years, the patient developed recurrent lesions and in August 2018, treatment with Bevacizumab with 10 mg/kg/day was started. The patient had not yet performed a control bronchoscopy, but showed a significant clinical improvement in the airway obstruction.

Learning Points/Discussion

Recently, this medication has been shown to be a promising new alternative in cases of severe recurrent respiratory papillomatosis.

ESPID19-0751
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Respiratory syncytial virus in hospitalized children in greece (2004-2018)

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Background and Aims:

Respiratory Syncytial Virus (RSV) is a common cause of bronchiolitis and pneumonia during winter months, especially in children < 2 years of age. The rate of RSV infection among children hospitalized with respiratory infection was examined retrospectively.

Methods:

During a 14-year period (July 2004 to July 2018) 10.490 nasopharyngeal aspirates from children hospitalized with acute respiratory infection were analysed. The laboratory, demographic and epidemiological data were recorded using the LIS. The age distribution of children was: < 1 month 1399; 1-6 months 5448; 6-24 months 1232; 2-5 years 1919 and > 5 years 492. RSV was detected by direct immunofluorescence or immunochromatography assay. Pearson chi-square test was used for statistical analysis.

Results:

Of the tested samples, 31,1% (3258/10490) were RSV (+) without statistically significant difference (p>0,05) between boys [30,4% (1773/5830)] and girls [31,9% (1485/4660)]. The percentage of positive samples according to age was: < 1 month 37,0% (517/1399); 1-6 months 37,1% (2023/5448); 6-24 months 28,2% (347/1232); 2-5 years 18,3% (352/1919); >5 years 3,9% (19/492). The seasonal distribution was characterized by epidemic peaks from December to April [96,3% (3137/3258)]. The longitudinal trend analysis of RSV infection during the 16 years showed a statistically significant in the rate of positive samples (p<0,05) in the last 5 years [July 2013-June 2018; 22,7% (981/4314)] compared to the previous period [July 2004-June 2013; 36,9% (2277/6176)].

Conclusions:

RSV is a major cause of lower respiratory tract infections in children < 2 years of age, mainly during winter months. The lower virus detection over the last 4 years could be attributed to improved preventive measures of virus distribution or due to sampling bias.

Systematic Review Registration:

None

ESPID19-0731
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Mycoplasma pneumoniae-induced rash and mucositis and steven johnson syndrome: two faces of the same medal or distrinct forms?

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Background

Mycoplasma pneumoniae (Mp) is a common cause of pulmonary infections in children. Although the majority of cases are mild, some patients may experience extrapulmonary complications, such as severe mucositis, resembling erythema multiforme or Steven Johnson Syndrome (SJS).

Case Presentation Summary

We report the case of a previously healthy 9-year-old girl who presented fever, respiratory symptoms and painful oral lesions. In the previous 5 days she was treated with Amoxicillin clavulanate and Clarithromycin because of a left basal pneumonia diagnosed in the in the Emergency Department. Despite the antibiotic therapy the clinical condition worsened and she was admitted to our Hospital. On admission she suffered from bilateral conjunctivitis, severe oral mucositis with ulcerated areas and superficial ulcerations of the lips and tongue and one lesion around the anal area. The differential diagnosis included 1) Stevens–Johnson Syndrome (SJS) related to the antibiotics 2) infection-related multiform erythema 3) Kawasaki Syndrome (KS). Because of the pneumoniae a therapy with Levofloxacin was started in order to avoid the administration of beta lactam antibiotics and macrolides. Microbiological and viral investigation were performed: HIV, herpes viruses, cytomegalovirus, Epstein-Barr virus and parvovirus B19 infections were ruled out. Skin biopsy was negative for herpes simplex virus and varicella zoster virus. Echocardiography ruled out KS. Mp DNA was detected from throat swab specimens. Her diagnosis was subsequently revised to Mp-Induced Rash and Mucositis (MIRM). Over the following days her general conditions gradually improved, she resumed to feed and the mucous membranes slowly healed.

Learning Points/Discussion

Distinguishing between MIRM and drug etiologies of SJS may be clinically useful; recognizing MIRM as infection-triggered, rather than drug-triggered, disease enables more specific counseling about triggers, prognosis, and recurrence risk and could lead to distinct, evidence based treatment strategies.

ESPID19-0639
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

A severe mucocutaneous manifestation of mycoplasma pneumoniae infection in a 5-year-old boy

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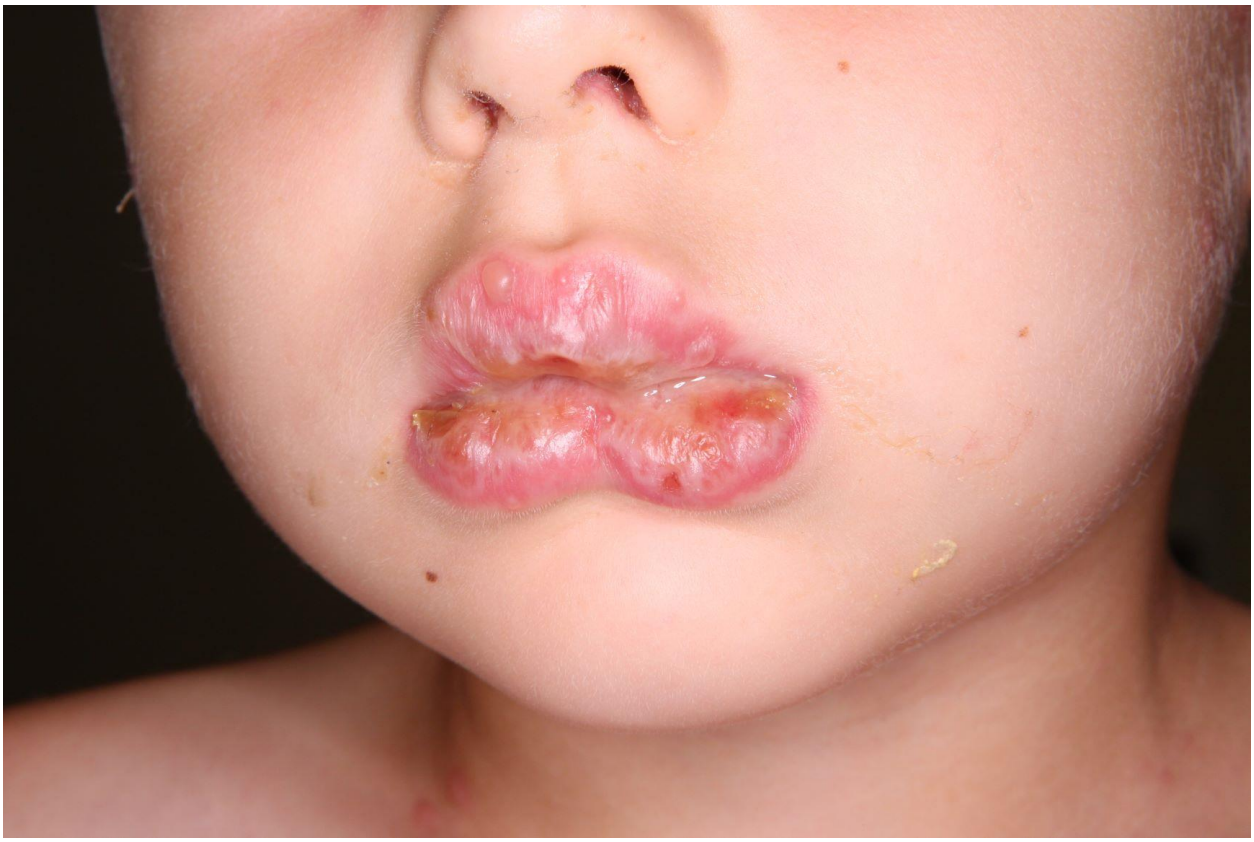
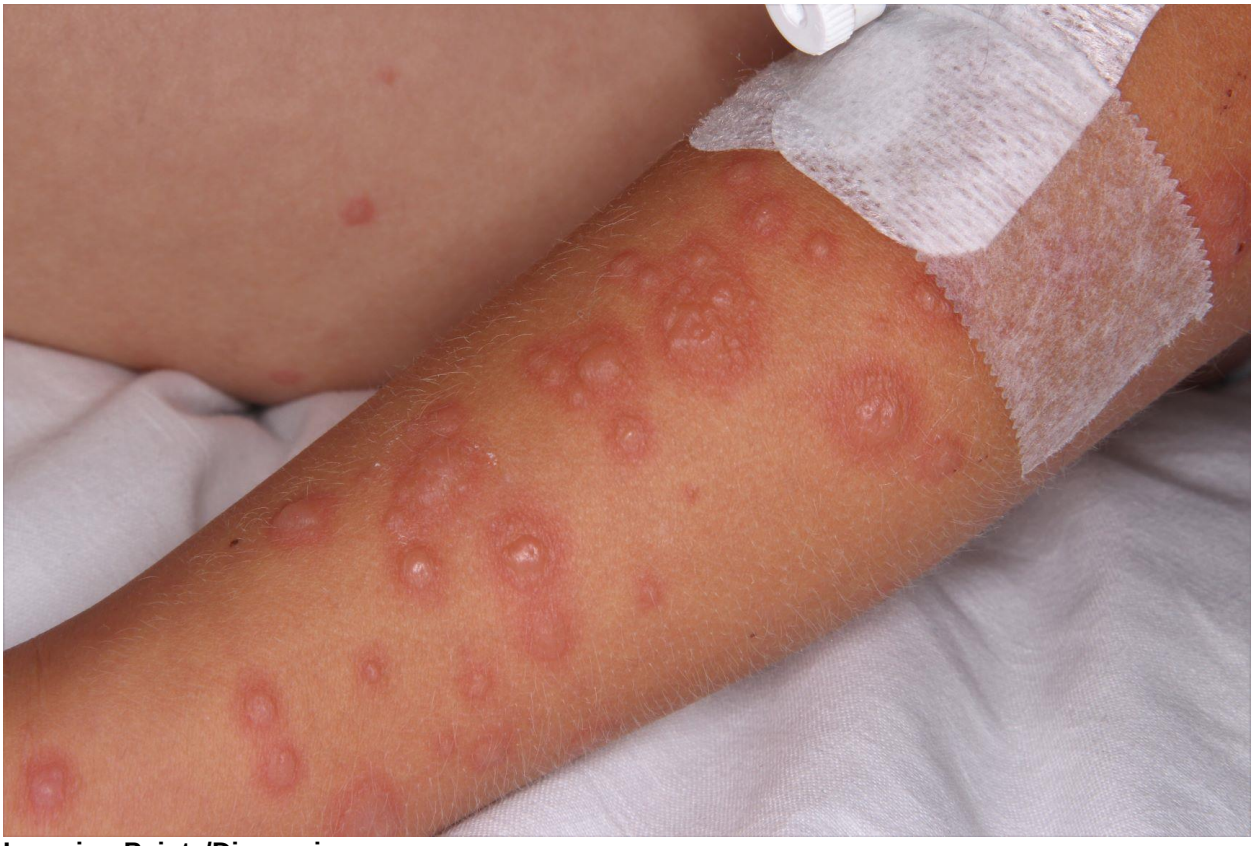
Background

Mucocutaneous complications may develop in up to one-third of patients with M. pneumoniae infections. They include erythema multiforme (EM), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and, recently defined, Mycoplasma-induced rash and mucositis (MIRM). In some patients, mucous membranes and skin involvement is more prominent than respiratory symptoms, whereas we should still target the infectious agent with the treatment.

Case Presentation Summary

Five years old boy was admitted to a hospital with high fever, cough, and vesicular rash. On admission his general condition was severe; he presented with dyspnea, crepitations over his left lung, decreased oxygen saturation, numerous vesicular lesions on the skin and multiple painful sores (vesicles, erosions) on mucous membranes of the lips and oral cavity, the nose, the eyes, and the penile glans. Laboratory tests revealed moderately elevated inflammatory markers, whereas chest X-ray showed interstitial pneumonia of the left lung. PCR test for *M. pneumoniae* from the boy's throat was positive, and further seroconversion of IgM and IgG antibodies confirmed the etiology. The boy improved significantly within a few days of treatment with clarithromycin and prednisone.





Learning Points/Discussion

M. pneumoniae infection may be responsible for > 60% of cases of *erythema multiforme maior*. Another recently defined entity characterized by severe mucosal involvement is Mycoplasma-induced rash and mucositis (MIRM). Target lesions and vesicles on the skin plus severe mucosal sores in children with respiratory tract infection should raise suspicion of mycoplasmal infection and requires an appropriate antibiotic regimen.

ESPID19-0551
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Risk factors and outcomes among children admitted to a paediatric intensive care unit with respiratory syncytial virus bronchiolitis

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Background

Acute bronchiolitis is a common indication for hospital admission among children less than two years of age and the most common aetiological agent is Respiratory Syncytial Virus (RSV). Paediatric Intensive Care Unit (PICU) admission is required in 3-6% of hospitalised infants

Methods

Data was collected prospectively for all patients admitted with RSV-bronchiolitis from 2004-2017 at a tertiary paediatric hospital. Data recorded included demographic variables, background, management and outcome. Categorical variables were analysed using Chi-squared test. Continuous variables were analysed using Man-Whitney test.

Results

There were 2851 admissions with RSV-bronchiolitis during the study period. The total number of admissions per season significantly increased over the 13-year study period ($p<0.0001$, r^2 0.85). Of total admissions, 396 (13.9%) required PICU care. Lower birth weight and gestational age, younger age, history of neonatal intensive care unit admission, oxygen dependence, Palivizumab use, multiple birth, existing medical conditions, and higher number of siblings had significant positive association with PICU admission. Male gender, breast feeding, crèche attendance, number of cohabitants and exposure to passive smoke had no significant association. The length of stay of those admitted to PICU was significantly longer (median 10 vs 4 days, $p<0.001$). PICU admission was associated with a lower rate of discharge home (88% vs 98%) and a higher rate of death (2.5% vs 0.08%), $p<0.0001$.

Conclusions

The burden of hospital admissions with RSV bronchiolitis is considerable and appears to be increasing. RSV remains a significant cause of PICU admission and mortality in young children. In contrast to other studies of factors for PICU admission and outcome in RSV bronchiolitis, male gender, exposure to cigarette smoke and overcrowding had no significant association. Improved RSV prophylaxis and treatment are keenly awaited.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0423
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Mycoplasma pneumoniae-induced mucocutaneous disease: a prospective longitudinal cohort study

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[3]Children's Hospital Lucerne, Division of Infectious Diseases, Lucerne, Switzerland
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Background

To report the occurrence and clinical presentation of *Mycoplasma pneumoniae*-induced mucocutaneous disease in a prospective longitudinal cohort study of children with community-acquired pneumonia (CAP).

Methods

We investigated *M. pneumoniae*-induced mucocutaneous disease among 152 children enrolled during a prospective longitudinal CAP study from May 1, 2016, to April 30, 2017 at the University Children's Hospital Zurich. Infection with *M. pneumoniae* was diagnosed by polymerase chain reaction (PCR) in pharyngeal samples and confirmed with the measurement of peripheral blood immunoglobulin (Ig) M antibody-secreting cells (ASCs) by enzyme-linked immunospot (ELISpot) assay.

Results

Mucocutaneous eruptions developed in 10 (23%) cases of CAP positive for *M. pneumoniae* by PCR (n=44), all of whom tested positive for specific IgM ASCs. *M. pneumoniae* PCR-negative CAP cases had skin manifestations in 3% (p<0.001). The spectrum of *M. pneumoniae*-induced mucocutaneous disease included *M. pneumoniae*-induced rash and mucositis (MIRM; n=3/44, 7%), urticaria (n=2, 5%), and exanthematous skin eruptions (n=5, 11%). Two cases had ocular involvement as sole mucosal manifestation (bilateral anterior uveitis and non-purulent conjunctivitis). Cases with *M. pneumoniae*-induced mucocutaneous disease had longer prodromal fever (p=0.02) and higher CRP levels (p=0.04) than cases with *M. pneumoniae* CAP without skin manifestations. They were also more likely to require oxygen (p=0.007), hospitalization (p=0.01), and to develop long-term sequelae (p=0.03).

Conclusions

Mucocutaneous disease occurred in one out of four cases with *M. pneumoniae* CAP, significantly more frequent than in CAP of other etiology. *M. pneumoniae*-induced mucocutaneous disease was associated with increased systemic inflammation, morbidity, and higher risk of long-term sequelae.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT03613636

ESPID19-0166
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

The prevalence and clinical characteristics of pertussis-associated pneumonia among infants in botswana

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Background

There are scant data on the prevalence and clinical course of pertussis disease among infants with pneumonia in low and middle-income countries. While pertussis vaccination coverage is high (≥90%) among infants in Botswana, human immunodeficiency virus (HIV) infection affects nearly one-third of pregnancies.

We aimed to evaluate the prevalence and clinical course of pertussis disease in a cohort of HIV-exposed uninfected (HEU), HIV-unexposed uninfected (HUU), and HIV-infected infants with pneumonia in Botswana.

Methods

Children 1–23 months of age admitted to a tertiary care hospital (Princess Marina Hospital, Gaborone, Botswana) with pneumoniabetween April 2012 and June 2016 were included. Nasopharyngeal swab specimens obtained at enrollment were tested by a previously validated in-house real-time polymerase chain reaction assay that detects a unique sequence of the porin gene of *Bordetella pertussis*.

Results

*B. pertussis*was identified in 1/248 (0.4%) HUU and 3/110 (2.7%) HEU children 1-23 months of age. All pertussis-associated pneumonia cases occurred in infants <5 months of age (prevalence, 1.0% [1/103] in

HUU and 4.8% [3/62] in HEU infants). *B. pertussis*was not detected from the 33 HIV-infected children with pneumonia.No HEU infants with pertussis-associated pneumonia were taking co-trimoxazole prophylaxis at the time of hospital presentation. One HUU infant required intensive care unit admission for mechanical ventilation, but there were no deaths.

Conclusions

The prevalence of pertussis was low among infants and young children with pneumonia in Botswana. Although vaccination against pertussis in pregnancy is designed to prevent classical pertussis disease, reduction of pertussis-associated pneumonia might be an additional important benefit.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0135
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Exchange transfusion treatment for severe pertussis in infants: a single medical center experiance (2015-2018)

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Background and Aims:

Severe pertussis in infants is characterised by leukocytosis with lymphocytosis, pulmonary hypertension and/or pneumonia. The aim of our retrospective study was to identify factors associated with poor outcome and to assess impact of exchange transfusion (ET) on in-hospital mortality over a 4 years period (January 1st, 2015, to December 31st, 2018).

Methods:

We retrospectively examined hospital records including demographic data, clinical presentations, diagnostic tools, management and outcomes of all infants with total white blood cell (WBC) count over 30 x 10^9/L and *Bordetella pertussis* proven using PCR from nasopharyngeal or tracheal aspirate.

Results:

We identified 16 infants with severe pertussis, 5 had received ET and 2 had died. The mean age was 2.9 months. Patients receiving ET had the median WBC and relative lymphocyte counts of 101 x 10^9/L and 58%, respectively, in comparison to 43 x 10^9/L and 77%, respectively, among infants who did not receive ET. One patient was diagnosed with pulmonary hypertension. Fatal cases were infants who had rapid rise in WBC count within 24 hours, developed pneumonia, renal failure and refractory cardiogenic shock.

Conclusions:

Rapid rise in WBC count within 24 hours and development of pneumonia can be associated with poor outcome in infants with severe pertussis. Although ET will lower the high WBC count, presence of other factors (prematurity, low birth weight, pneumonia) may impact in-hospital mortality nevertheless.

Systematic Review Registration:

N/A

ESPID19-0028
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Unusual presentation of mycoplasma pneumonia in a young child

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Background

Mycoplasma pneumonia is a common cause of community acquired pneumonia (CAP) in school children. We report a case of pneumonia with empyema due to mycoplasma in a 2 year old child. This case is unusual due to 2 reasons, the young age of presentation and the unusual complication of empyema.

Case Presentation Summary

A 2 year old male child was brought with fever and cough since 8 days and breathlessness since 4 days. He had received oral amoxiclav for 4 days prior to admission. On admission,child had tachycardia of 170/min and tachypnea with reduced air entry on right side. CBC revealed Hb 8.7 ,total leucocyte count 9220 with 75% polymorphs. Xray chest showed right sided pneumonia with pleural effusion. USG chest reported consolidation with moderate pleural effusion, with no septations. USG guided pleural tap was suggestive of an exudate. Gram staining ,AFB staining and Genexpert for Myobacterium TB and culture were negative. The child was started on IV Ceftriaxone. After 48 hours, high grade fever persisted and tachypnea increased. USG done at 48 hours showed increase in the fluid collection. Intercostal drain(ICD) was inserted and 300 ml serous fluid was drained. Inj Vancomycin and Azithromycin were added. Over next three days, pleural fluid gradually decreased and ICD was removed on 6th day of insertion Mycoplasma IgM came positive (>27) by CLIA. Vancomycin was stopped and azithromycin given for total 6 days. Complete resolution occurred after treatment.

Learning Points/Discussion

Pediatricians need to be aware of mycoplasma pneumonia as causative agent of CAP in preschool children and also its presentation as empyema. Diagnostic testing is challenging especially in resource limited setting. Hence it should be a differential of a non responding pneumonia with standard regimens.

ESPID19-0016
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Radiological aspects and etiology of community-acquired pneumonia in hospitalized children

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Background and Aims:

Community-acquired pneumonia (CAP) remains the leading cause of death in children worldwide. The role of chest radiograph (CXR) in CAP etiological diagnosis is debatable. We aimed to assess distinct radiological findings among children aged less than 5 years hospitalized with radiologically-confirmed CAP with bacterial or exclusively viral infection determined in a prospective and thorough investigation.

Methods:

Radiological findings of children hospitalized with radiologically-confirmed community-acquired pneumonia were assessed in regard to the prospectively determined etiology in this cross-sectional study. CXR was obtained upon admission, when clinical data, nasopharyngeal aspirate and blood sample were collected to investigate etiology (11 viruses, 8 bacteria). CXR was read by an independent pediatric radiologist blinded to clinical and etiological information.

Results:

Of 165 patients, 158 (95.8%) and 18 (10.9%) had pulmonary infiltrate and pleural effusion, respectively. Pulmonary infiltrate was classified as alveolar (n=152) or only interstitial (n=6). Patients with only interstitial infiltrate did not have pleural effusion. Overall, median (IQR) age and length of disease were 18 (9-28) months and 7 (4-12.5) days, respectively and bacterial (n=86; 52.1%) and exclusively viral (n=79; 47.9%) infections were diagnosed. Pneumococcal was the most frequent bacterial infection (24.2%). Rhinovirus (24.8%), parainfluenza viruses (21.8%) and respiratory syncytial virus (19.4%) were the most common viral pathogens. Among the 152 patients with alveolar infiltrate, 81 (53.3%) and 71 (46.7%) had bacterial or exclusively viral infection. Among the 6 patients with only interstitial infiltrate, 2 (33.3%) and 4 (66.7%) had bacterial or exclusively viral infection.

Conclusions:

Children with radiologically-confirmed pneumonia with alveolar pulmonary infiltrate may have either bacterial or exclusively viral infection.

Systematic Review Registration:

Not applicable

ESPID19-0459
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Hospitalizations related to respiratory syncytial virus in children under 1 year old in the vahnsi network during 6 consecutive seasons (2012/2013 to 2017/2018, valencia, spain)

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Background

Respiratory viral infections such as Respiratory Syncytial Virus (RSV) cause an important number of hospitalizations in infants.

Methods

The Valencia Hospital Network for the Study of Influenza and other respiratory viruses (VAHNSI) conducts annually a prospective, active-surveillance hospital-based study. The current analysis was restricted to patients <1 year old (y.o.) from 2012/2013 to 2017/2018 seasons (November to April, September to June in the 2017/2018 season).

All consenting admissions of non-institutionalized patients, resident in a participating hospital catchment area, not discharged within 30 days and hospitalized within 7 days of the onset of symptoms were included in the study and swabbed. Samples were tested by real-time reverse transcription polymerase chain reaction (RT-PCR). Patient information was collected by interviewing legal tutors and/or by clinical records review.

Results

Of the 2202 children <1 y.o. included in the study, 761 (35%) were positive for RSV. Positivity rates ranged from 14% in the 2013/2014 season to 48% in the 2015/2016. The overall (all seasons) highest positivity rate (39%) was detected in children 2 moa (42%). The RSV positivity rate did not differ between preterm and term children (34% in both groups). 9 (1.2%) cases were admitted to the ICU, 4 (0.5%) of them required mechanical ventilation and 1 (0.1%) died during hospitalization.

Conclusions

Between 3 or 4 out of 10 hospitalized children <1 y.o. were positive for RSV. Most of the infections were detected in children 2 moa. The RSV positivity rate did not differ according to prematurity status. Several complications were detected among RSV cases.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0452
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Hospitalizations related to picornaviruses infections in patients under 18 years old in the vahnsi network during 4 consecutive seasons (2014/2015 to 2017/2018, valencia, spain)

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Background

Respiratory infections are the main cause of morbidity and mortality worldwide. Picornaviruses, such as rhinovirus (RhV) or enterovirus (EV), play a significant role in the respiratory pathology of young children.

Methods

The Valencia Hospital Network for the Study of Influenza and other respiratory viruses (VAHNSI) conducts annually a prospective, active-surveillance hospital-based study. The current analysis was restricted to admitted patients <18 years old (y.o.) from 2014/2015 to 2017/2018 seasons (November to April, September to June in the 2017/2018 season).

All consenting admissions of non-institutionalized patients, resident in a participating hospital catchment area, not discharged within 30 days and hospitalized within 7 days of the onset of symptoms (ECDC ILI-case definition was required for those ≥5 y.o.) were included in the study and swabbed. Samples were tested by real-time reverse transcription polymerase chain reaction (RT-PCR). Patient information was collected by interviewing legal tutors and/or by clinical records review.

Results

RhV infections (N=388) were distributed as follows: 50% in children <1y.o., 14% in 1 y.o., 22% in 2-4 y.o. and 14% in 5-17 y.o. For EV (N=54) the distribution was 22%, 37%, 22% and 19%, respectively. The length of hospitalization (LoH) was 3(2-5) days for RhV and 3(2-3) for EV. RhV and EV were mainly admitted due to bronchial disorders. 8 RhV cases were pneumonia. Annual variability was detected with the highest incidence rate in the 2014/2015 (0.46 x100,000 person-week) season for EV and in the 2017/2018 season (1.92 x100,000 person-week) for RhV.

Conclusions

RhV infections occurred in younger patients than EV and had longer LoH. Picornaviruses infections were mainly admitted due to bronchial disorders. High variability was detected among age groups and seasons.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0210
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Circulation of influenza virus subtypes in children attending a tertiary care hospital in bucharest romania, in two consecutive influenza seasons

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Background and Aims:

Good understanding of the seasonal circulation of influenza strains is essential for establishing evidence-based vaccination policies. Pediatric patients may be at particularly high risk for acquiring infection and developing complications.

Methods:

The National Institute for Infectious Diseases “Prof.Dr. Matei Balș” (Bucharest, Romania) has been conducting an active epidemiological surveillance study of hospitalized influenza cases for the past two years as part of the GIHSN network. The circulating strains in children during the influenza season 2017/18 were analysed by RT-PCR and compared with those from the 2016/17 season. The study included 337 pediatric patients with influenza-like illness in 2017/18 and 152 in 2016/17.

Results:

In the 2017/18 season, 178 (52.8%) patients tested positive for influenza. We recorded intense circulation of B viruses (61.8% of positive cases): B/Yamagata was the dominant lineage (88.1% of subtyped B strains); A/H1 predominated among A viruses (85.5% of subtyped strains). This is in contrast to the circulation observed during the 2016/17 influenza season in the pediatric population attending the same hospital, when we exclusively identified A/H3 (23% of influenza cases) and B/Victoria viruses (77%).

In the 2017/18 season, influenza A viruses circulated predominantly in younger children (median age and interquartile range: 3 [2, 4] years), and B viruses in older children (median age: 5 [2, 8] years), p=0.007, U=2873.5, r=-0.2, a trend that was also present during the preceding influenza season in our study.

Conclusions:

We have identified an intense circulation of B viruses, particularly in older children. Continued surveillance of influenza is warranted to provide robust data that are informative for local policies.

Acknowledgement

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Systematic Review Registration:

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

The clinical impact of exophiala on children with cystic fibrosis

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Background and Aims:

Exophiala species are increasingly isolated in paediatric cystic fibrosis (CF) patients, though clinical significance is unknown. We conducted a retrospective survey to determine the impact of *Exophiala* isolation on clinical condition (FEV1% predicted, body mass index (BMI)), and treatment burden (annual intravenous antibiotic days) in paediatric CF patients. We compared these patients to CF controls, and reviewed effectiveness of treatment strategies.

Methods:

Electronic notes were analysed for all paediatric CF patients isolating sputum *Exophiala* more than once at Royal Manchester Children's Hospital (RMCH) from 2012 to 2015. Clinical data covering demographics, BMI, spirometry, intravenous antibiotic days and *Exophiala* treatment were collected from 12 months before until 12 months after first isolation. Cases had 3 age matched controls.

Results:

Exophiala was isolated from 16 children, mean age 11.8yrs, 7 females. Prior to *Exophiala* isolation there was no significant difference between cases and controls for BMI, FEV1% predicted or annual intravenous antibiotic days ($p = 0.76$, $p= 0.57$ and $p=0.72$ respectively). Following isolation, there was no significant change in clinical parameters. Cases had a higher burden of *Candida* species (75% vs 23% controls) and *Aspergillus* species (44% vs 31% controls). *Exophiala* treatment was attempted in 9 patients, tolerated in 6, with 4 (67%) eradicating *Exophiala*, all of whom took posaconazole.

Conclusions:

Exophiala isolation was not seen in children with a worse clinical condition and once isolated, *Exophiala* did not appear to negatively impact lung function, BMI or intravenous antibiotic days. It was however associated with isolation of other fungi. Eradication, when attempted, was often not tolerated but when successful, posaconazole was used. Based on this small study, should we be concerned about *Exophiala* isolation in paediatric CF?

Systematic Review Registration:

n/a

ESPID19-1084
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Respiratory mycoplasma pneumoniae infections – challenges and clues in differential diagnosis

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Background and Aims:

M. pneumoniae is a significant causative agent of community-acquired pneumonia (CAP) in children and young adults, accounting for 30-40% of cases. It usually cannot be distinguished from other causes of atypical CAP based on clinical presentation, although extrapulmonary manifestations often suggest *M. pneumoniae* infection. The aim of the study was to assess possible differences in age, clinical presentation, epidemiology and laboratory findings between confirmed cases of *M. pneumoniae* CAP and negative ones.

Methods:

Patients younger than 18 years with radiologically verified pneumonia and obtained PCR for *M. pneumoniae* from nasopharyngeal swab were included in the study from October 2014 to October 2018 at the University Hospital for Infectious Diseases, Zagreb. Seasonality, clinical characteristics, chest x-ray findings and laboratory parameters were retrospectively analyzed and compared between PCR positive and negative group. P-value <0,05 was considered statistically significant.

Results:

There were 166 patients, of whom 41% were PCR positive and 59% PCR negative for *M. pneumoniae,* with median age of 8,7 years and 5,7 years, respectively. Cough and fever were dominant symptoms in both groups, while gastrointestinal symptoms were more frequent among PCR positive samples (p<0,018). There was no significant difference between WBC count, CRP and PCT values among two groups. Increased number of *M. pneumoniae* CAP was observed during colder months, with a peak during November, while *M. pneumoniae* negative CAP showed less prominent seasonal variations.

Conclusions:

It is a challenge to distinguish *M. pneumoniae* CAP from atypical CAP caused by other agents. Laboratory findings are usually not helpful in establishing diagnosis. Age of the patients, presence of extrapulmonary manifestations and prominent seasonality could be the clue to suspect *M. pneumoniae* infection and perform further tests (PCR or serology).

Systematic Review Registration:

N/A

ESPID19-1081
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

High rate of methicillin resistance among staphylococcus aureus isolates from spanish children with community-acquired pneumonia

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Background and Aims:

Staphylococcus aureus (SA) is an infrequent cause of community-acquired pneumonia (CAP). Methicillin-resistant SA (MRSA) is uncommon in Spain (3-10%), but could be increasing due to migration from high-prevalence countries. We aimed to describe the epidemiology and antibiotic resistance of pediatric SA-CAP in Spanish children.

Methods:

Retrospective multicenter study including patients <17 years with SA-CAP admitted to 4 tertiary hospitals in Madrid during 2008-18.

Results:

Twenty-four cases were included: median (IQR) age 10.9 (5.4-29.5) months, 15 (63%) male. SA strains were isolated from blood cultures in 13 (54%) and detected in pleural fluid in 11 (46%; 6 by culture, 4 by PCR, 1 by both). MRSA accounted for 6/24 (25%) cases, and 4/24 (16.7%) were clindamycin-resistant. Initial empiric therapy was inadequate in 18/24 (75%). MRSA was more frequently isolated in the last two years of the study (50% vs 12.5%, p=0.13). Eleven (46%) patients had complications: 10 (42%) pleural effusion (7 empyema) and 1 pulmonary necrosis, and 17/24 (71%) needed intensive care unit (ICU) admission. Non-invasive and invasive mechanical ventilation was initiated in 7/24 (29%) and 1/24 (4%), respectively. All patients survived. Mean hospital length of stay was 15.8 days (SD: 10.14). Compared to MSSA, MRSA pneumonia affected younger children (median age 3.5 vs 19 months; p=0.004), with non-significant higher rates of ICU admission (100% vs 61%, p=0.13), 30-day readmission (33% vs 0%, p=0.05), foreign parental origin (67% vs 22 %, p= 0.14) and clindamycin resistance (33% vs 11%, p=0.25).

Conclusions:

SA-CAP is severe and affects mainly infants. Infections by MRSA are emerging among younger patients and tend to be more severe. Empiric therapy in young children with suspected SA-CAP should cover the possibility of methicillin and clindamycin resistance.

Systematic Review Registration:

ESPID19-0940
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Rsv infections in the first year of life: a twin-based clinical model approach to better understand disease severity

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Background and Aims:

RSV infection is the most common cause of severe LRTI in the pediatric population worldwide. Age, weight, GA, and siblings are major risk factors for RSV-associated LRTI. Our aim was to identify other risk factors by comparing twins within their pair to adjust for the above risk factors and for the environment.

Methods:

We retrospectively identified (Jun 2012-Dec 2017) pairs of twins of whom at least one was admitted for a PCR-confirmed infection. A severe infection was defined as requiring hospitalization for feeding support, and respiratory support triggered by blood acidosis (pH < 7.35, PCO_2 > 6.7 kPa). In another sample of twins, antibody levels at birth were tested and compared in cord blood using an IVD serology Kit VRS IgG (Elisa IgG R-Biopharm IVD).

Results:

Fifty-four children were included in the study (mother 32±6y, 74% spontaneous pregnancies, GA 34±4w, birth weight 1888±762g [695-3540], 54% girls, maternal feeding 78%, 74% siblings (n=2.1±1.9)). Among the 54 patients (11% chronic respiratory disease), 8 without symptom, i.e. 46 sick: 5 (11%) ambulatory managed, and 41 (89%) hospitalized (14 (30%) in PICU, 27 (59%) in pediatric wards). Among the 46 with disease, 36 (78%) required O2 (2% invasive ventilation (IV), 28% nasal high flow (NHF), and 48% standard O2), 16 (30%) required a nasogastric tube for feeding and 10 (19%) required perfusion. Among

the twin pairs, 56%, 48%, and 44% differed for hospitalization (none/pediatric/PICU), nutritional care (none/NGT/perfusion), and level of respiratory support (none/NHF/IV), respectively. RSV IgG levels at birth were highly correlated for 90% of all pairs.

Conclusions:

Our results highlight that genetic and environmental factors may also influence the severity of RSV infections. Antibody level variations at birth may not account for this observation.

Systematic Review Registration:

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Diagnostic imaging of pediatric parapneumonic pleural effusions and empyema in germany (2010 to 2018) - too frequent use of computed tomography?

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Background and Aims:

Systematically obtained data on imaging procedures of pediatric parapneumonic pleural effusions (PPE) and empyema (PE) are limited.

Methods:

In cooperation with the German Surveillance Unit for Rare Diseases in Childhood (ESPED), we collected patient and clinical data on children <18 years of age with PPE/PE (effusion persistence >7 days or requiring drainage) from all pediatric hospitals in Germany, 2010 to 2018. We analyzed the frequency of performed imaging procedures by chest radiography (CXR), ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI), stratified by age and by therapeutic management (χ^2-test).

Results:

In total, 1724 children with PPE/PE (median age: 5 years, interquartile range 3-10) were included and received at least one imaging procedure: CXR: 1714 (99%), US: 1670 (97%), CT: 619 (36%) and MRI: 113 (7%). Ninety-nine percent of the children received CXR, regardless of age (Fig.1). The proportion of US decreased with increasing age, from 99% (age <1 year) to 94% (13-17 years), whereas the proportion of CT increased from 30% to 45%. The use of CT increased with therapeutic invasiveness: 20% for non-invasive therapy, 36-41% for pleural puncture/drainage/intrapleural fibrinolysis and 60% for surgical therapy.

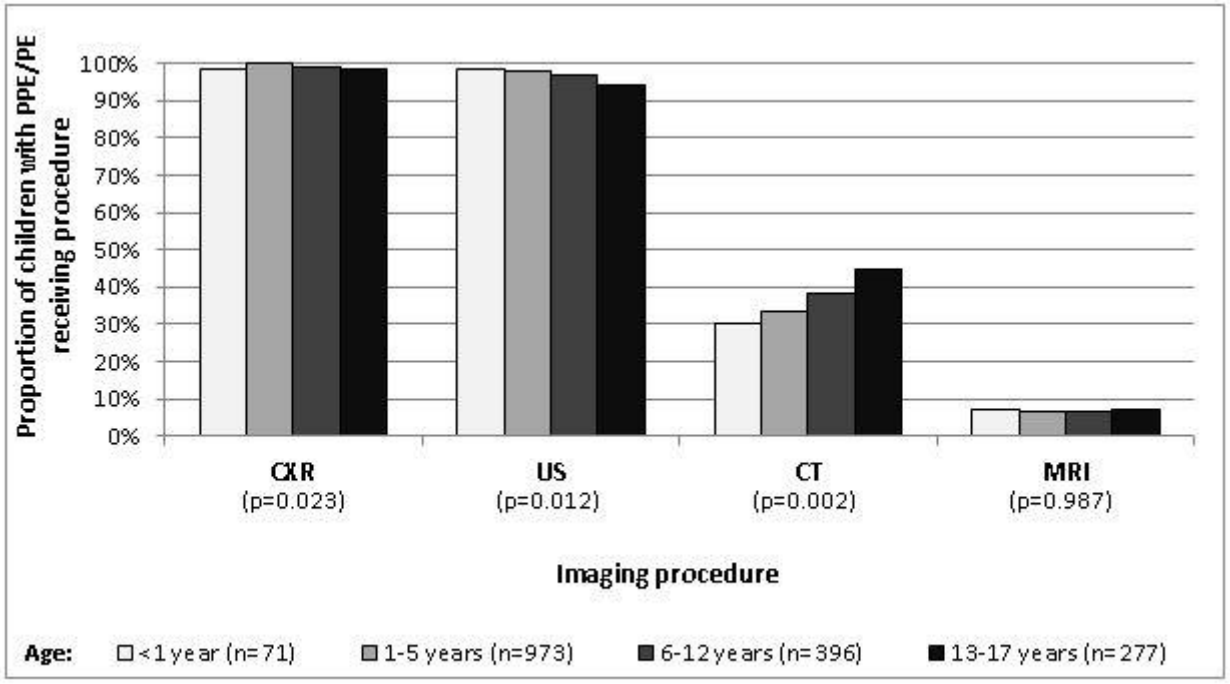

Fig.1: Diagnostic imaging of 1717 children with PPE/PE, stratified by age (Germany, 2010-2018)

Conclusions:

The use of CT in 36% of children with PPE/PE is clearly higher than the 25% indicated in an European expert survey (Hafen et al., 2016). Furthermore, one fifth of children without invasive therapies received CT. As CT results in high radiation exposure, its use should be restricted to children with complicated PPE/PE, necessitating surgical procedures, or presenting with parenchymal complications such as lung abscess or necrotizing pneumonia.

Systematic Review Registration:

N/A

ESPID19-0760
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Bordetella pertussis and co-infection with other respiratory pathogens – a clinically important association?

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Background and Objective

Bordetella pertussis infection has recently increased in prevalence despite good global vaccination coverage. Children presenting with a respiratory illness may receive alternate diagnoses before pertussis is considered. Testing for and detection of other respiratory pathogens may influence outcomes in pertussis disease. We review the literature describing the epidemiology and influence of co-infection in pertussis disease. Co-pathogens of interest are rhinovirus, RSV, influenza [A & B], parainfluenza [1-4], HMPV, adenovirus, coronavirus, streptococcus pneumoniae, and haemophilus influenzae.

Methods

Cochrane, EMBASE, MEDLINE and CINAHL were searched for English language articles published since 2008 reporting paediatric data. Studies were included for review if they reported results from children tested for both pertussis and another of the respiratory pathogens of interest, and if prevalence of co-infection in those with pertussis could be extracted from the data. Additionally, we looked for studies commenting on the clinical differences between those with co-infection and those with sole pertussis disease

Learning Points Discussion

Our data demonstrate that co-infection with another respiratory pathogen may be common in pertussis disease. Conclusions about the epidemiology or influence of co-infection on pertussis disease cannot be drawn. Further studies are needed to explore this association.

- 29 studies report prevalence of co-infection in confirmed pertussis cases, ranging from 0.2-90%. Most studies report test results from children presenting with either suspected pertussis, bronchiolitis or acute respiratory illness.

- Of the studies that simultaneously tested for multiple respiratory pathogens rhinovirus, respiratory syncytial virus and adenovirus were frequently found.

- 15 studies commented on the differences in clinical characteristics or outcomes of children with sole pertussis infection compared to children with pertussis co-infection. Six studies report no clinical difference compared to four studies reporting different demographic or clinical characteristics.

ESPID19-0637
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Lung ultrasound for early diagnosis of severe pneumonia in critical paediatric patients. Preliminary results of a randomized clinical trial.

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Background

Aims: To compare the utility of lung ultrasound (LUS), with respect to chest X-Ray (CXR), in the diagnosis of severe community and nosocomial pneumonia in the Paediatric Intensive Care Unit (PICU).

Methods

Prospective, randomized, blinded, interventional clinical trial, June 2017-march 2019. Inclusion criteria: patients (7 days-18 years) with suspected community pneumonia (CP) or nosocomial pneumonia (NP) admitted at PICU. Pneumonia diagnosis was based on clinical signs, radiological findings (group 1-experimental: LUS; group 2-control: CXR) and analytical data (Procalcitonin). Images recorded were assessed later a paediatric trained on LUS and a senior radiologist, both blinded to patient condition and clinical data.

Results

106 cases were recruited; 40 males (57.1%), mean age: 22.12 months. Patients randomization: group1-LUS= 37 (52.9%), and group 2-TXR= 33 (47.1%). Final diagnosis in suspicious CP [u1] (n=78) was: bacterial pneumonia in 28 patients, viral pneumonia in 22, and no pneumonia in 20. LUS sensitivity and specificity for pneumonia was 98.7% and 87.2%, and 90.2% and 73.3% for CXR. LUS allowed an early diagnosis than the CXR in 28 patients. The number of CXR in group 1-LUS resulted in 1.8/patient, with respect to 2.5 in group 2-CXR, p= 0.075. NP was confirmed in 18 of the 28 with initial suspicious. Sensitivity and specificity were also higher for group1-LUS than for CXR (96.7% and 85% vs 89.2 and 74%); with an early diagnosis for LUS in 9 patients; and lower rate of CXR in group1-LUS (2.1 vs 2.7, p= 0.084).

Conclusions

LUS showed a better sensitivity and specificity for CP and NP diagnosis than CXR in this preliminary analysis. LUS seemed to allow an early diagnosis of pneumonia in some cases. LUS leads to a lower irradiation of paediatric patients.

Clinical Trial Registration (Please input N/A if not registered)

PI16/01040

ESPID19-0626
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Extensive mycobacterium abscessus pneumonia in an immunocompetent infant

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Background

Pulmonary infections from non-tuberculous mycobacteria (NTM) typically present in patients with cystic fibrosis, underlying lung pathology, or immunodeficiency. Immunocompetent children typically have skin and soft tissue infection, cervical lymphadenitis, and rarely pulmonary infection. Although exact incidence is not known, NTM are an emerging pathogen. We describe the first extensive pneumonia with culture-confirmed *Mycobacterium abscessus* in an otherwise completely normal infant.

Case Presentation Summary

A 6-month old Hispanic female born at 38 weeks gestation via uncomplicated spontaneous vaginal delivery presented at age 4 months with 2-month history of cough and failure to thrive despite broad-spectrum antibiotic therapy. Our evaluation revealed an afebrile infant with heart rate 80 beats/min, respiratory rate 40 breaths/min with peripheral pulse oximetry of 98% on HFNC. She had nasal flaring, intercostal and subcostal retractions, but no wheezing nor rales. CT scan of the lungs showed large posterior bilateral perihilar opacities with sparing of pulmonary periphery and bases. Bronchoalveolar lavage and lung biopsy were performed as patient had no response to broad-spectrum antibiotic therapy. *Mycobacterium abscessus* was isolated from gastric aspirate and pleural fluid. Lung biopsy showed pleural and sub-pleural fibrosis, mixed focal neutrophilic aggregate, but no evidence of congenital lung malformation. Extensive immunologic testing, cystic fibrosis testing, and wide genetic testing by Dr. Holland's lab at NIH were negative. She responded to 12 months of clarithromycin and amikacin.

Learning Points/Discussion

Mycobacterium abscessus subsp. a*bscessus* can cause extensive pulmonary disease in young infants without immunodeficiency or underlying lung pathology, confirmed by culture, in this first case in English literature to our knowledge. We describe the first successful treatment of this presentation with combination antibiotic therapy without surgical intervention.

ESPID19-0603
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Community-acquired pneumonia after the introduction of 13-valent pneumococcal conjugate vaccine

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Background and Aims:

Pneumococcal conjugate vaccines (PCV) have reduced pneumonia caused by *Streptococcus pneumoniae*. However, their impact in respiratory infections caused by other bacteria has been barely studied. Our aim was to describe the changes in the epidemiology of community-acquired pneumonia (CAP) and its complications since the commercialization of the 13-valent PCV in 2010.

Methods:

Retrospective review of patients aged 1 month-16 years with culture-confirmed CAP admitted to La Paz Hospital (Madrid, Spain) in 2010-18.

Results:

We included 69 patients (66% male, 81% below 5 years, median age 32±35 months): 67% (44/67) *S. pneumoniae*, 19% (13/67) *Streptococcus pyogenes* and 15% (10/67) *Staphylococcus aureus*. Twenty percent had coinfection with respiratory viruses, which were less common in pneumococcal pneumonia (5%, vs 46% and 60%, $p<0.001$). Bacteria were isolated in blood culture (57%), pleural fluid (39%) or both (4%). There were no differences regarding age among the three bacteria. CAP numbers remained unchanged, but *S. pneumoniae* decreased (69% vs 31%, $p=0.019$) and *S. aureus* increased (30% vs 70% p=0.038) in the last three years of the study. Clinical data were available for 65 patients, 63 of whom (92%) required hospital admission (mean stay 12.2 days) and 28 (43%) intensive care. Sixty percent (39/65) developed complications, mainly pleural effusion/empyema (34/65, 52%), sepsis (9/65, 14%) and necrosis (8/65, 12%). Twenty-nine patients with pleural effusion required chest drainage (85%). The rate of complications, ICU admission and need of respiratory support was different among the three bacteria (Table 1), being Pneumococcal pneumonia less severe.

Table 1. Clinical data of patients, according to ethiology.

	S. pneumoniae n=42	*S. pyogenes* n=13	*S. aureus* n=10	
Bacteremia	**67% (28)**	7.7% (1)	**70% (7)**	p=0.03
Complications	50% (21)	**92% (12)**	60% (6)	p=0.025
Pleural effusion	45% (18)	**92% (12)**	40% (4)	p=0.08
Sepsis/shock	7% (3)	**46% (6)**	0	p<0.001
Intensive care admission	31% (13)	**85% (11)**	40% (4)	p=0.003
Respiratory support	12% (5)	**61% (8)**	**60% (6)**	p<0.001
Chest drain	31% (13)	**92% (12)**	40% (4)	p<0.001
Viral coinfection	4.8% (2)	**46% (6)**	**60% (6)**	p<0.001

Conclusions:

After 13-valent PCV introduction we have observed a decreased in pneumococcal pneumonia and an increase in staphylococcal pneumonia. *S. pyogenes* and *S. aureus* CAP causes complications often than pneumococcal CAP.

Systematic Review Registration:

N/A

ESPID19-0573
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Chest radiograph (cr) in children hospitalized with lower respiratory infections (lrti) due to rsv infection

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Background and Aims:

When performed, CR raises many doubts on its interpretation, and practical implications. The aim of this study was to retrospectively verify the concordance between the CR results and the WHO criteria for chest radiographs, and its influence on the antibiotic use. Additionally, the correlation with laboratory and clinical course was assessed.

Methods:

Hospitalized children with LRTI between January 2016-June 2018 were included. CRs were firstly evaluated by the radiologists influencing clinical decision-making process. Then retrospectively a team of pediatricians experienced in radiograph evaluation according to the pneumonia WHO criteria (P-WHO-C) performed the reevaluation of CR in a blinded manner. RSV infections were diagnosed by rapid antigen test and/or polymerase chain reaction.

Results:

CR was performed in 81 children (aged 12 days-91 months, median 4 months) with confirmed RSV infection. Alveolar or non-alveolar pneumonia was initially diagnosed in 60 children. After verification, WHO criteria were fulfilled only in 21 (26%) cases (including 3 cases initially classified as “no pneumonia”), 1 case was excluded. Sensitivity and specificity of initial CR assessment for P-WHO-C was 85.7% and 30.5%, respectively. Children with P-WHO-C showed higher CRP levels (median 20.7 vs. 6.1 mg/dL, **p=0.037**), but there were no differences in terms of laboratory (white blood cells count, absolute neutrophil count, procalcitonin), and clinical (breath rate, heart rate, oxygen saturation at admission, length of stay) parameters. Initial antibiotic treatments were started in 37 (46%) children, including 6 (7.5%) alveolar, 5 (6%) non-alveolar pneumonia cases, and 44% patients (26/59) with no pneumonia.

Conclusions:

In children with LRTI due to RSV much attention should be put on CR interpretation and the use of the WHO criteria for chest radiographs might help to avoid unnecessary antibiotic therapy.

Systematic Review Registration:

non-applicable

ESPID19-0525
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Access to palivizumab against respiratory syncytial virus among high-risk children in english hospitals

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Background and Aims:

Bronchiolitis due to respiratory syncytial virus (RSV) is the most common reason for hospital admissions in infants in England. Passive immunisation using palivizumab (Synagis®, MedImmune) is recommended for high-risk infants during the RSV season (October-March in England). It is not known what proportion of eligible children in England are treated with palivizumab.

Methods:

We used the Hospital Treatment Insights (HTI) database which incorporates hospital admission and pharmacy dispensing records for 43 hospitals in England. Eligible children were identified based on chronological and gestational age, and if their medical records indicated chronic lung disease (CLD), congenital heart disease (CHD), or severe combined immunodeficiency (SCID).

We calculated the proportion of children prescribed at least one dose of palivizumab in infancy. We modelled the odds of treatment according to gestational age, birth weight, sex, ethnicity, age and presence of CLD, CHD or SCID using logistic regression model.

Results:

We identified 7078 potentially eligible children, of which 4802 had complete information on risk factors. 83% of eligible children had CHD, 46% had CLD, 2% had SCID. 876 eligible children (18%) were prescribed ≥1 dose of palivizumab. The odds of treatment were four times higher for children with CLD compared to children without, 90% higher for children with SCID, and there was no difference between children with and without CHD (table 1).

Table 1 – Adjusted odds of palivizumab treatment in eligible children in 43 English hospitals by risk factors of interest (with 95% confidence intervals)

Risk factor	Odds Ratio (95% confidence interval)
Sex	
Female	1
Male	1.05 (0.90, 1.24)
Ethnicity	
White	1
Black	**1.75 (1.32, 2.31)**
Asian	0.76 (0.56, 1.04)
Mixed/other	1.15 (0.84, 1.58)
Congenital heart disease present (yes vs.no)	0.94 (0.77, 1.15)
Chronic lung disease present (yes vs.no)	**4.19 (2.91, 6.02)**
Severe combined immunodeficiency present (yes vs.no)	1.89 (0.98, 3.62)
Gestational age	
<28 weeks	**3.11 (1.69, 5.70)**
28-31 weeks	**2.24 (1.25, 4.02)**
32-36 weeks	1.24 (0.76, 2.02)
37+ weeks	1
Birth weight	
<1500g	**2.94 (1.41, 6.14)**
1500-2499g	1.60 (0.84, 3.05)
2500g-3499g	1.43 (0.87, 2.37)
3500+g	1
Age at start of RSV season	
<1 month	0.78 (0.59, 1.04)
2-3 moths	**3.01 (2.23, 4.07)**
4-5 months	**2.39 (1.78, 3.22)**
6+ months	1

Conclusions:

We found that palivizumab is infrequently prescribed to eligible children. Further research is needed to explore variation in clinical and coding practice between hospitals and to compare long-term respiratory outcomes in treated and untreated children.

Acknowledgement: Funded by the Wellcome Trust. HTI is maintained by IQVIA.

Systematic Review Registration:

NA

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E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Acute exacerbation of chronic suppurative lung disease in children. Is cough swab a reliable diagnostic tool?

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Background and Aims:

Cough swabs samples following inhaled hypertonic saline are routinely used in children with acute exacerbation of chronic suppurative lung disease (CLSD). The diagnostic accuracy of these samples at the specific group of patients has not been evaluated. Our aim was to evaluate whether cough swabs following inhaled hypertonic saline from children with acute exacerbation of CLSD provide reliable microbiological results, using a new nested, multiplex reverse transcription PCR syndromic diagnostic panel.

Methods:

On-going prospective case-control study since November 2018. The BioFire® FilmArray® Pneumonia Panel (BioFire Diagnostics, Biomerieux) was used to compare bacterial yield of cough swabs samples from children with acute exacerbation of CLSD and age-matched previously healthy children hospitalized with clinical or/and radiological evidence of low respiratory infection, comprising the healthy control group.

Results:

Eleven children with acute exacerbation of CSLD and 9 controls were included. The microbiological yield did not differ (Table 1), while the median number of detected microorganisms in both groups of children was 4.

Table 1: Detected microorganisms in patients and controls

Microorganisms	Nº of microorganisms in CLSD patients (n=11)	Nº of microorganisms in controls (n=9)	P
Haemophilus influenzae	8	4	0.36
Moraxella catarrhalis	5	3	0.67
Staphylococcus aureus	5	2	0.37
Streptococcus pneumoniae	3	3	1.00
Streptococcus pyogenes	1	3	0.28
Pseudomonas aeruginosa	1	0	1.00
Human Rhinovirus/enterovirus	8	5	0.64
Parainfluenzae virus	3	1	0.59
Adenovirus	1	1	1.00

Microorganisms	Nº of microorganisms in CLSD patients (n=11)	Nº of microorganisms in controls (n=9)	P
Respiratory Syncytial Virus	0	1	0.45

Conclusions:

According to these preliminary data, microbiological results from cough swabs probably reflect upper respiratory flora and may not represent reliable samples. Although a larger cohort is needed, we further plan to evaluate cough swabs in CLSD children by comparing them with concomitantly obtained bronchoalveolar lavage samples.

Systematic Review Registration:

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Hospital invoicing based on nordic diagnosis related groups works well concerning infant bronchiolitis treated on the ward but not in the intensive care unit

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Background and Aims:

Bronchiolitis is the leading cause for hospitalisation in infancy and for that reason, the hospitalisation costs are high. We carried out a retrospective case-control study, which evaluated the hospitalisation costs of inpatient bronchiolitis treatment and the nursing intensity measured by the patient classification system (RAFAELA®).

Methods:

We identified 44 bronchiolitis patients treated in the paediatric intensive care unit (PICU) for bronchiolitis at less than 12 months of age between 2010 and 2015 (cases). For each case we selected two controls treated on the paediatric ward (n=88). We collected patient's treatment data, hospital invoicing data, which was based on Nordic Diagnosis Related Groups (NordDRG), or on the expensive categories and RAFAELA® points. As statistical analyses, we used median with minimum and maximum values, Mann-Whitney U test for non-normally distributed continuous variables and Spearman test for correlations between continuous variables.

Results:

For cases treated in the PICU, hospital invoicing was most often based on expensive categories. For controls treated on the ward, invoicing was most often based on NordDRG. Median total costs were €6352 (min-max 1330-30,554), and median length-of-stay in hospital (LOS) was 8.5 days (3-18) in cases, and respectively, €2009 (768-6027) and 3 days (1-8) in controls. The average RAFAELA® points were 20 (12-24) in cases and 15 (9-19) in controls. The higher RAFAELA® points were associated only to the treatment with nasal continuous positive airway pressure (nCPAP) and mechanical ventilation during PICU admissions and to the treatment with supplementary oxygen and naso-gastric tube during ward admissions. RAFAELA® points did not correlate with the hospitalisation costs.

Conclusions:

Current NordDRG categories should not be used in hospital invoicing when PICU admission is needed for bronchiolitis, though they work well in ward settings.

Systematic Review Registration:

N/A

ESPID19-0441
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Analysis of pediatrics hospitalizations due to influenza in two consecutive seasons 2016/2017 and 2017/2018 in a defined polish population.

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Background and Aims:

This study aimed to analyze the causes of hospitalization in children with influenza, based on a defined Polish population.

Methods:

This was a retrospective analysis (based on hospital records) of causes of hospitalization in children under 18 years of age with influenza, treated on the Infectious Diseases Ward of the Children's Hospital in Poznan, Poland in two consecutive flu seasons from October 2016 to June 2018. The ward serves almost the entire child population of the Greater Poland region (10% of the Polish population).

Patients were identified using the ICD-10 codes. Influenza was diagnosed based on one of the two tests: the immunochromatography-based rapid diagnostic tests or molecular tests (PCR).

Results:

A total of 209 children were hospitalized for influenza complications: 140 with influenza type A and 69 with type B. The median age of admitted patients was 62 months (range from 3 weeks to 17 years).

Three-fourts of children had no risk factors for severe course of influenza (no chronic diseases). Median lenght of hospitalization was 6 days. The commonest complications were vomiting (23%), followed by pneumonia (18%), neurological symptoms (13%) and hematological complications (12%). Oseltamivir was used in the treatment of 97% of patients.

Conclusions:

The results presented here serve to remind us that influenza may to lead to severe complications in unvaccinated children and adolescents, and demonstrate the benefits of influenza vaccination.

Most children hospitalized with influenza were immunologically healthy.

Systematic Review Registration:

N/A

ESPID19-0397
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Demographic, perinatal and childhood hospitalisation characteristics of hospitalised pertussis vaccine failure cases in new zealand: a case series study

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Background

Host characteristics that influence risk of pertussis vaccine failure are still not thoroughly understood. A greater understanding of host risk factors for pertussis vaccine failure has the potential to improve pertussis prevention strategies. We describe demographic, perinatal and childhood hospitalisation characteristics of paediatric pertussis vaccine failure cases.

Case Presentation Summary

A case series study design was used to describe all hospitalised cases of paediatric (5 months to four years old) pertussis vaccine failure occurring in New Zealand between 2006 and 2016. Hospitalisation, demographic and perinatal data was sourced from three large national data sets linked by unique identification number.

Of the 504,984 pertussis vaccinated paediatric population, 85 (0.2%) were hospitalised for pertussis disease during the study period. None were admitted to neonatal intensive care units or died from pertussis. Median age at pertussis hospitalisation was 15 months (Table 1). The median socioeconomic deprivation quintile was 4, indicating low socioeconomic status. Twenty-one (25%) cases were born prematurely; seventeen (20%) were of low or very low birth weight (less than 2500 g); and eleven (15%) had either a moderately low or very low five minute Apgar score (6/10 or less). Fifty-six (66%) had at least one hospitalisation between 92 days old and four years old; 70% were hospitalised for respiratory diseases not including pertussis.

Table 1 Case demographics

Characteristic	Value n=85
Median age at pertussis hospitalisation, interquartile range	15, 16
Socioeconomic deprivation (NZDep13) quintile median, interquartile range	4, 2

Learning Points/Discussion

Our findings suggest perinatal and demographic factors may influence risk for pertussis vaccine failure, but there is need to test these hypotheses statistically. Further work is being undertaken to identify predictive host factors for pertussis vaccine failure.

ESPID19-0363
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Fatal case of malignant pertussis with hyperleukocytosis and multi-organ failure in unvaccinated infant

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Background

Despite a widespread vaccination program, pertussis continues to be a common worldwide infection, that can be particularly severe in young infants, with frequent hospitalizations and occasional deaths. We here report a fatal case of malignant pertussis in an infant who underwent repeated exchange transfusions (ET) and eventually died due to severe complications.

Case Presentation Summary

A 3-month old girl was admitted to ICU of Children's Clinical University Hospital with a 10-day history of rhinitis and persistent, paroxysmal cough 5 days prior admission. She was vaccinated only with BCG. On examination, her respiratory rate was 52 breaths/min, oxygen saturation was 94% in room air, heart rate was 150 beats/min. A chest radiograph showed bilateral pneumonia. Her WBC count was 87.37x10^3/μL (53.2% lymphocytes, 38.8% neutrophils), which over the next 20 hours increased to 104.34x10^3/μL. Because of suspected severe pertussis, patient was treated with oral Azithromycin (10mg/kg/day) and underwent 1st double volume ET according Great Ormond Street Hospital guidelines. After that, WBCs was 49.73 x10^3/μL, however in next 30 hours it doubled to 102.31x10^3/μL and patient developed respiratory distress, requiring mechanical lung ventilation and 2nd ET, during which, patient's condition rapidly worsened with hypotension, low oxygen saturation, poor peripheral perfusion and oliguria. The WBCs dropped to 19.14x10^3/μL, but after 30 hours was 85.25 x10^3/μL, therefore 3rd ET was done and haemodialysis started due to anuria. On 8th day of hospitalization, patient became unresponsive to stimulus and brain death protocol was started and finished on 9th day of hospitalization. *Bordetella pertussis* was diagnosed by PCR on nasal secretions.

Learning Points/Discussion

Early ET has been suggested a useful therapeutic modality in children with severe pertussis, however, severe leucocytosis is a prognosticator of poor outcome and mortality rate approaches 80%.

ESPID19-0290
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Should be on the alert in infants with cytomegalovirus infection in the lower respiratory tract

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Background

Common variable immune deficiency (CVID) is a disease that disrupts the immune system and is characterized by low levels of immunoglobulin subgroups and failure in antibody-producing B lymphocytes and plasma cells. We report a case of 6-month-old patients with pneumonia due to CMV and Bocavirus and he was later diagnosed as CVID and underwent bone marrow trasplantation (BMT).

Case Presentation Summary

The patient, who was admitted with fever, cough, wheezing and frequent breathing, and hospitalized with the diagnosis of acute bronchiolitis. Then he was admitted to the intensive care unit on the 5th day of treatment with no clinical improvement. He was treated with antibiotherapy for pneumonia and noninvasive nasal cpap therapy and other supportive treatments for other respiratory problems for 8 days in the intensive care unit. His nasopharengeal swab was evaluated multiplex polymerase chain reaction (PCR) for respiratory viruses and positive for Bocavirus. There was no growth in his blood and urine culture. His blood CMV PCR was found to be positive (400 copy) and intravenous ganciclovir treatment was ordered and his clinical condition and pneumonia was improved. His immunoglobulin levels were found to be low (IgA: 4 mg/dl (4.4-84), IgG: 18 mg/dl (232-1411), IgM: 115 mg/dl (0-145), Anti-HBs: 2 U/L) and his lymphocyte subgroups were also found to be low (CD3: %31,60 (%60-85), CD4: %21,14 (%29-59), CD8: %7,24 (%19-48), CD19: %66,59 (%11-16), CD20: %66,51 (%11-16), NK: %1,79 (%5-15), CD45: %99,46 (>%90-100), CD14: %0.09 (<%2). He was diagnosed with as a common variable immune deficiency and later underwent succesful BMT.

Learning Points/Discussion

It should be kept in mind that if unusual pathogens are detected in the lower respiratory tract infections immunodeficiency syndromes must be thougt.

ESPID19-0152
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Clinical presentation of respiratory illness with enterovirus d68 in taiwan

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Background

Enterovirus-D68 (EV-D68) has been endemic with a small number of positive cases in Taiwan for some years. Local detailed respiratory presentation was lacked**.** This study characterized the clinical course in patients admitted to the medical center and regional hospital in Taichung during 2015.

Methods

Retrospective chart review of patients with confirmed EV-D68 infection admitted to the medical center and regional hospital in Taichung with respiratory symptoms in the second half year of 2015. Past medical history, clinical presentation, management, and course in hospital were collected and analyzed. Simple demographic data and clinical symptoms were also collected from patient confirmed EV-D68 infection visited to clinics in Taichung.

Results

Eight patients were included (2 adults and 6 children with median age 6.3 years). Two children had a prior history of asthma or recurrent dyspnea, and one had other preexisting medical comorbidities. One children were admitted to the pediatric intensive care unit. Cough, rhinorrhea, tachypnea and fever were the most common clinical symptoms among inpatients, while influenza like illness(ILI) was prevalent in outpatients.

Conclusions

EV-D68 infection resulted in respiratory presentations of asthma-like illness in the hospitalized pediatric population. Patients with a prior history of asthma or recurrent dyspnea appear to be more severely affected.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0105
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Pneumocystis pneumonia in taiwan from 2014 to 2017: clinical manifestations and outcomes between pediatric and adult population

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Background and Aims:

Pneumocystis pneumonia (PJP) is a severe and lethal opportunistic infection in the immunocompromised patients. Due to the increasing usage of immunosuppressants, the incidence of non-HIV related PJP has increased in recent years. However, there's little research regarding the children with PJP. The aim of this study is to understand PJP more among pediatric population.

Methods:

We retrospectively reviewed the medical records of the patients with PJP in NTU hospital from 2014 to 20 17. Diagnosis is made if the patient met all of the following criteria: 1. Presence of relevant pulmonary symptoms and signs, 2. Pulmonary infiltrate on CXR or CT, 3. Detection of Pneumocystis. jiro verci from respiratory specimen via PCR, 4. Received relative antibiotics for PJP.

Results:

20 children and 132 adults were enrolled in this study. The most common underlying disease among child ren included malignancy (40%), post-transplant (30%), and primary immunodeficiency (20%). The major underlying disease in adults including malignancy (36%), HIV with AIDS (31%), and aut oimmune disease (24%). There's no significant difference in the clinical manifestations, mortality, and complication between pediatric and adult. But children tend to have lesser chance of using alternative antibiotics, methylprednisolone and inhaled NO in treating PJP. The chance of associated CMV disease is also significantly lower in children.
Risk factors for mortality including: malignancy or autoimmune disease, lower lymphocyte count and albu min, co-infection with CMV.

Conclusions:

There's no significant difference between children and adult with PJP in clinical manifestation and outcom es. But children tend to have lesser chance of using alternative antibiotics, methylprednisolone and inhaled NO in treatment. The chance of associated CMV disease is also significa ntly lower in children.

Systematic Review Registration:

N/A

ESPID19-0098
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Chornic and acute infectious triggers in immunocompetent children

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Background and Aims:

During epidemic seasons the causative agents are quickly identified and unified treatment guidelines are easily created and covered. Outside epidemic however the etiological profile could be in a very broad spectrum and thus it is difficult to have unified guidelines.

Methods:

A real life observational study for 6 months (outside winter) on 74 children dived in 4 groups: 24 children with bronchial asthma (BA), 20 with chronic wet cough (CWC), 24 with bronchiolitis and bronchitis (AB) and 10 healthy children (HC) as a control. We collected serum, nasopharyngeal and deep throat swabs from specific pathogen detection (culture examination, PCR, ELISA).

Results:

In the HC we didn't identify any pathogens in the throat samples. In 20% of the nasal swabs we cultured *Staphylococcus aureus*. In 33% of the patients from the AB group we found only viruses (RSV, RV and hMPV), in 25% we found combined infection with virus and bacteria (mainly *Moraxella catarrhalis* and *Streptococcus pneumoniae*). The BA group in 25% we found only viruses (Adenovirus, RV and RSV). In 56% of the cases *Streptococcus pneumoniae* was confirmed in the throat swabs vs. only 33% for isolated *Moraxella catarrhalis.* Only in 10% of the CWC group we found viral infection (hMPV, Adenovirus and RV), 50% had *Streptococcus pneumoniae* and the rest 40% - polymicrobial etiology incl. *S.aureus, H.influenzae, S. pyogenes, E.aerogenes*.

Conclusions:

The most prevalant bacteria found was *M. catarrhalis* and *S. pneumoniae* (non vaccine serotypes), while RV, RSV and Adenoviruses are the predominant viral cough triggers ouside winter season.

Systematic Review Registration:

Acknowledgements This work was supported by a grant from the Medical University of Sofia (Council of Medical Science, project no. 7770/2017, grant no. 106/2018).

ESPID19-0097
E-Poster Viewing - May 7-10 - E-Poster Hours

Lower respiratory infections and pneumonia

Seasonal variations of etiology of pneumonia in hospitalized children in bulgaria

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Background and Aims:

The correct identification of pathogens causing community acquired pneumonia (CAP) in childhood is crucial for timely and adequate treatment. We analyzed the seasonal etiological profile of pneumonia in children for three consecutive years, after introduction of pneumococcal vaccine in Bulgaria.

Methods:

We evaluated prospectively the data for the last 3 consecutive years (2016-2018), 285 immunocompetent children hospitalized with radiographically confirmed pneumonia. We specifically looked for prior antibiotic use and immunization status. The laboratory data included – CRP, full blood count, sputum culture examination, PCR and/or serology for respiratory viruses, Chlamydia and Mycoplasma.

Results:

As expected the lowest number of hospitalized patients with CAP is during summer, and for 3 years we found viral pathogen (adenovirus) only in one patient. RSV is more often isolated during autumn, while influenza and hMPV more during winter (p=0.02). More co-infected patients (bacteria and virus) were found during winter and spring (p=0.01). For *Streptococcus pneumoniae* we couldn't find any seasonal prevalence (p=0.5), while for *Mycoplasma pneumoniae* we found main prevalence during spring and early summer (p=0.000). Maybe these seasonal fluctuations of viruses and *M.pneumoniae* are behind the finding that there is no viral co-infection with *M.pneumonia*. More combined infections were found during winter (p=0.04).

Conclusions:

Based on our study we think that maybe we should reevaluate our treatment guidelines and first line of antibiotic choice for CAP in children in late spring and early summer should be macrolide. Winter patients would benefit from the standard first choice treatment with beta lactam with added supportive symptomatic therapy as in viral co-infection.

Systematic Review Registration:

Acknowledgements This work was supported by a grant from the Medical University of Sofia (Council of Medical Science, project no. 7771/2017, grant no. 107/2018).

ESPID19-0605
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Yellow fever cases in children in a tertiary care center in são paulo in 2018

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Background

Yellow Fever (YF) is a disease caused by a *Flavivirus* and transmitted by arthropod bite. It is endemic in Africa and South America. YF is vaccine preventable but has high morbidity and mortality in susceptible individuals. There was an outbreak of YF in Brazil in 2017/2018 leading to concern of re-urbanization of the disease. Vaccine campaigns happened in areas without previous vaccine recommendation.

Case Presentation Summary

We had sixteen patients with suspected YF in a tertiary care center in São Paulo in 2018. One case was confirmed, eight were ruled out and seven were vaccine reactions.

One viremic patient confirmed with PCR had hepatitis and came from an endemic area. He was vaccinated three days before the beginning of the symptoms. We could not identify if the virus was wild or vaccine-type. The child was dismissed with normal liver function.

Two cases of vaccine related disease were laboratory confirmed. A child nine-months-old was admitted with fever, vomit and respiratory distress three days after vaccination. Laboratories showed aspartate-aminotransferase 21,151U/L, myositis and metabolic acidosis. Bilirubin levels were normal. A twelve-year-old adolescent presented with headache and vomit twenty days after vaccination. YF-IgM was positive in cerebrospinal fluid. Both cases were severe but patients recovered without sequelae. The other five cases had fever and mild adverse effects after vaccination.

Learning Points/Discussion

The majority of cases of YF during the epidemic in Brazil were in adults. Despite the high mortality rate, our patients had a good outcome.

The increased frequency of cases of vaccine reaction might be due to a high number of people vaccinated in the campaign.

Some patients had hepatitis without jaundice, which is not the typical presentation of YF. It is important to suspect of YF even in anicteric patients

ESPID19-1195
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Dengue fever in tourists returning from endemic area: an italian pediatric case series

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Background

Dengue is a mosquito-borne disease frequently imported in Europe, where autochthonal outbreaks are potential since recent spreading of the vector. Primary infections usually produce a self-limited febrile syndrome. Secondary infections with different serotype, especially in children, may lead to severe shock syndrome with plasma leakage and hemorrhagic features. WHO 2009 revision defined warning signs (both clinical and laboratoristic features) to identify patients at risk of severe Dengue. Imported infections require prompt diagnosis to reduce the risk of autochthonous outbreaks, and diagnostic tools like rapid tests may be useful in these situations.

Case Presentation Summary

We describe a series of 4 children infected with viral serotype 3 during a journey to the Maldive Islands, who developed symptoms after returning to Italy. We obtained rapidly the diagnosis performing NS1 antigen test, then they were hospitalized, clinically and laboratoristically monitored for the presence of warning signs.
Lab tests reported thrombocytopenia, lymphopenia, elevated liver enzymes, and hyperferritinaemia, Interestingly, these datas were aligned with those in literature, reporting this association. Although not present among the WHO warning signs, hyperferritinaemia is considered a hallmark of extensive immune activation and it is reported as a possible predictor for severe Dengue.
In our case all patients were treated supportively and, as expected in primary infections, they developed no complications.

Learning Points/Discussion

We highlight the importance of considering Dengue infection in all febrile children travelling to endemic areas, since also in popular touristic destinations vector eradication may be incomplete where host structures coexist with local ones. So, also in non-endemic areas diagnostic tests should be available to early recognize all the cases. Awareness of a primary infection may help prevent future re-exposure in order to avoid reinfection with potentially severe clinical course.

ESPID19-0962
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Abdominal pain as presenting manifestation of neuroborreliosis in children

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Background

Lyme borreliosis is a tick-borne infection which affects the skin, joints, heart and nervous system. Children with a neuroborreliosis usually present with a facial nerve palsy or aseptic meningitis, but the spectrum of manifestations is wider.

Case Presentation Summary

PP, a 9- year-old male, was referred to our department with a 1-year history of abdominal pain, anorexia and loss of attention. He first presented severe continuos abdominal pain. A computed tomography (CT) scan of the abdomen, a gastroscopy and a colonoscopy were performed but no abnormalities were revealed. After 2 months the pain gradually remitted. Subsequently he presented anorexia with weight loss and poor scholar performance. At the physical examination reduced patellar reflexes were revealed. MRI showed leptomeningeal, cranial nerves and cauda equina contrast enhancement. A lumbar puncture was performed and a lymphocytic pleocytosis with hypoglycorrhachia and increased cerebro-spinal-fluid (CSF) protein level were found. Lyme neuroborreliosis was considered and IgG antibody test against Borrelia was positive in both serum and CSF. Intravenous ceftriaxone treatment 3 gr daily was given for 21 days. 8 weeks later a lumbar puncture showed normalised cell count and reduced protein concentration in the CSF. MRI was repeated showing a remarkable improvement. At the follow-up, 10 weeks after the end of the treatment, the patient gradually regained appetite and a slight improvement of the attention was observed.

Learning Points/Discussion

The early clinical symptoms of Lyme neuroborreliosis may be nonspecific and can point to a wide spectrum of disease. Although extremely rare in children, abdominal pain due to radiculitis could be the starting symptom of the infection.

ESPID19-0814
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Paediatric scrub typhus in nepal

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Background and Aims:

Scrub typhus is a rickettsial infection caused by Orientia tsutsugamushi and transmitted by tromboculid mites. It is an important cause of undifferentiated fever and is endemic to various regions of South East Asia. It causes multi-systemic disease and has similar features to typhoid fever, leptospirosis, and murine typhus. Our aim is to study the clinico-demographic profile of children diagnosed with scrub typhus in a tertiary care hospital in Nepal.

Methods:

The admissions of children (aged 2 months to 14 years) to the paediatric ward and ICU of Patan Hospital were reviewed. Between April 2017 and October 2018 a total of 24 patients were diagnosed as scrub typhus; confirmed IgM antibody positive by ELISA. Medical records were reviewed and information collected, including age, sex, clinical features, and total length of stay in hospital. The records of 4 patients were unobtainable.

Results:

Out of 20 children (n=20) 13 were female (65%) and 7 were male (35%). The mean age was 7.4 years. Average length of hospital stay was 9 days. 6 children (30%) were admitted to the PICU. Fever was present in 20 children (100%), abdominal pain in 9 (45 %), vomiting in 6 (30%), pneumonia in 5 (25%), shock in 4 (20%), oedema in 2 (10%), oliguria in 2 (10%), jaundice in 1 (5%), rashes in 1 (5%), signs of meningeal irritation in 1 (5%), and cerebellar signs in 1 (5%).

Conclusions:

Paediatric scrub typhus in this centre is consistent with the disease profile; often shows various clinical features, and can warrant prolonged admission and intensive care. The numbers here indicate that it remains an important differential in fever, and should be considered when evaluating any child in Nepal presenting with undifferentiated fever.

Systematic Review Registration:

N/A

ESPID19-0716
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Effectiveness of complementary medicine, quercetin, combined with standard of care in the treatment of patient with acute dengue fever: an open label randomized controlled trial

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Background

Dengue fever is a significant public health problem. There are no effective antiviral agents against dengue virus therefore the treatment remains supportive. Quercetin, a flavonoid, found naturally in vegetables and fruits have been reported to have anti-inflammatory and antiviral properties with potential to boost thrombopoiesis and erythropoiesis. However, there are limited studies to prove beneficial effects of quercetin as a complementary medicine in the treatment of dengue fever in children. This study aims to evaluate the beneficial effect of quercetin, plus standard of care in the treatment of acute dengue fever. The primary endpoint shall be the time of improvement of hemoconcentration, thrombocytopenia, resolution of clinical symptoms, and shorter hospital stay.

Methods

An open label randomized controlled clinical trial was conducted in a tertiary hospital. Patients age 7 to 18 with acute dengue fever were enrolled. Randomly into 2 groups either receiving the quercetin-containing capsule taken for 3 consecutive days plus standard of care (experimental group) or standard of care alone (control group) for acute dengue fever. Serial blood tests were taken within the treatment period.

Results

The study involved 64 patients (32 in each arm). Results showed that there was significant increase in the platelet counts of the experimental group (p value <0.001). There was also noted significant difference with regards to the resolution of symptoms (p value <0.05) and in the total number of hospital stay among the same group (p value <0.001) wherein they demonstrated lesser hospital stay. No incidence of infection or untoward effects on both treatment groups.

Conclusions

Complementary medicine, quercetin combined with standard of care is effective and safe in the management of patients aged 7 to 18 years old with acute dengue fever.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0599
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Diagnosing leptospirosis and the disease spectrum: a level ii hospital experience

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Background

Leptospirosis is a zoonotic infectious disease with a high incidence rate in semi-tropical climates such as that of Azores Islands, in Portugal. The Azores have a incidence rate of 11,1/100.000 and only one case was diagnosed between 1-14 years of age. Between 2016-2018 two children from São Miguel island were diagnosed with leptospirosis.

Case Presentation Summary

Case 1 A 13 year old boy was admitted with fever, chills, myalgias, headache, conjunctival suffusion and dark urine. Analysis demonstrated neutrophilia, reactive C protein (RCP) of 32mg/dL, proteinuria, high urobilinogen and normal renal function. The boy performed farming activities. Molecular biology study identified Leptospira spp. in the blood and urine. Ceftriaxone was initiated. Subsequent laboratory and clinical improvement was observed. Preliminary leptospira serologies were negative with seroconvertion verified three weeks later.
Case 2 A 15 year old adolescent was admited with high fever, myalgias, headache and abdominal pain. Blood analysis demonstrated neutrophilia, ascending RCP values reaching 30mg/dL and signs of non-oliguric renal lesion. He had been in contact with domestic dogs, pigs and rabbits. Molecular biology study identified Leptospira spp. in the blood and urine with negative preliminary serologies. Chest Xray revealed bilateral infiltrate. Antibiotic with ceftriaxone was initiated. Twelve hours later he started tachycardia and hypotension. Transfer to an ICU unit was performed. There was a subsequent clinical improvement.

Learning Points/Discussion

In areas with high rural exposure such as the Azores leptospirosis in pediatric age should be highly considered in the child or adolescent with fever, myalgias, headache and conjunctivitis and concomitant history of contact with potencially infected domestic animals/wild rodents. The diagnosis is made with serologic testic and supported with molecular techniques. An age-dependant association with disease's severity, as exemplified in the presented cases, should be considered.

ESPID19-0565
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Clinical use of the who revised dengue classification in a-tertiary hospital

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Background and Aims:

Background: Dengue infection is a major public health problem in South East Asia, including Thailand. Accurate diagnosis and appropriate management are essential steps to decrease mortality rate. In 2009, World Health Organization (WHO) presented the revised Dengue Case Classification by adjusting the diagnostic criteria for dengue infection to be easy to implement.
Objective: To evaluate the clinical use of WHO Dengue Case Classification 2009 for dengue infection in Bhumibol Adulyadej Hospital.

Methods:

Methods: A Retrospective descriptive study was performed in Pediatric Department of Bhumibol Adulyadej Hospital. Medical records of eligible patients who were aged under or 15 years old with laboratory confirmed with dengue infection between July 1, 2016 and October 31, 2017 were reviewed.

Results:

Results: There were 209 laboratory-confirmed dengue infections. Diagnosis was done by using the traditional (1997) classification, 170 cases (81.3%); by the revised classification, 29 cases (13.9%); and 10 cases (4.8%) by both classifications. In traditional classification group, the patients were classified as dengue fever (149; 87.7%), dengue hemorrhagic fever (18; 10.6%) and dengue shock syndrome (3; 1.7%), respectively. In this group, 126 cases (74%) received treatment according to the traditional guideline. In revised classification group, the patients were classified as dengue with warning signs 23 (79.3%), and dengue without warning signs 6 (20.7%). No patient was classified as severe dengue. All patients in revised classification group received treatment according to the revised guideline.

Conclusions:

Conclusions: The WHO Dengue Case Classification 2009 and its treatment guideline are applicable and friendly to be used and followed. Nonetheless, it may cause a burden to healthcare personnels especially in resource-limited settings. To modify the revised classification to each clinical setting may need to be done.

Systematic Review Registration:

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ESPID19-0305
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

Serial igm and igg levels after an acute infection with scrub typhus

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Background

Scrub Typhus is re-emerging in many parts of the world. Little is known about the persistence of IgM and IgG antibodies after an acute infection. In this study, we present serial serological data after an acute infection of scrub typhus.

Methods

Children < 15 years who were diagnosed with scrub typhus disease based on a positive scrub typhus IgM by ELISA were followed up serially and blood sampling done at 3, 6, 9 and 12 months for scrub typhus IgM and IgG. Graphs were plotted for both IgM and IgG to determine their trajectory and the duration it takes for the IgM results to become negative after an acute infection. Optical densitiy(OD) values of >0.5 were considered positive for both IgM and IgG.

Results

There were 103 children diagnosed with scrub typhus. IgM levels were available at baseline, 3, 6, 9 and 12 months for 103, 16, 22, 49 and 63; and IgG for 99, 15, 22, 49 and 61 children respectively. The mean OD values for IgM were 2.304(0.694), 0.714(0.448), 0.341(0.282), 0.294(0.282) and 0.358(0.425); and IgG were 1.369(0.956), 2.741(0.453), 1.861(1.095), 1.950(1.103), 1.947(1.014) at baseline, 3, 6, 9 and 12 months respectively. With serial plotting of the IgM, the mean duration of IgM to become negative after an acute infection was 4.6 months.

Conclusions

After an acute infection of scrub typhus, scrub typhus IgM takes about 4.6 months to become negative and IgG remains positive atleast till 12 months.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0050
E-Poster Viewing - May 7-10 - E-Poster Hours

Lyme Disease

The epidemiology and virology of dengue virus infection in children from primary health care of urban area in western java indonesia

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Background and Aims:

In endemic countries, most of dengue fever cases clinically resembles other diseases such as malaria, typhus, or just flu-like syndrome, it is important to detect dengue infection in patient with acute fever 1 to 4 day and which serotype of dengue virus that circulation to determine the risk of severe case of dengue to occur in primary health care

Methods:

patients 0-18 years old with acute fever from three Primary Health Centre in bandung city that represent three subdistricts with high dengue case form march to October 2018 with inclusion criteria: Fever at least 37.6^{o}C, 1-4 days, with or not taking antipyretics. Name, age, and sex, nutritional status, laboratorium examination was collected. Rapid NS1 antigen test is done as an additional check, nested RT-PCR assay for dengue virus (1-4) was perform from NS1 antigen positive patient. The collected data analyzed by independent t-test.

Results:

178 blood samples collected. 40 (22,5%) samples NS1 (+), mostly in 5-14 years old group, 17(42,5%) patient not done complete blood count because not suspected as dengue cases, mean body temperature higher in confirmed dengue virus cases (37,66 (±2,07) vs 38,33 (±0,83);p<0,005) while mean leucocyte count (8.964 (±5.369) vs 4803.91 (±2.197);p>0,005) and platelet count (239.218 (±99.402) vs 164.739,13 (±98.259);p>0,005) is lower. from 40 NS1(+) patient, 17(42,5%) showed all serotype of dengue can be found, with 8(47,05%) Den 3.

Conclusions:

Incidence of dengue cases in acute febrile patient is quite high, all serotype of dengue virus found, the risk of secondary dengue virus infection is imminent, its strongly suggest for the government to make a policy to supports use of rapid NS1 antigen at primary health center expecially in endemic area for early detection and prevention for the community.

Systematic Review Registration:

N/A

ESPID19-0222
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Etiological structure of the causative agents of bloodstream infections

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Background

In a retrospective study from 2009 to 2017 was studied identified etiological pattern of bacteremia.

Methods

Only for the period allocated 655 pathogens cultured from blood cultures 515 patients aged from 3 weeks to 18 years old.

Results

According to the results of the study, the proportion of gram-negative bacteria was 31.7%, gram-positive bacteria-61.9%, fungus -6.4%.

The spectrum of gram – negative bacteria in the family Enterobacteriacae (n=86) is diverse: Escherichia – 10.5%, Salmonella – 5.8%, Shigella – 25.6%, Proteus mirabilis – 1.15%, Providencia stuartii – 1.15%, Serratia – 15.1%, Klebsiella – 27.9%, Enterobacter – 10.5% and others – 2 (2,3%).

Gram-negative non-fermenting bacteria were isolated in 102 (16.7%) episodes of bacteraemia. Among them dominated Acinetobacter – 47.1%, Pseudomonas – 20.6%, Achromobacter – 12.7% and Stenotrophomonas maltophilia – 7.8%.

The structure of gram-positive bacteria (n=404) was dominated by staphylococci (62.1%), with the most frequently isolated coagulase-negative types (84.5%). In the structure of all staphylococci (n=251), S. aureus was found with a frequency of 15.1%, the most common was S. epidermis – 63.3% of cases. Streptococci (n=66) were dominated by Str. pneumonia (27.3%) and Str. agalacia (19.7%) and Str. viridans groups (15.2%). Enterococci were isolated in 31 patients (5.1%), with almost the same frequency dominated by Enterococcus faecalis and Enterococcus faecium (41.9% and 38.7%, respectively). During the study period, 7 (1.1%) strains of Corynebacterium were isolated.

Conclusions

Among the isolated microorganisms, staphylococci prevailed, the 2nd place in the frequency of isolation was occupied by non-fermenting bacteria and the 3rd place-bacteria of the Enterobacteriacae family.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESPID19-1114
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Unexplained fever in an 8-week-old infant. Usefulness of n-terminal pro-brain natriuretic peptide (nt-probnp) as a diagnostic tool.

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Background

Kawasaki disease (KD) in young infants is rare and often incomplete, leading to a delayed diagnosis and higher rate of complications.

Case Presentation Summary

An 8-week-old previously healthy infant was brought to Hospital with 1-hour history of fever and fussiness. She didn't look toxic and physical exam (PE) was normal. Laboratory tests: 13,050 leucocytes/mm^3, C-reactive protein (CRP) 191.8 mg/L, procalcitonin 4.87 ng/mL. Urine and cerebrospinal fluid (CSF) analyses were normal. Sepsis was suspected and she received 7-day intravenous antibiotics. On day 2 she still had high fever, grunting and tachycardia. ECG and chest X-ray were normal. From day 3, she had no fever and clinical status improved. Viral and bacterial tests were negative. At discharge, she was symptom-free with normal PE and acute phase reactants (APR) decreased (CRP 62.6 mgL, procalcitonin 0.49 ng/mL).

She was well at home. On day 14 her temperature was 38.2º C. PE showed paleness, macular rash on trunk and thighs, II/VI systolic murmur and slight conjunctival hyperemia. Laboratory tests: 16,290 leucocytes/mm^3, 756,000 platelets/mm^3, hemoglobin 8.9 gr/dL, albumin 24 gr/L, CRP 218.5 mg/L, procalcitonin 0.61 ng/mL, N-terminal pro-brain natriuretic peptide (NT-proBNP) 8,096 ng/L. An echocardiogram revealed dilatation and saccular aneurysms in both coronary arteries (Z-Score +6.4 and +4.09). She received one dose of intravenous inmunoglobuline with immediate resolution of fever. On day 20, APR were normal and NT-proBNP value was 520 ng/L.

Learning Points/Discussion

KD in infants may lead to coronary complications even with a short duration of fever. NT-proBNP is a marker of cardiomyocyte stress; early measurement in infants with fever, elevation of APR and negative cultures may lead to an earlier suspicion and treatment of KD.

ESPID19-1092
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Brain abscess debut in a previously asymptomatic infant

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Background

Brain abscesses are rare in childhood. Mechanism of spread includes contiguous, hematogenous or following penetrating head injury and it defines the causative pathogens. Invasive disease caused by Group A Streptococcus (GAS) has recently been described; however, brain abscesses caused by GAS are uncommon.

Case Presentation Summary

We present the case of a brain abscess in a 10-month-old girl with positive culture for GAS and unknown origin.

She developed abrupt left eye ptosis and right hemiparesis, without other symptoms (either fever or cold). The level of consciousness was not altered. The complete blood count and acute-phase reactants were normal. The Magnetic Resonance found a lesion with peripheral enhancement in the pons´ and midbrain´s left-side with extension to thalamus.

There was no history of recent infections or travels. There were no founds in the cardiological and ORL examination. Hemoculture, Interferon Gamma Release Assay (IGRA), HIV-analysis and basic inmunology study were normal. The biopsy´s histopathology was compatible with a brain abscess. In the culture of the biopsy sample, *Streptococcus pyogenes* was isolated.

Due to the results, systemic corticosteroid and broad-spectrum antibiotics were implemented during 6 weeks: cefotaxime (replaced with penicillin after the culture result), vancomicine and metronidazole. Levetiracetam was additionally started to prevent seizures and was discontinued before discharge.

During the hospitalization, clinical improvement was gradually observed. Before discharge, ptosis was almost solved, she presented good arm mobility being able to pick up big things. Some difficulties for walking were still present. Currently, the girl has regular follow-up appointments in the outpatient setting with almost completely solved symptoms.

Learning Points/Discussion

Brain abscess are uncommon in childhood and a high level of suspicion is needed since signs and symptoms are not pathognomonic. GAS is an unusual brain abscess´ causative pathogen.

ESPID19-1002
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Imported case of cutaneous leishmaniasis caused by l. Tropica.

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Background

Armenia is an endemic region for visceral leishmaniasis caused by Leishmania infantum. According to the European Region of WHO data, in our region cutaneous leishmaniasis can be also caused by the same causative agent. There are reported approximately 20-40 cases of visceral leishmaniasis annually, but we omit the cases of cutaneous leishmaniasis. An unusual case about neglected disease is presented below.

Case Presentation Summary

A 10-month-old female infant was admitted to ‘‘Nork’’ ICH with 3.5-4.0cm diameter ulcer on her right cheek covered by white crust. She had no fever or other systemic symptoms. Laboratory data: CBC was normal. The family members were Syrian refugees and had immigrated to Armenia when the child was 1 month old. At that time, she had only 1-2mm papule. During several months the papule was progressing and turned into crusted ulcer, which was gradually enlarging. The ulcer swab sampling microscopy was negative. The lesion estimated as pyoderma by dermatologists. The treatment was started with local and systemic antibacterial drugs. The treatment was ineffective, ulcer was progressing. Consulting of infectious disease specialist was done: biopsy of ulcer approved cutaneous leishmaniasis caused by L. tropica parasite, which is not typical to our region. The treatment was started with Meglumine Antimoniate IM. Though the patient was recovered, the healing process resulted in atrophic scarring.

Learning Points/Discussion

We assume the swab sampling was the cause of late diagnosing of this case. The lesion biopsy with microscopy or qPCR is the main method to diagnose cutaneous leishmaniasis as recommends WHO. We also suggest to take into consideration the imported cases.

ESPID19-1001
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Infective endocarditis in a tertiary hospital in spain: clinical, microbiological and therapeutic features in the last 10 years

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Background and Aims:

Infective endocarditis (IE) is a rare and difficult to diagnose entity, associated with high mortality and morbidity. The clinical characteristics, microbiology and management of IE at a tertiary Spanish centre are presented.

Methods:

A retrospective study of paediatric cases (patients <16 years-old) diagnosed between 2008 and 2018 in the Paediatric Hospital Virgen del Rocío, Seville, Spain was performed. The clinical presentation, past medical history of congenital heart defect, time of admission, microorganisms isolated, treatment and outcome were reviewed.

Results:

A total of 12 patients were diagnosed with IE (58.3% males, 41.7% females). Mean age was 8.3 years +/- 5.2 SD. The most frequent clinical presentation was fever of unknown origin (33.3%), with a median time for diagnosis of 15 days (IQR 8-25). An underlying congenital heart defect was identified in 83.3% of cases. IE was associated to prosthetic material in 33.3% of cases. The causative organism was found in 11 cases (91.6%). The most frequent isolated organism was *Staphylococcus aureus* (25%). 18-FDG PET-CT was used to support IE diagnosis in 3 cases finding metastatic complications in all of them. Median treatment length was 42 days (IQR 36.7-47). The most used antibiotics were cloxacillin and gentamicin (58.3%). 33.3% required surgical treatment. Resolution was achieved in all patients; 33.3% patients had a recurrent episode and no fatal outcomes were reported.

Conclusions:

IE in our cohort shows a similar microbiology as reported in series from other regions. IE diagnosis remains challenging reflected by the high median time for diagnosis reported, thus a high level of clinical suspicion is required in patients with compatible symptoms and risk factors. 18-FDG PET-CT could be a valuable aid in diagnosis of IE and its complications.

Systematic Review Registration:

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ESPID19-0921
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Novel genetic determinants of streptococcus dysgalactiae subsp. Equisimilis strains isolated in vietnam

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Background

Streptococcus dysgalactiae subsp*. equisimilis* (SDSE) previously considered to be a commensal bacterium, is currently recognized as a causative agent of about 60% of infections caused by groups C and G streptococci. In order to identify novel genetic determinants in the genomes of SDSE, the strains isolated in Vietnam were analyzed using next generation sequencing and bioinformational analysis.

Methods

Four SDSE strains isolated from schoolchildren were used. The strains were cultured in Todd-Hewitt Broth containing 0,2% of yeast extract. Streptococcal DNA was isolated by phenol/chloroform extraction. Whole genome sequencing was done using MiSeq technology, and bioinformational analysis was done using SPAdes, BLAST, and GenBank databases.

Results

The genome sequences of four SDSE strains were determined, and numerous DNA fragments which were previously undescribed for SDSE were revealed. Most of the fragments were presented by migrating genetic elements such as bacteriophages, transposons, plasmids, integrative conjugative elements, etc. The numerous genes involved in recombination events such as integrases and recombinases were also identified. For the first time the resistance genes to antibacterial drugs (*tetS*, *tetT* – resistance to tetracycline, and *lsaE*, *lnuB* – to lincosamides) were determined in the studied SDSE strains. Bioinformational analysis suggested that most of the novel genetic determinants were acquired from other gram-positive bacteria (*S. pyogenes*, *S. pneumoniae*, *S. aureus*, etc.) by the horizontal transfer. Importantly, some of the genes could be acquired from bacterial strains causing animal infections such as *S. suis* and *S. equi*.

Conclusions

Given that horizontal gene transfer, including virulence gene transfer, associated with migrating genetic elements, is a driving force of streptococcal evolution, an emergence of novel virulent SDSE clones is expected.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0887
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Influence of panton-valentine leukocidine and mec a genes on staphylococcus aureus infections in hospitalized children

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Background

S. aureus (SA) containing Panton-Valentine Leukocidine (PVL) gene and MecA gene (responsible for resistance to Methicillin (MRSA)) is associated with the invasiveness of the infection, different clinical expression, distributional difference in various age groups and among community-acquired (CAI) and hospital-acquired infections (HAI). According different epidemiological studies, prevalence of PVL toxin has low rates in Western Europe.

Methods

The PVL and the MecA genes were tested among invasive and non-invasive SA infection cases in children under 18 years (0.1 to 215 months, mean 82 months) hospitalized in the Hospital of Lithuanian University of Health Sciences Kauno klinikos since 1st of October 2012 to 30th of September 2015.

Results

PVL and MecA gene expression was detected in 42.7% (67/157) and 11.6% (14/121) of all SA cases retrospectively. PVL expressing cases were associated with the invasive SA infections (p=0.027, OR 2.059), MecA gene hadn't shown effect on invasiveness (p >0.05). Only presence of MecA was associated with multiple SA foci (p=0.012, OR 4.05), PVL had no influence. PVL expression was more common in the older (p <0.001, median age 109 vs. 24 month) and MecA was related to the younger age (p=0.01, median age 8 vs 70 month). MecA was unrelated to the origin of the infection (CAI or HAI), mostly of PVL positive cases were CAI 98.5% (66/67) p< 0.001, OR 22.65.

Conclusions

There were high rates of PVL positive *S. aureus* cases in our study. PVL was related to the invasiveness of SA infections, occurred in older children and mostly among community-acquired infections. MecA gene was associated with multiple SA foci and its occurrence at younger age.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0820
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Molecular antimicrobial resistance surveillance for gram negative bacteria in a pediatric oncology unit

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Background

Infections caused by highly-resistant bacteria in pediatric oncology patients significantly increase morbidity, length of stay, mortality rates and costs allocated to healthcare systems. There is an urgent need to reduce the spread of these bacteria in pediatric oncology patients. The aim of this project was to use molecular diagnostics directly to clinical samples as a tool for active surveillance of antimicrobial resistance in a pediatric oncology department.

Methods

This study was conducted in a 20-bed pediatric oncology department, located in a tertiary-level general hospital. All patients hospitalized for at least 7 days were included. Stool samples were collected between June and October 2018 and stored at -80oC until processed. The presence of resistance genes to antibiotics was assessed using PCR following DNA isolation directly from stool samples. One carbapenemase, *blaKPC*, and one extended spectrum beta lactamase, *blaCTXM*, were evaluated. Patients found negative for the resistant genes studied, were re-evaluated after at least one month for probable colonization.

Results

A total of 22 patients were screened at least once. Seven patients (32%) found to carry *blaKPC* and 2 out of 22 patients(9%) were *blaCTXM* positive. Among the patients found negative for carbapenamase (n=15), 9 were re-evaluated for a second time and 4 out of 9 were screened a third time. All patients found at the initial screening negative, remained negative for *blaKPC/CTXM* during all subsequent testing.

Conclusions

Direct implementation of a targeted and customized rapid molecular detection assay to clinical samples was effective to recognize the burden of bacterial resistance in this clinical setting endemic to highly resistant bacteria. These results are part of a multidisciplinary research to integrate molecular methodologies into surveillance and develop efficient strategies to combat spread of antimicrobial resistance.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0734
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Community-acquired pneumonia caused by m. Pneumoniae is frequent in hospitalized children under 5 years old and can cause severe disease

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Background and Aims:

M. pneumoniae (Mpn) causes Pediatric Community-Acquired Pneumonia (PCAP). Usually, *M. pneumoniae* is considered to cause mild infections, to be typical of older children and adolescents and to be infrequent in children under 5 years old. Our aim is to describe a prospective survey of hospitalized patients with PCAP, with a focus on the incidence and characteristics of *M. pneumoniae* PCAP.

Methods:

151 patients admitted with PCAP were prospectively recruited in 2 hospitals in Madrid, Spain, from April-2012 to March-2015. An extensive microbiological work-up was performed, including two paired samples of serology for Mpn and PCR in nasopharyngeal aspirate (NPA). Both, seroconversion and/or the presence of nucleic material in NPA were considered diagnostic. Epidemiological, clinical, analytical, image and severity data were investigated.

Results:

29 patients had Mpn. Median age was 60 months (IQR 42-93), 14 (48%) were below 60 months (range 17-58, median 42). 7 (24%) had asthmatic exacerbation. The radiography showed WHO “consolidation end-point” in 28 (96%). Biomarkers values were: median leucocytes11700/µL (IQR 6970-19700), median neutrophils7500/µL (IQR 4200-15950), median albumin3.6 g/dL (IQR 3.4-3.6), median sodium137 mmol/L (IQR 135-138), median CRP44 mg/L (IQR 20-110), median procalcitonin0.3 (IQR 0.11-1.17). 3 patients (11%) were admitted to PICU. Paraneumonic pleural effusion (PPE) was diagnosed in 13 (45%), one of them with complicated effusion and chest drainage.

Conclusions:

1. In hospitalized children and adolescents with PCAP, *M. pneumoniae* is a major causal agent, including children from 17 months onwards.

2. PPE and asthmatic exacerbation are very usual in PCAP associated with *M. pneumoniae*.

3. The elevation of analyzed biomarkers is slight in these cases.

4. The typical image is WHO “consolidation end-point” (consolidation, alveolar infiltrate or pleural effusion) and rarely “other infiltrates”.

Systematic Review Registration:

No

ESPID19-0725
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

A score to differentiate atypical bacteria of typical bacteria pediatric community-acquired pneumonia

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Background and Aims:

To discriminate atypical bacteria (Atbacteria) from typical bacteria (Tbacteria) origin at diagnosis of pediatric community-acquired pneumonia (PCAP) in children and adolescents is an unresolved problem in the usual clinical practice. Our aim is to describe, with a prospective survey of children and adolescents hospitalized with PCAP, with an extensive microbiological and analytical study, a score that can differentiate these pathogens.

Methods:

We recruited 151 patients, previously healthy, except asthma, in 2 hospitals in Madrid, Spain, from April-2012 to March-2015. An extensive microbiological work-up, with molecular and conventional techniques, was performed in blood, pleural fluid and nasopharyngeal aspirate. Several blood biomarkers were obtained and correlated with the agents detected. A score described elsewhere has to be used previously to rule out viral origin.

Results:

We diagnosed 9 with Tbacteria and and 32 with Atbacteria. The variables significantly associated with Tbacteria were assigned values according the relative-risk and P-value of the association with Tbacteria.

- CRP>100mg/L (yes5, no0)
- Procalcitonin>1.5ng/mL or albumin<3.1g/dL or sodium<135mmol/L (yes5, no0)
- Leucocytes>15000/microL (yes1, no0)
- Neutrophyls>10000/microL (yes1, no0)

The points have to be added. With a score <6, probability of Abact is 100%. If score is >6, probability of Tbact is 100%. If score is 6-8, both are possible. AUC is 0.92 (CI 95% 0.82-1). The positive LR is 8.3, the negative LR, 0.19.

Conclusions:

1. A score with C reactive protein, procalcitonin, seric albumin and sodium, leucocyte and neutrophyl counts can accurately discriminate atypical bacteria of typical bacteria PCAP.

2. This score can improve the choice of empiric antibiotic therapy in PCAP hospitalized children and adolescents and contribute to the appropriate antibiotic stewardship.

3. This score could be included in the PCAP diagnostic and therapeutic guidelines.

Systematic Review Registration:

No

ESPID19-0597
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Molecular genetic characteristics of escherichia coli o55 isolated from children in saint-petersburg

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Background

Escherichia coli strains associated with diarrhea have been classified into six groups based on clinical, epidemiological and molecular criteria: enteropathogenic (EPEC), enteroinvasive (EIEC), enterotoxigenic (ETEC), enterohaemorragic (EHEC), enteroaggregative (EAEC), and diffusely adherent (DAEC) strains. Detection of genes encoding for O-, H-antigens and virulence factors is considered to be reliable procedure for characteristics of pathogenicity of diarrheal *E. coli* (DEC) isolates.

Methods

Six strains of *E. coli* serological group O55, isolated from faecal samples of 2-6 years old children hospitalized with diarrhea, were studied. Bacterial DNA was isolated by phenol/chloroform extraction. Routine molecular techniques were done as previously described.

Results

Molecular serotyping revealed that six *E. coli* strains belonged to three variants. One strain belonged to O55: H7 (rfb_{O55}, $fliC_7$), four strains - to O55: H6 (rfb_{O55}, $fliC_6$), and one strain – to O55: H21 (rfb_{O55}, $fliC_{21}$) variant. The strain of O55: H7 variant belonging to EHEC group, possessed *stx1* gene encoding for Shiga-like toxin 1 and *eae* gene encoding for adhesion factor - intimine. This strain was isolated from a 6-year old child with a symptom of hemocolitis. Four strains of *E. coli* O55: H6 isolated from children with enteritis had *eae* gene and belonged to EPEC group. The strain of *E. coli* O55: H21 also isolated from a child with enteritis had the set of virulence genes (*astA, pet, aap, aggR, aatA, aafA*) and belonged to the EAEC group.

Conclusions

Molecular serotyping and detection of virulence genes not only expand analytical and diagnostic capabilities of laboratory diagnosis of acute intestinal infections, but also reveal significant genetic diversity of DEC pathogens. This is extremely important for rational treatment, targeted preventive measures and for minimizing errors in etiological interpretation of acute intestinal infections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0574
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

A score to differentiate viral from bacterial pediatric community-acquired pneumonia

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Background and Aims:

To discriminate viral from bacterial pediatric community-acquired pneumonia (PCAP) is a challenging problem in the usual clinical pediatric practice. Our aim is to describe, with a prospective survey of children and adolescents hospitalized for PCAP, with an extensive microbiological study that was correlated with epidemiological, clinical, analytical and radiographic data, a score to differentiate viral from bacterial origin of PCAP.

Methods:

We recruited 151 previously healthy children, except asthma, in 2 hospitals in Madrid, Spain, from April-2012 to March-2015. An extensive microbiological work-up, including molecular techniques, was performed. Only the presence of genetic material of atypical bacteria, respiratory syncitial virus, metapneumovirus, parainfluenza and influenza virus in nasopharyngeal aspirate was considered diagnostic, but not other viruses. Traditional bacterial cultures were also included.

Results:

At least an agent was detected in 72: typical-bacteria 9, atypical-bacteria 32 and viruses 38. Antibiotics were received in 96%. Variables significantly-associated with bacteria were assigned values according relative-risk and P-value of the association with bacteria:
- Age>48months (yes4, no1)
- >3.5days with fever (yes3, no1)
- Absence of PCV (yes1, no2)
- Wheezing (yes1, no3)
- WHO radiographic “consolidation end-point” (yes3, no1)
- Leucocytes>15000/microL (yes3, no1)

The points are multiplied. With score <6, probability of virus is 100%. AUC is 0.88 (CI 95% 0.81-0.96). The positive LR is 2.2 and the negative 0.14. A potential saving of 55% of antibiotic use is feasible.

Conclusions:

1. A score with a few of simple epidemiological, clinical, analytical and radiographic data can discriminate reasonably viral from bacterial pediatric community-acquired pneumonia.

2. This score can improve the empiric therapy in pediatric community-acquired pneumonia in hospitalized children and adolescents and contribute to the appropriate antibiotic stewardship.

3. This score could be included in the pediatric community-acquired pneumonia diagnostic and therapeutic guidelines.

Systematic Review Registration:

No

ESPID19-0547
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

A prospective study of community-acquired pneumonia in children and adolescents in spain: high tase of mycoplasma pneumoniae and viruses and a low rate of coinfection

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Background and Aims:

The coinfection rate usually reported in pediatric community-acquired pneumonia (PCAP) in hospitalized patients is around 30%. Recently, only respiratory syncitial virus (RSV), metaneumovirus (hMPV), parainfluenza (PIV) and influenza (flu) viruses are considered real pathogens in PCAP. Bocavirus, coronavirus, enterovirus and rhinovirus are not considered etiological agents since they are as frequent in asymptomatic children as in PCAP. There are doubts about adenovirus. Our aim is to describe a prospective survey of hospitalized patients with PCAP, with a focus on the incidence of coinfections.

Methods:

Children and adolescents with PCAP were recruited in 2 hospitals in Madrid, Spain, from April 2012 to March 2015. An extensive microbiological work-up was performed: blood cultures, PCR for *S. pneumoniae* in blood, two paired samples for serology of atypical bacteria and PCR for 16 viruses, *M. pneumoniae* and *C. pneumoniae* in nasopharyngeal aspirate (NPA). When available, culture and *S. pneumoniae* antigen in pleural fluid were performed. Seroconversion or the presence of nucleic material of atypical bacteria, RSV, hMPV, PIV and flu were considered diagnostic.

Results:

We studied 151 patients, median age 41 months (IQR 19-70), 66% under 60. At least a pathogen was detected in 72 (48%) of the patients. The agents were: typical bacteria 12% (*S. pneumoniae* 10%), atypical bacteria 41% (*M. pneumoniae* 37%) and viruses 49%. *M. pneumoniae* was detected in 14% of patients under 60 . Coinfection was detected in 7 patients (10%).

Conclusions:

1. Viruses and *M. pneumoniae* are the more frequent pathogens causing PCAP in hospitalized patients.
2. *M. pneumoniae* is an usual agent in PCAP in children under 5 years.
3. The coinfection rate of PCAP is not as high as usually reported.

Systematic Review Registration:

No

ESPID19-0460
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Direct identification of pathogens from pediatric blood culture bottles using an in-house maldi-tof ms protocol

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Background

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) is widely used for direct identification of pathogens from positive blood culture bottles. However, the commercial kit designed to remove substances interfering with spectrometric analysis from the bottle is costly prompting many laboratories to develop different in-house (IH) preparation methods. The objective of this study was to evaluate the accuracy of direct identification of microorganisms from positive pediatric blood culture bottles by MALDI-TOF MS using an IH protocol developed at Sidra Medicine.

Methods

MALDI-TOF MS analysis was directly performed on positive BD BACTEC Peds Plus/F bottles (June to December, 2018) using a processing protocol involving blood cell lysis with 1% SDS and protein extraction with 70% ethanol to generate a microbial pellet suitable for spectrometric analysis. On average, the procedure required 30 minutes. Identification thresholds to species and genus levels were set at ≥ 1.8 and ≥ 1.6, respectively. Organisms with a score ≥ 1.6 were deemed as correctly identified for clinical reporting purposes. All samples were simultaneously assessed by conventional bacteriological procedures.

Results

Direct MALDI-TOF MS analysis was performed on 155 positive pediatric blood culture bottles. Of 142 monomicrobial bottles, 87% and 94% of microorganisms were identified to the species and genus levels, respectively. Compared with conventional methods, 96% gram-positive organisms and 90% gram-negative organisms were correctly identified. Ninety-six percent of microorganisms recovered from clinically significant bacteremic episodes were correctly identified. A correct identification of a single pathogen was achieved in 85% of the polymicrobial blood culture bottles.

Conclusions

MALDI-TOF MS analysis performed directly on positive pediatric blood culture bottles processed with an IH user-friendly method provided an accurate and rapid identification of pathogens and was easily integrated into the standard laboratory workflow.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0335
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Detection of pathogens in children with suspected central nervous system infection with biofire® filmarray® meningitis/encephalitis pcr multiplex panel: 2-year experience

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Background

Rapid identification of pathogens that cause central nervous system (CNS) infections could benefit patient care and facilitate better use of antibiotics. The aim of the study was to describe the experience with the use of a rapid multiplex CNS PCR panel.

Methods

A retrospective analysis of results of cerebrospinal fluid (CSF) multiplex PCR (Biofire® FilmArray® Meningitis/Encephalitis panel) (FA) in children with clinical suspicion of meningitis or encephalitis was performed over a 2-year period (2016-2018) in a tertiary pediatric hospital. This panel enables rapid automated cerebrospinal fluid testing for 14 common viral, bacterial and yeast pathogens that cause CNS infections. Conventional microbiological procedures were performed in addition to the multiplex panel in all children who were included in the analysis.

Results

During the study period, FA was performed on CSF samples from 85 children. 46(54,1%) were boys and the median age was 12 months (IQR: 1,5-89,75). FA was positive in 35/85 cases (41,2%) and detected in positive samples: *Enterovirus* 27 (77,1%), *Parechovirus* 3 (8,6%), *N.meningitidis* 2 (5,7%), *S.agalactiae* 1 (2,9%), *S.pneumoniae* 1 (2,9%), *Human herpes Virus* 6 (HHV-6) 1 (2,9%). In children <12 months (42/85, 49.4%) the most frequent pathogens detected were *Enterovirus* (72,7%) and *Parechovirus* (13,6%). In children> 12 months the most frequent pathogens detected were *Enterovirus* (84,6%), *S. pneumoniae* (7,7%), *N. meningitidis* (7,7 %). There was no any discrepancy between the panel and the conventional culture regarding detection of bacterial pathogens. The median hospitalization time in FA positive for viruses and negative samples were 5,78 days (IQR:3-6) and 11,4 days (IQR: 5-13) respectively (P-value<0.0001).

Conclusions

FA use in children with clinical suspicion of CNS infection could guide clinical decisions and reduce significantly hospitalization time compared to standard diagnostics.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0196
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

The prevalence of specific pathogenic carriage of bacteria in the nasopharynx of the children with respiratory tract infections in the primary clinics

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Background

The nasopharynx is an ecologic reservoir for bacterial pathogens in children. The purpose of this study was to assess the nasopharyngeal carriage of specific pathogens in children with acute respiratory infection (ARI) and to compare the pathogens between upper respiratory tract infection (URI) and lower respiratory tract infection (LRI).

Methods

Nasopharyngeal aspirates were collected for the TaqMan-PCR assay to determine the pathogenic bacteria from 1056 children with ARI, aged 0 to 16 years from January 2015 to April 2016 at the primary clinics in Sejong, Korea. ARI (n=1056) was divided in URI (n=891) or LRI (n=165).

Results

In URI, mixed *S. pneumoniae* and *H. influenzae* (59.0 %) pathogen was the most common prevalent. *S. pneumoniae* (20.7 %) was second, and *H. influenzae* (7.3 %) was third. In LRI, mixed *S. pneumoniae* and *H. influenzae* (50.9 %) was also the most common prevalent. The second was *S. pneumoniae* (20.0 %), and the third was mixed *S. pneumoniae* and *H. influenzae* and *M. pneumoniae* (11.5 %). According to the age of 0-3, 3-7 and 3-16 years, mixed *S. pneumoniae* and *H. influenzae* pathogen was the most common prevalent across three age groups in URI. But the variability of mixed pathogens showed a tendency of increasing with older age. *S. pneumoniae* was the most common single bacterial pathogen in both groups (20.7 % vs 20.0 %). Pneumococcal conjugate vaccination did not affect the pathogenic bacteria prevalence in LRI (p=0.41).

Conclusions

Mixed *S. pneumoniae* and *H. influenzae* pathogen was the most prevalent nasopharyngeal pathogenic carriage, and *S. pneumonia* was the most common single pathogen in both URI and LRI. The variability of mixed nasopharyngeal pathogenic bacteria carriage increased with aging.

Clinical Trial Registration (Please input N/A if not registered)

IRB FILE No : 2017-11-048

ESPID19-0123
E-Poster Viewing - May 7-10 - E-Poster Hours

Microbiological diagnostic tools

Can quantitative c reactive protein assist in early identification of a bacterial infection in short duration fever in children?

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Background

CAN QUANTITATIVE CRP ASSIST IN EARLY IDENTIFICATION OF A BACTERIAL INFECTION IN SHORT DURATION FEVER IN CHILDREN?

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Fever is a common presentation of infection in children but distinguishing between a viral and a bacterial fever can be a diagnostic challenge. Prevalence of malaria complicates the issue in the tropics. Antibiotic use in a patient who has a self-limiting viral illness or malaria increases adverse effects and antimicrobial resistance. But quick diagnosis of a bacterial infection for early institution of antibiotics is equally important to reduce morbidity and mortality.

AIMS AND OBJECTIVES-

To evaluate the usefulness of quantitative C Reactive Protein in distinguishing non-bacterial from bacterial infections to assist decision in starting antibiotics in acute febrile illness.

Methods

Quantitative CRP was measured between 2nd to 4th day of fever in 80 children aged 1 to 5 years with or without other symptoms. Diagnosis of bacterial or parasitic (malarial) etiology was done by clinical assessment along with appropriate microbiological, radiological and biochemical / haematological criteria (excluding the CRP). The CRP value was then correlated with the diagnosis (bacterial vs non-bacterial) and a cut-off value for the CRP was obtained with the best sensitivity and specificity to distinguish bacterial and non-bacterial infection.

Results

RESULTS:

A CRP value >15 mg/dl was suggestive of a bacterial infection with a specificity of 75 % and a sensitivity of 67.5 %.

Conclusions

C Reactive Protein value used in conjunction with other clinical and laboratory parameters may aid in differentiating bacterial from non-bacterial infections and guide need for early antibiotic administration.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0602
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Public health impact and cost-effectiveness of a nine-valent gender-neutral human papillomavirus vaccination program in france

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Background

In France, nine-valent HPV vaccination is recommended routinely for 11-14-year-old girls and as a catch-up for 15-19-year-old girls. The objectives of the study were to assess the public health impact and cost-effectiveness of a nine-valent gender-neutral vaccination (GNV) compared with girls-only vaccination program (GOV).

Methods

A published HPV disease transmission dynamic model accounting for herd protection effects with a 100-year time horizon was adapted and calibrated to French data. Epidemiological and economic outcomes were assessed which included disease cases averted, quality-adjusted life years (QALY). Costs and incremental cost-effectiveness ratio (ICER) were measured in 2017 Euros (€). A coverage rate of 26.2% among girls and boys was assumed for the GNV program, based on the current female coverage rate in France. A scenario analysis was conducted by considering higher vaccination coverage rate (60%). Deterministic sensitivity analyses were performed.

Results

Over 100 years, GNV resulted in an additional reduction of 9,542 and 3,070 additional cervical cancer cases and deaths, 6,935 and 1,178 additional anal cancer cases and deaths and a reduction of additional 1,276,724 genital warts compared with current program (Table 1). The ICER was 29,343€/QALY. At a higher coverage rate (60%), GNV would prevent 17,286 and 4,338 additional cancer cases and deaths (cervical and anal), and over two million cases of genital warts compared with GOV with an ICER of 47,335€/QALY. Base case results were sensitive to higher discount rate (6% versus 4%) and a shorter duration of protection (20 years versus

lifetime).

Table 1: HPV 6/11/16/18/31/33/45/52/58-related diseases cases and deaths avoided with girls only vaccination versus screening and nine-valent gender-neutral vaccination program versus girls-only program over 100 years considering a 26.2% vaccination coverage rate. Only HPV related diseases included in the summary of product characteristics are included in the base-case analysis.

Health outcome	**HPV 6/11/16/18/31/33/45/52/58-related disease events prevented**		**HPV 6/11/16/18/31/33/45/52/58-related deaths avoided**	
	Girls only vaccination vs screening only	**Additional Disease events avoided with GNV vs girls only**	Girls only vaccination vs screening only	**Additional Deaths avoided with GNV vs girls only**
Genital warts (females)	1,400,915	**338,607**	-	-
Genital warts (males)	1,021,488	**938,117**	-	-
CIN 1	144,430	**27,648**	-	-
CIN 2/3	237,874	**44,178**	-	-
Cervical cancer	51,946	**9,542**	15,754	**3,070**
Vaginal cancer	478	**105**	89	**20**
Vulvar cancer	673	**145**	125	**27**
Anal cancer (females)	11,807	**3,351**	1,681	**530**
Anal cancer (males)	2,943	**3,584**	515	**648**

Conclusions

In France, GNV has a significant impact in terms of public health benefits and is considered cost-effective compared with girls only vaccination at low and high coverage rates.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0977
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Potential public health impact model assessing a switch back to use of the 13-valent infant pneumococcal conjugate vaccine in belgium on children under 18 years

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Background

As pneumococcal disease represents a significant healthcare burden, 13 valent (PCV13) and 10 valent (PCV10) pneumococcal vaccines are available globally. After 4 years of use of PCV13 in regional infant immunization programs in Belgium, the Flanders and Wallonia/Brussels regions switched to PCV10 in 2015/2016. Since this time, an increase in invasive pneumococcal disease (IPD) caused by serotype 19A, which is contained in PCV13 but not in PCV10, has been observed in Belgium. We evaluated the potential public health impact of switching back to PCV13 in Belgium on children <18 years.

Methods

A model was developed using observed IPD incidence trends in Belgium to predict future serotype behavior under PCV13 or continued PCV10 use.

Serotype specific IPD incidence trends were obtained from the National Reference Laboratory for Pneumococci Surveillance. Rates for hospitalized pneumonia and hospitalized otitis media were derived using differentials to IPD from observed data in Finland and assumed to be proportional to IPD.

Results

By switching back to PCV13 use in the regional immunization programs in Belgium, over 28,000 cases of pneumococcal disease and 17 deaths can be avoided in children <18 years (Table 1). The majority of disease that may result in death was predicted to occur in children <5 years over the next 10 years.

Conclusions

Based on observed serotype behavior in Belgium, a switch back to PCV13 in regional pneumococcal vaccination programs is predicted to reduce disease and mortality compared to continued use of PCV10. Our findings are reinforced by recent recommendations by the Belgian Superior Health Council who have recommended switching back to PCV13 use due to the higher level of protection against disease.

Clinical Trial Registration (Please input N/A if not registered)

N / A

ESPID19-0957
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Clinical and economic impact of use of the 13-valent pneumococcal vaccine over the current infant pneumococcal vaccination environment in poland

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Background

As *Streptococcus pneumoniae* represents a substantial public health burden two infant pneumococcal vaccines are available protecting against 13 (PCV13) and 10 (PCV10) serotypes. A Polish pneumococcal infant national immunization program (NIP) was introduced in 2017 using PCV10. While PCV13 is in private market use at 23% of total pneumococcal vaccination, this rate is declining. We evaluated the impact of switching to a PCV13 NIP versus a “mixed-use” environment in Poland.

Methods

A model using observed, serotype-specific invasive pneumococcal disease (IPD) incidence trends was developed. IPD trends were taken from observed data in Finland (PCV10) and the United Kingdom (PCV13). The trends were applied to Polish baseline IPD incidence to estimate future serotype behavior under each vaccine. Pneumonia and otitis media rates were predicted based on proportional change relative to IPD from baseline rates from the National Institute of Public Health and GUS Statistics Poland.

Results

Over 10 years, switching to a full PCV13 NIP versus the current market share mix between PCV10 (77%) and PCV13 (23%) was estimated avoid 200,000 cases of disease and save >5,000 lives. If the PCV13 market share continues to decrease there will be declining clinical and cost benefit from the vaccination program. With either vaccine at 100% of market share, PCV13 is predicted to be cost-saving versus PCV10 (Table 1).

Conclusions

Switching to PCV13 in Poland’s infant pneumococcal NIP is predicted to save lives and reduce medical costs versus a split market share between PCV13 & PCV10. Because the vaccine program benefits decline as market share of PCV13 decreases, the comparative clinical and economic benefit of a PCV13 NIP increases. Due to these benefits in Poland, a switch to a PCV13 NIP should be considered.

Clinical Trial Registration (Please input N/A if not registered)

N / A

ESPID19-0900
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Epidemic potential of the emerging meningococcal serogroup w sequence type-11 clonal complex: a mathematical modeling study in england and in france

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Background and Aims:

The recent emergence of strains belonging to the meningococcal serogroup W (MenW) sequence type-11 clonal complex and descending from the South American strain sub-lineage (MenW:cc11) has caused alarm. However, the epidemiological characteristics of MenW:cc11 have not yet been quantified.

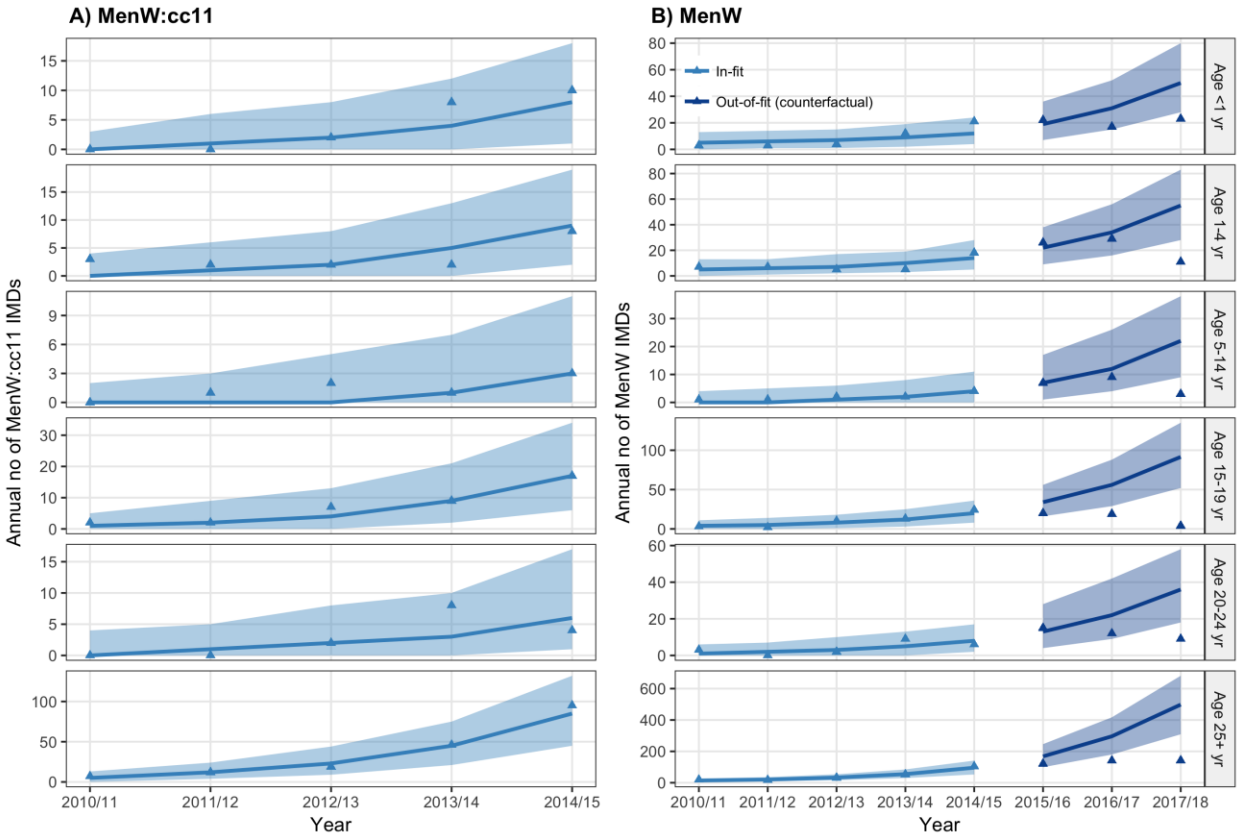
Methods:

We designed a mathematical model of MenW transmission, carriage, and infection to analyze the recent epidemiology of invasive disease caused by MenW:cc11 strains and by other MenW strains in England and Wales and in France. Using state-of-the-art statistical inference methods, we confronted that model with incidence data to estimate the transmissibility and the invasiveness of MenW:cc11.

Results:

During the epidemiological years 2010/11–2014/15 in England and Wales, the transmissibility of MenW:cc11 relative to that of non-MenW:cc11 was estimated at 1.20 (95% confidence interval: 1.15–1.26). The invasiveness of MenW:cc11 relative to that of non-MenW:cc11 was also found to exceed unity and to increase with age, with point estimates ranging from 4 in children aged 0–4 years to 19 in adults aged ≥25 years. During the years 2015/16–2017/18, which followed the introduction of the MenACWY vaccine in adolescents aged around 14 years and of the 4CMenB vaccine in infants, the observed cases of MenW disease were lower than those predicted by counterfactual model simulations of no vaccination (Figure). Assuming that the epidemiological traits of MenW:cc11 estimated in England and Wales were similar during 2012–2016 in France, MenW:cc11 was estimated to have emerged in late 2011 (95% confidence interval: early 2011–mid-2012) in France.

Figure: Data and model simulations of MenW invasive diseases in England and Wales.



Conclusions:

Our study provides the first estimates of MenW:cc11 invasiveness and transmissibility. Such estimates may be useful to anticipate changes in MenW epidemiology and to adapt vaccination strategies.

Systematic Review Registration:

N/A

ESPID19-0823
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Public health impact and cost-effectiveness analysis of a human papillomavirus gender neutral nine-valent catch up vaccination cohort in belgium

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Background

In Belgium, human papillomavirus (HPV) vaccination is reimbursed for catch-up cohorts for 13-18-year-old girls. The objectives of the study were to assess the public health impact and cost-effectiveness of a gender-neutral nine-valent vaccination (GNV) catch-up cohort compared with a girl-only catch-up cohort at the national level.

Methods

A published HPV disease transmission dynamic model accounting for herd protection has been adapted and calibrated for Belgium. The model considered the occurrence of cervical intraepithelial neoplasia, cervical, vaginal, vulvar and anal cancers, and recurrent respiratory papillomatosis, penile and oropharyngeal cancers. A 3-dose schedule and a vaccination coverage rate (VCR) of 50% were used in the base case analysis for both cohorts. Various deterministic sensitivity analyses on key parameters (incidence of genital warts and HPV related cancers, VCR, duration of protection and vaccine cost) were performed.

Results

A switch to a HPV GNV catch-up cohort resulted in an additional reduction of 17,148 cervical intraepithelial neoplasia cases; 2,252 and 593 cervical cancer cases and deaths; 1,506 and 336 additional anal cancer cases and deaths and 185,043 additional genital warts compared with current program in girls cohort only over a period of 100 years. In the base case analysis, the incremental cost-effectiveness ratio (ICER) of the nine-valent HPV for boys and girls versus girls only was 7,889€/QALY; the ICER for this analysis when a low (5%) VCR was tested was 3,805€/QALY. Additional sensitivity analyses showed that results were still cost-effective (below the threshold of 33,000€/QALY).

Conclusions

Based on this modelling study, a switch to a GNV catch-up 13-18-year-old cohorts using the nine-valent vaccine demonstrated additional benefits in terms of public health impact and was considered a cost-effective strategy compared to the current catch-up program in Belgium.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0822
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Public health and economic impact of gender-neutral nonavalent vaccination and catch-up vaccination in hong kong

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Background

The Hong Kong (HK) government will implement a vaccination program for preventing human papillomavirus (HPV)-related diseases with the nonavalent HPV (9vHPV; types 6/11/16/18/31/33/45/52/58) vaccine in females aged 10-12 years. A high proportion of cervical cancer (CC;15.94%) in HK is attributable to types 52/58, which is typical in the region. Gender-neutral vaccination (GNV) provides direct protection to males against HPV infection and associated diseases. We estimated the public health impact and cost-effectiveness of 3 immunization strategies with 9vHPV vaccine: female-only vaccination (FOV), GNV, and catch-up GNV.

Methods

A validated HPV-type dynamic transmission model simulated 9vHPV vaccination in 12-year-old females, and 12-year-old females and males with and without catch-up up to 18 years old at 70% uptake (30% for catch-up) in the HK population over 100 years for the prevention of HPV-related cancers; cervical lesions (CIN-1/2/3); vulvar lesions (VaIN); and genital warts (GW). Costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs) were estimated; cost-effectiveness assessed at a threshold of 1.0xGDP for HK (359,996 HKD).

Results

Model results suggest that 9vHPV GNV vaccination would avert 1,009 CCs, 640 CIN-2/3s, 235,497 GWs, and 440 anal cancers compared with FOV over 100 years (**Table**). Further cumulative reductions in incidence were demonstrated with catch-up vaccination. Cost-effectiveness with the 9vHPV vaccine was demonstrated with GNV compared to FOV (ICER of 223,096 HKD/QALY), and with catch-up GNV against GNV (30,312 HKD/QALY). After including penile and head/neck cancers, ICER of catch-up GNV vs GNV was 25,375 HKD/QALY.

Table. Cumulative Reduction in HPV-Related Disease Incidence for GNV vs FOV, and GNV Catch-up vs GNV with the 9vHPV Vaccine Over 100 Years

	Cumulative reduction in HPV-related disease incidence (% reduction)	
HPV-related disease	9vHPV GNV vs 9vHPV FOV	9vHPV GNV Catch-up* vs 9vHPV GNV
Cervical cancer	1,009 (4.5)	1,498 (5.1)
CIN-1	181 (7.4)	245 (6.7)
CIN-2/3	640 (6.9)	846 (6.2)
Vaginal cancer	2 (3.2)	5 (5.6)
VaIN-2/3	3 (3.9)	5 (6.3)
Vulvar cancer	5 (3.1)	10 (5.5)
Genital warts (female)	38,982 (33.2)	11, 621 (5.1)
Genital warts (male)	196,515 (51.1)	22,854 (4.4)
HPV6/11-related CIN-1	147 (30.9)	34 (4.1)
Anal cancer (female)	106 (4.6)	106 (4.0)
Anal cancer (male)	334 (14.6)	98 (4.0)
Head and neck cancer (female)	129 (4.8)	117 (3.8)
Head and neck cancer (male)	1193 (16.2)	301 (3.8)
Penile cancer	569 (24.9)	54 (2.5)
	Deaths prevented	
Cervical cancer	334 (4.1)	504 (4.9)

9vHPV, nonavalent HPV vaccine; CIN, cervical intraepithelial neoplasia; FOV, female-only vaccination; GNV, gender-neutral vaccination; HPV, human papillomavirus; VaIN, vaginal intraepithelial neoplasia.

*Catch-up vaccination with the 9vHPV vaccine assumed a 2-dose schedule in individuals 13-14 years old and a 3-dose schedule for those 15-18 years old.

Conclusions

9vHPV catch-up GNV provides the maximum public health benefit and is cost-effective in HK compared with GNV, which is more cost-effective compared with FOV. GNV with or without catch-up should be considered in HK over FOV.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0710
E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Epidemiological impact of a gender-neutral hpv vaccination compared to a females only program in portugal

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Background

In Portugal, HPV vaccination was included in the National Immunization Program (NIP) for 13-years old girls in 2008 using the 4-valent HPV (4vHPV) vaccine. In 2017 the 4vHPV vaccine was replaced by the 9-valent HPV (9vHPV) vaccine and the age for vaccination was anticipated for 10-years old. The aim is to assess the epidemiological impact of gender-neutral HPV vaccination (GNV) (2 doses, 10-years) with the 9vHPV vaccine compared with the current NIP (girls only, 2 doses, 10-years).

Methods

A published HPV disease transmission dynamic model accounting for herd protection with a lifetime horizon (100 years) was adapted and calibrated (incidence and mortality rates for all the diseases considered) for Portugal. Epidemiological outputs assessed were genital warts (GW), cervical intraepithelial neoplasia, cervical, vaginal, vulvar and anal cancers; and penile and oropharyngeal cancers. Demographic inputs were obtained from Statistics Portugal and annual all-cause mortality rates were extracted from the Portuguese Mortality table 2014-2016.

Results

The implementation of a GNV program using the 9vHPV vaccine will significantly reduce the epidemiological burden by averting additional 342,535 cases and 1,222 deaths in the female and male population compared to females only vaccination. The reduction of GW would happen within the first 5 years of the program, while the reduction in the incidence and mortality from HPV-related cancers would be more gradual, reflecting the fact that these diseases have slower progression.

Conclusions

The extension of HPV vaccination to boys would amplify the reduction in HPV related diseases in addition to the significant reductions already provided by the current girls only program. This strategy would further accelerate the reduction of HPV-related diseases in Portugal as it contributes to significant additional impact in women's health, beyond the expectable men protection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Estimating the clinical and economic impact of maintaining use of 13-valent pneumococcal conjugate vaccine (pcv13) in the philippines

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Background and Objective

Pneumococcal conjugate vaccines (PCV) have demonstrated a remarkable public health impact around the world. In 2014, PCV13 was introduced in the Philippines Expanded Program on Immunization (EPI). This study evaluated the public health and economic impact of maintaining PCV13 compared to switching to the 10-valent pneumococcal conjugate vaccine (PCV10).

Methods

A decision-analytic model was adapted to estimate health outcomes and associated health-care costs for each pneumococcal conjugate vaccination program. Disease incidence at the time of potential switch for invasive pneumococcal disease (IPD), pneumonia (PNE) and acute otitis media (AOM) was obtained from the published literature. For modeled PCV13 trends, incidence was adjusted by year based on serotype-specific estimates of years to 90% reduction according to a published meta-analysis. Finland serotype trends were used to model PCV10 clinical impact for all ages. Costs, utility weights, and risk of disease-specific complications were derived from published sources.

Learning Points Discussion

In the base case, continued use of PCV13 would result in significantly fewer cases of pneumococcal disease than switching to PCV10 over a 10-year time horizon (See Table 1). PCV13 was found to be cost-saving compared with PCV10 in the base case and PCV13 remained cost-effective across a number of scenario analyses. Over a 5-year time horizon, 13,067 cases of IPD, 235,563 cases of AOM, 121,719 cases of pneumonia, and 2,168 deaths were estimated to be averted when using PCV13, compared with PCV10.

Continued use of PCV13 in The Philippines EPI is estimated to provide greater public health benefit and economic savings compared with switching to PCV10. It is important that policy makers consider potential implications of disease re-emergence of non-covered serotypes when considering modifications to vaccination strategies.

Table 1: Total estimated cases and costs associated with PCV13 vs PCV10 in The Philippines over a 10 year period

	PCV13	PCV10	Incremental
Number of Cases			
IPD	38,898	80,154	-41,257
Pneumococcal PNE	1,823,857	2,167,447	-343,590
AOM	1,732,739	2,397,691	-664,952
Deaths	14,688	21,636	-6,948
Quality Adjusted Life Years	761,133,514	761,116,188	17,326
Direct Medical Costs			
Vaccination	₱ 41,845,586,364	₱ 37,316,336,496	- ₱ 4,529,249,869
IPD	₱ 2,008,694,143	₱ 4,293,622,905	-₱ 2,284,928,763
Pneumococcal PNE	₱ 17,108,810,570	₱ 19,833,233,537	-₱ 2,724,422,967
AOM	₱ 463,063,146	₱633,322,617	-₱ 170,259,471
Total Costs	₱ 61,426,154,224	₱ 62,076,515,556	**- ₱ 650,361,332**

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Modelling studies

Estimating the population health and economic impact of introducing a pneumococcal conjugate vaccine in malaysia

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Background and Objective

Pneumococcal disease is a vaccine preventable bacterial infection that causes potentially fatal conditions. Vaccination represents the best approach towards minimizing its population health impact. Malaysia is considering making pneumococcal vaccinations mandatory for children under two years of age. This study assesses the potential impact of adapting the available pneumococcal conjugate vaccines (13-valent and 10-valent) on population health and related costs in Malaysia.

Methods

A previously published decision-analytic model was adapted to estimate the outcomes of population health and various costs. Current disease incidence for invasive pneumococcal disease (IPD), pneumonia (PNE) and acute otitis media (AOM) was obtained from the published literature. For each vaccination program, health outcomes and associated health-care costs were estimated. The scenarios of initiating PCV13 versus PCV10 and the status quo (no pneumococcal vaccine) were compared. Finland serotype trends were used to model PCV10 clinical impact and UK serotype trends for PCV13. The current analysis is based on the societal perspective over a 5 year time horizon.

Learning Points Discussion

PCV13 use for those ≤2 years old in Malaysia has the potential to avert 125,660 cases of pneumococcal disease compared with PCV10 (Table 1). PCV13 is estimated to cost an incremental US$89,893,794 in the acquisition of vaccine and offset -US$140,611,502 on pneumococcal-related medical care and lost productivity. Compared with PCV10, PCV13 shows cost-saving potential. Compared with the status quo of no vaccination, the incremental cost per QALY gained to introduce PCV13 was US$1,958.

Introduction of a pneumococcal vaccine is found to have high public health impact to the entire population in Malaysia. PCV13 is highly cost effective in the prevention of pneumococcal disease and improving quality of life compared to the status quo (without pneumococcal vaccine) and is cost-saving compared with PCV10.

Table 1: Total estimated cases and costs associated with PCV13 vs PCV10 in Malaysia over a 5 year period

	PCV13	PCV10	PCV13 vs PCV10
Number of Cases			
IPD	2,923	3,623	**-700**
Pneumococcal PNE	1,366,928	1,382,485	**-15,557**
AOM	329,785	438,951	**-109,166**
Deaths	4,991	5,229	**-238**
		Total Cases Averted	**-125,660**
Vaccine acquisition cost, USD	331,902,426	242,008,632	**89,893,794**
Costs of medical care, USD			
IPD	22,697,412	27,908,074	**-5,210,662**
Pneumococcal PNE	1,026,986,354	1,041,878,641	**-14,892,287**
AOM	187,936,951	249,178,062	**-61,241,111**
Cost of productivity lost, USD	786,187,789	845,455,231	**-59,267,442**
		Total Cost Reduction	**-$140,611,502**
Total Costs, USD	2,355,710,932	2,406,428,640	**-50,717,708**
Total QALYs Gained	127,761,531	127,760,784	**747**
Cost/QALY			**PCV13 Dominant**

*PNE, Pneumonia; AOM, Acute Otitis Media; IPD, Invasive Pneumococcal Disease; QALY, Quality Adjusted Life Years

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E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Cost-effectiveness of a national immunization program with the 13-valent (pcv13) pneumococcal conjugate vaccine compared with the 10-valent (pcv10) pneumococcal conjugate vaccine in south korea

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Background and Objective

Globally, pneumococcal disease represents a significant public health and economic burden. In South Korea, the 7-valent pneumococcal conjugate vaccine was introduced in 2003 and was replaced with PCV10 and PCV13 in 2010. In 2014, a physician choice infant national immunization program (NIP) using a 3+1 schedule with PCV10 and PCV13 was implemented to prevent invasive pneumococcal disease (IPD) and non-invasive pneumococcal acute otitis media and pneumonia. Given this unique situation, we performed a cost-effectiveness evaluation to elucidate which vaccine will provide greater public health impact if included in an NIP.

Methods

Using an established population based forecasting model, we estimated the impact of introducing either PCV13 or PCV10 into the South Korean NIP in 2015. Vaccine impact was estimated based on fit regression equations to the historic impact of PCV13 from 2010 to 2015 in Korea given high uptake of PCV13, and PCV10 impact was estimated and varied based on experiences in countries with PCV10 NIPs; notably Finland and The Netherlands. Pneumococcal disease incidence and costs were derived from the published literature and the Korean Health Insurance Review and Assessment (HIRA) database.

Learning Points Discussion

In the base case analysis, over 5 years PCV13 was estimated to avert 550,000 more cases of pneumococcal disease compared to PCV10, driven by broader serotype coverage and less replacement from serotypes 3 and 19A. This translated to a net cost-savings of $24.3 million USD despite PCV13's higher cost. Sensitivity analysis found ICERs ranging from cost-saving to $7,300 USD per QALY for PCV13 compared to PCV10. In conclusion an NIP using PCV13 was estimated to have a more substantial public health impact and be cost-saving compared to a program with PCV10 due to broader serotype coverage.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Modelling studies

Determining the effectiveness of the 13-valent pneumococcal conjugate vaccine (pcv13) against serotype 3: a modelling approach

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Background and Objective

Over 90 different serotypes of the bacterium *Streptococcus pneumoniae* exist, causing a variety of pneumococcal diseases. While PCV13 contains a serotype 3 (ST3) antigen, evidence of vaccine effectiveness (VE) has varied, with some studies suggesting 0% VE. Some countries using PCV13 have reported constant circulation of ST3 disease. However, a recent meta-analysis estimated VE of ST3 IPD (VE_{IPD}) to be 63.5%. The objective of this study is to recalibrate a transmission dynamic model to determine ST3 VE.

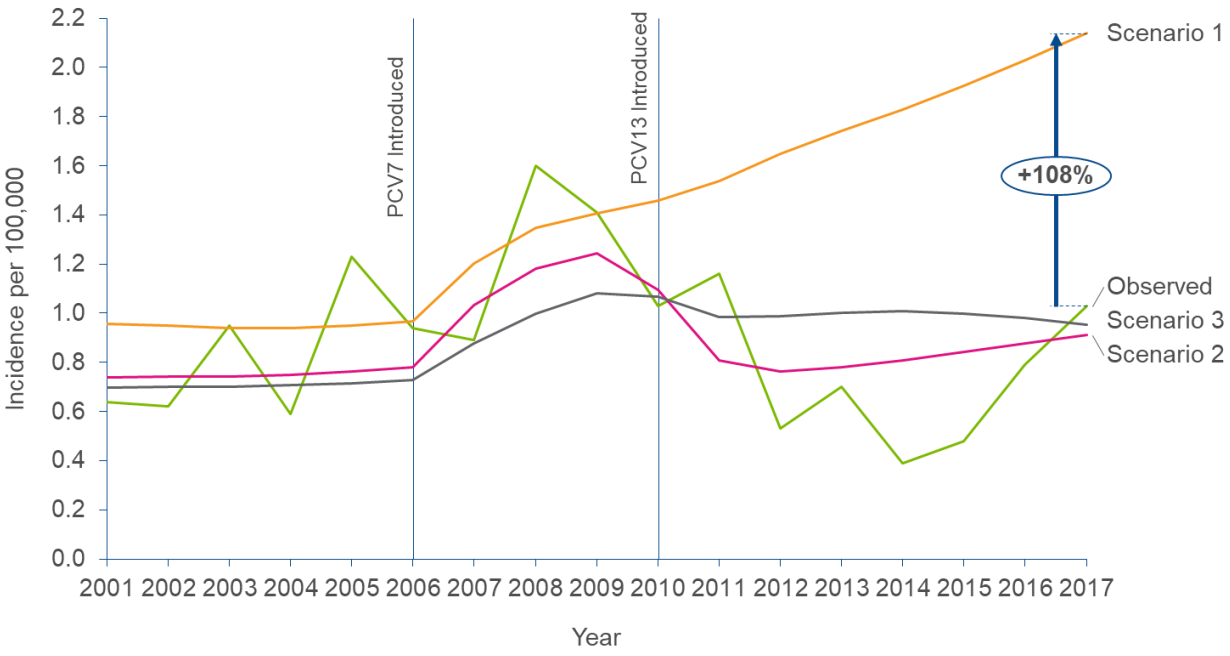
Methods

A published dynamic model leveraging United Kingdom surveillance data from 2001-2017 was recalibrated to estimate ST3 VE_{IPD} (direct protection) and carriage VE (indirect protection; $VE_{carriage}$). Scenarios included: (1) PCV13 has 0% $VE_{carriage}$ and VE_{IPD}; (2) 63.5% VE_{IPD}; $VE_{carriage}$ calibrated based on observed IPD incidence across all age groups; and (3) VE_{IPD} and $VE_{carriage}$ calibrated. VE estimates for all other serotype groups were as seen in the previous analysis.

Learning Points Discussion

Scenario 2 had strongest fit in 0-2 year olds estimating $VE_{carriage}$= 6.1% (Figure 1). Calibration of VE_{IPD} (30.1%) and $VE_{carriage}$ (19.1%) in scenario 1 was also a strong fit. Assuming PCV13 had 0% $VE_{carriage}$ and VE_{IPD} estimated that 2017 ST3 IPD incidence would be 108% higher than was observed in 0-2 year olds (2.14 vs 1.03-per-100,000). This would correspond to an additional 92 cases of ST3 in ages 0-2, and over 1,800 cases over all ages.

Figure 1: Estimated versus Observed Serotype 3 Incidence in 0-2 Year Olds in The United Kingdom



The model calibration procedure fit best when the VE_{IPD} and $VE_{carriage}$ estimates were greater than 0%. Predicted VE_{IPD} matched well to a meta-analysis of ST3 effectiveness. Further research is necessary to better understand the complex transmission dynamics and evolution of serotype epidemiology.

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Modelling studies

Persistence of pertussis toxin antibodies (pt-igg) in children vs adults after pertussis
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Background

The knowledge of kinetics of PT-IgG after pertussis disease and appropriate diagnostic cut-off values for single-sample methodology is limited. We aimed to model kinetics and persistence of PT-IgG among children and adults with pertussis.

Methods

Pertussis was confirmed by culture and/or PCR and/or PT-IgG >100IU/mL or PT-IgG 40-100IU/mL and PT-IgA ≥12IU/mL (last pertussis immunisation >1year ago). PT-IgG concentrations were measured by ELISA (Euroimmun®) at the enrolment, 1year, 2year and 3year after disease. PT-IgG kinetics was described by biexponential (assuming IgG production by short-lived and long-lived plasma cells resulting in biphasic decay – rapid initial, slower second phase) and power function decay (assuming many different IgG production sites and decay rates) model (Teunis et al. 2016) separately for children (<18years) and adults. Proportion of patients with PT-IgG level above cut-off was estimated from 3000 simulations.

Results

Pertussis was diagnosed in 22 patients (mean (SD) age 21.6 (17.2) years), by typical clinical symptoms plus serology (17/22) or PCR (5/22).
According to biexponential model (Figure), adults compared with children had higher peak PT-IgG (median (IQR) 397(274-518) vs 289(193-368) IU/mL; p=0.005), longer time to reach peak PT-IgG (16(16-18) vs 13(13-13)days; p=0.0006), shorter PT-IgG half-life in initial (21(17-36) vs 336(332-452)days; p<0.001) and second decay phase (4.2(3.3-4.3) vs 7.1(6.8-7.5)years; p<0.001). More children than adults had PT-IgG >40 (77% vs 55%) and >100IU/mL (55% vs 31%) at 1year. Power function decay model yielded similar differences between adults and

children.

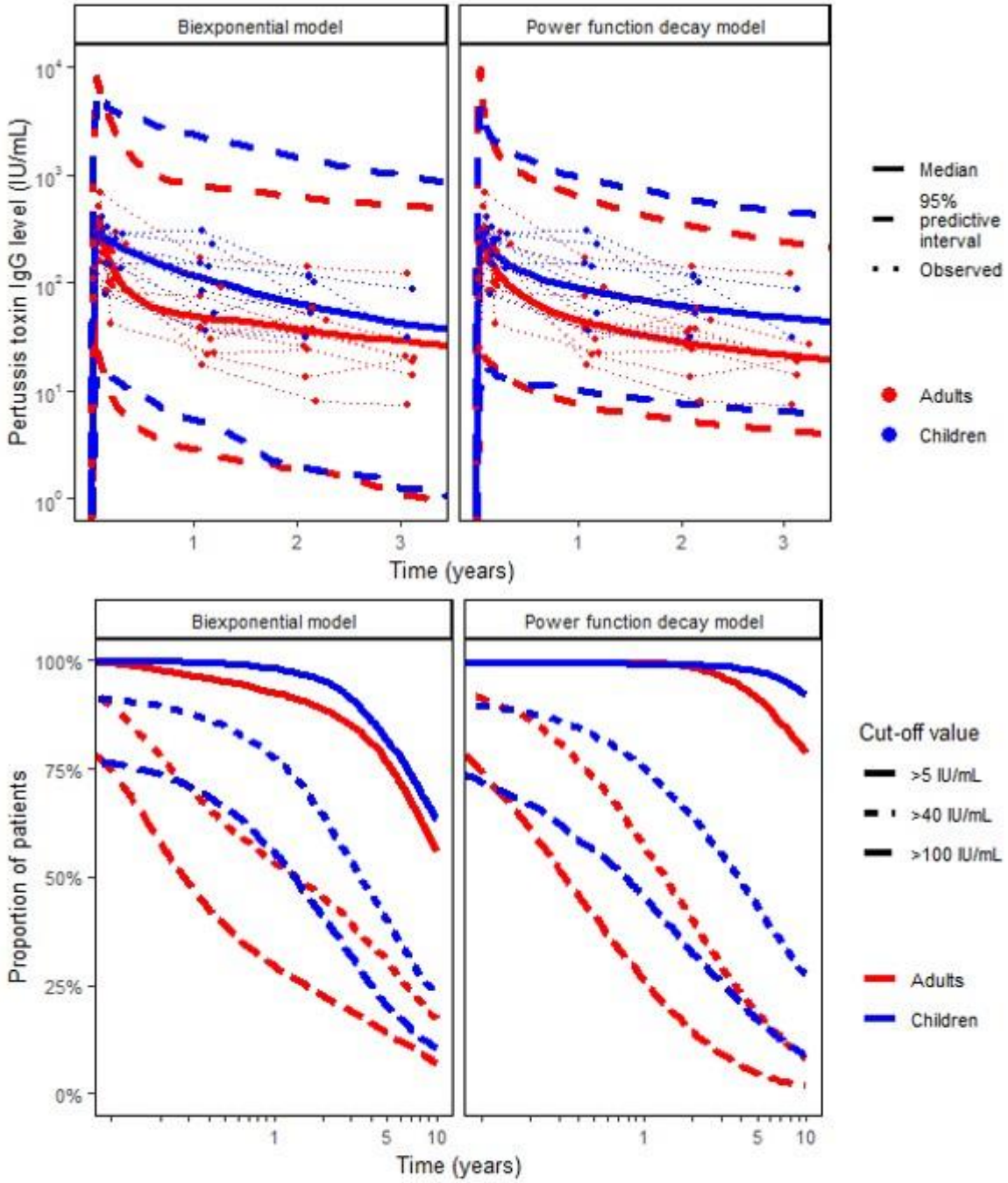

Figure. Predicted concentrations of PT-IgG (IU/mL) after the onset of infection (upper panel) and proportion of patients with PT-IgG level above cut-off value (lower panel) in adults (red lines) and children (blue lines) using biexponential (left panels) and power function decay model (right panels).

Conclusions

Following pertussis disease peak PT-IgG is higher and time to reach peak level longer, but decrease of PT-IgG faster in adults than children. Therefore, diagnostic cut-off value of single-sample PT-IgG serology >100IU/mL may not be universally acceptable in all age groups.

(Funded by Estonian Science Foundation, grant 9259)

Clinical Trial Registration (Please input N/A if not registered)

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E-Poster Viewing - May 7-10 - E-Poster Hours

New research approaches

The global accelerator for paediatric formulations (gap-f): incentivizing the development and uptake of optimal paediatric drug formulations in low- and middle-income countries

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Background

Paediatric drug development (for HIV, tuberculosis, viral hepatitis, malaria and other infectious diseases) lags behind that of adults due to several challenges. Paediatric products are costly to develop and manufacture, while markets in low- and middle-income countries are small and fragmented, which discourages investment. Because infants and young children cannot swallow tablets or capsules, acceptable palatability is difficult to achieve. Drug doses need to be tailored to a child's drug metabolism and weight, and drug approvals do not often acknowledge dosing approaches based on weight bands.

Case Presentation Summary

Through enhanced coordination across stakeholders and sectors, the Global Accelerator for Paediatric Formulations (GAP-f, www.gap-f.org) brings value and efficiency across the product development lifecycle to:

- Prioritize and evaluate:
  Increase collaboration and develop clear prioritized drug portfolios; ensure that efficient, cost-effective clinical trials are completed; establish safety, dosing and efficacy (when needed) across all relevant weight bands; and ensure that relevant regulators approve products for use.

- Develop:
  Establish and maintain business relationships, coordinate these across all parties, and launch product development to deliver products faster.

- Deliver:
  Ensure that products are introduced in a coordinated manner and that healthcare providers are familiar with treatment regimens, and support improved safety monitoring.

Learning Points/Discussion

The GAP-f:

- Provides a sustainable mechanism to ensure that the most needed optimal paediatric formulations are developed and made available to children in a timely manner
- Works across the life cycle of drug development in order to prioritize, evaluate, develop and deliver optimal formulations for paediatric populations

- Accelerates delivery of safer, more effective and more durable new treatment regimens so that more children have access to the same standard of care as adults

Acknowledgments

Authors thank partners and stakeholders who have contributed to developing the GAP-f. This paper is submitted on behalf of GAP-f partners.

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New research approaches

Burden of respiratory syncytial virus (rsv) infection in the first two years of life: community cohort study

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Background and Aims:

Bronchiolitis caused by respiratory syncytial virus (RSV) is the most common reason for hospital admissions in infants. The community burden of RSV is less well understood. We link serological data to questionnaires and routinely collected health data to estimate the community burden of RSV in children aged <26 months in England.

Methods:

We used blood samples collected around age 13 and 26 months linked to questionnaire data and primary and secondary care records from the Born in Bradford cohort study. Blood samples were tested for RSV postfusion F antibodies. We fitted finite mixture models to classify children as with or without serological evidence of past RSV infection. We modelled the odds of RSV infection by age 13 and 26 months using logistic regression according to a child's age, ethnicity, date of blood sample and contact indicators (e.g.: childcare, number of older siblings).

Results:

The study included 476 children. By age 13 months, 249 children (52.2%) had serological evidence of past RSV infection, 91 of whom (36.5%) had been in contact with healthcare with an RSV-related condition during peak RSV season. Having older siblings, Pakistani ethnicity, date of sampling and attending formal childcare were predictive of RSV infection (table 1). By age 26 months, 408 children (85.6%) had serological evidence of past RSV infection. 159 children (33.4%) were newly infected in the

second year of

Table 1 – Burden of RSV in a community setting by age 13 and 26 months

	Serological evidence of past infection by the age 13 months (vs no evidence)	Serological evidence of new infection at the age 13-26 months (vs no evidence)	Serological evidence of any past infection by the age 26 months (vs no evidence)
Number of children in the model	476	227	476
	Odds ratios with 95% confidence intervals		
Sex			
Male	1	1	1
Female	1.20 (0.81, 1.77)	1.65 (0.86, 3.18)	1.42 (0.81, 2.47)
Ethnic group			
White British	1	1	1
Pakistani	1.66 (1.00, 2.75)	0.57 (0.28, 1.17)	0.83 (0.44, 1.57)
Other	1.61 (0.83, 3.13)	1.08 (0.36, 3.23)	1.63 (0.60, 4.46)
Date of blood sample			
Oct-Dec	1	1	1
Jan-Mar	3.36 (1.92, 5.87)	1.02 (0.37, 2.81)	1.64 (0.65, 4.13)
Apr-Jun	2.71 (1.57, 4.68)	0.62 (0.26, 1.47)	1.01 (0.46, 2.23)
Jul-Sep	1.50 (0.89, 2.52)	0.35 (0.16, 0.77)	0.55 (0.27, 1.10)
Age at measurement	1.16 (0.96, 1.39) *(age centred around 12 months)*	1.18 (0.92, 1.51) *(centred around 24 months)*	1.16 (0.93, 1.45) *(centred around 24 months)*
Number of older siblings			
0	1	1	1
1	2.50 (1.52, 4.11)	2.31 (1.03, 5.20)	3.82 (1.82, 7.99)
2	1.46 (0.83, 2.56)	1.63 (0.72, 3.68)	1.65 (0.81, 3.37)
3+	2.11 (1.19, 3.75)	3.10 (1.19, 8.07)	3.23 (1.40, 7.43)
Attending any formal care			
No	1	*Not included in the final model*	*Not included in the final model*
Yes	2.12 (1.18, 3.82)		

All odds ratios were adjusted for risk factors listed in the table.

life.

Conclusions:

Around half of children are infected with RSV during the first year of life, and one in seven children remain unexposed after their second year. Evaluation of future RSV vaccination programmes should take the burden and dynamics of RSV in the community into account.

Acknowledgment: Funded by the Wellcome Trust.

Systematic Review Registration:

NA

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Novel diagnostics

Changing trends of antimicrobial susceptibility in children of culture-positive typhoid fever at a tertiary care hospital of north india: a silver lining in the dark

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Background and Aims:

Typhoid fever remains an important public health problem in developing countries like India with majority of population belonging to low socioeconomic status and living under constrained sanitation infrastructure. Typhoid fever can lead to increase in complications and morbidity if not treated with appropriate antimicrobial agents. The effective treatment of typhoid fever is becoming increasingly difficult in India due to the emergence of drug resistance especially to ciprofloxacin.But the silver lining in the dark is the reappearance of sensitivity to drugs like chloramphenicol,ampicillin and co-trimoxazole.Hence this study was undertaken to look at the current sensitivity pattern to various drugs in typhoid/paratyphoid fever.

Methods:

All the culture positive typhoid/paratyphoid fever cases in children during 2015–2018 presenting to our hospital were included in the study.Antimicrobial susceptibility was done against chloramphenicol, ampicillin, co-trimoxazole, ciprofloxacin, ofloxacin, levofloxacin, cefixime,ceftriaxone and azithromycin as per corresponding CLSI guidelines for each year.

Results:

Over the 4 years from 2015-2018,a total of 15,800 blood cultures were collected from children visiting hospital and having fever.Out of these,salmonella was isolated in 404 patients.Out of these 404 isolates,344(85.1%) were salmonella typhi and rest 60(14.9%) were salmonella paratyphi.Males were 284 (70.3%) and females 120(29.7%).Over these years more than 90% isolates showed susceptibility to ampicillin,cotrimoxazole and chloramphenicol and almost 100% sensitivity to ceftrioxone,azithromycin and cefixime.Ciprofloxacin resistance was seen in more than 95% of isolates

Conclusions:

Decreasing multidrug-resistant strains and increase in susceptibility to Ampicillin, Chloramphenicol, and Cotrimoxazole were noted in our study. These changing trends highlight the need for better preventive measures, including proper sanitation and judicious use of antibiotics, adhering to correct dosage and duration, rather than searching for novel treatment options. Vaccination should be ideally promoted in endemic areas.

Systematic Review Registration:

not registered

ESPID19-0945
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Novel Diagnostics

Necrotizing granulomas in histopathology and a tricky differential diagnosis.

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Background

Granulomas are a common histopathology finding in several diseases such as tuberculosis, sarcoidosis, Crohn's disease and cat scratch's disease. Necrotizing granulomas can be found in infectious diseases, and, particularly in tuberculosis. However, this isn't always the case.

Case Presentation Summary

A 12 year-old boy was referred to our Pediatric Infectious Disease Unit. He had a personal history of IgA deficiency and cutaneous mastocytosis. He was diagnosed of necrotizing granulomatous mesenteric lymphadenitis after presenting with a low grade fever for two weeks associating abdominal pain in his right lower quadrant during the previous week. Abdominal ultrasound found enlarged mesenteric lymph nodes and the pathology showed necrotizing granulomas with acid fastness bacteria inside. He started treatment for tuberculosis that was discontinued after Mantoux, IGRAs and PCR came negative for *Mycobacterium.* Serology for *Bartonella henselae* was positive and he was subsequently started on azithromycin showing clinical and imaging improvement. Autoinflammatory conditions and malignancies were ruled out. Five months later, an ultrasound was performed that showed a colonic wall thickening. He was referred to our gastroenterology unit and diagnosed of Crohn's disease based on the colonoscopy findings.

Learning Points/Discussion

Granulomas are a common finding in several infectious and autoimmune and autoinflammatory conditions. Collaboration between an interdisciplinary team is the key to diagnose complex patients. Acid fast bacilli can be found accidentally in samples and are not always responsible for granulomas; therefore, a broad differential diagnosis other than infection needs to be kept in mind in case of atypical findings

ESPID19-0656
E-Poster Viewing - May 7-10 - E-Poster Hours

Novel Diagnostics

An unusual case of a serious tropical infection after a period of latency in a returning traveller

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Background

Melioidosis is a systemic infection caused by Gram-negative bacterium *Burkholderia pseudomallei*, which is endemic in South East Asia and Northern Australia. It is transmitted through direct contact with contaminated soil or water. Diabetes mellitus, chronic renal disease and thalassemia are risk factors for clinical disease. Melioidosis is often subclinical, but can present with abscesses, pneumonia, septicaemia and encephalitis, with a high mortality rate. Clinical presentation can mimic tuberculosis. The incubation period may be several days to years. Microbiological confirmation can be difficult, potentially leading to delays in diagnosis and treatment.

Case Presentation Summary

A 17-year-old girl, with a recent diagnosis of Type 1 Diabetes Mellitus presented with fever and lower leg swelling. Seven months earlier she had been travelling in Thailand and spent time washing elephants. The week after becoming symptomatic she developed new respiratory symptoms and worsening leg swelling and fevers. She was treated empirically with intravenous co-amoxiclav. Imaging showed multiple intramuscular abscesses of both ankles, right foot osteomyelitis and multiple pulmonary and intrasplenic abscesses. *Burkholderia pseudomallei* was isolated in both blood culture and wound swab. Time between initial presentation and confirmation of diagnosis from the reference laboratory was 24 days. She was treated with 6 weeks of intravenous meropenem, followed by 6 months of co-trimoxazole. Plastic surgery input was required due to progressive deep ulceration with muscle loss to the bone of both legs.

Learning Points/Discussion

- Better awareness of melioidosis and its associated risk factors within the medical community could increase timely recognition and treatment, and also improve health advice to those travelling to endemic regions.
- Where melioidosis is a differential diagnosis, the use of selective media is valuable.
- The relationship between specific co-morbidities and the host immune response is not yet fully understood.

ESPID19-0989
E-Poster Viewing - May 7-10 - E-Poster Hours

Novel Diagnostics

Lyme disease, known, but still difficult to diagnose (case report)

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Background

Lyme disease, WELL-KNOWN, BUT STILL DIFFICULT TO DIAGNOSE (CASE REPORT)

Svitlana Nykytyuk, PhD, Natalia Haliyash , PhD Garijan Tania PhD, Sergiy Klymnyuk MD, PhD

I. Horbachevsky Ternopil State Medical University, Ternopil, Ukraine

Case Presentation Summary

The patient: 16-year-old male who was treated in infection diagnostic department during 1 month.

Complaints: Patient reported pain in the left ankle joint of the left feet. Any contact with *B. burgdorferi* was not indicated. His medical history included: 1 month before admitting to the hospital, there was a rash and pain in the left ankle joint. Pain syndrome was so intense, that he could not sleep at night. Neurological pathology was not detected. Tick bite wasn't recalled. Objective data: Redness and edema of the left feet, neckling. Heart-tone arrhythmical. HR 90 in 1 min, lungs were clean. Abdomen was soft, not painful. The patient was at consultations by a neurologist, orthopedics,, hematologist. Differential diagnosis with collagenosis, Multiple sclerosis, Rheumatoid arthritis

Fibromyalgia, chronic fatigue, leukemia was carried out.Imunological test :

IgM-positive to B.burgdorfery, OspB**,** p41positiv. Diagnosed: Lyme disease, erythema migrans, artritis.

Conclusion. 1.This case shows difficulties of diagnosis Lyme disease in children, that require more careful approach. Arthritis may be one of the manifestation of lyme diseases .

2.A two-step diagnosis is necessary to be done: the first step is based on a ELISA with positive result, which must be confirmed by the more specific Western blot test.

Learning Points/Discussion

Lyme disease, B.burgdorfery, Elisa test, western blot test

ESPID19-0502
E-Poster Viewing - May 7-10 - E-Poster Hours

Novel Diagnostics

Comparative characteristics of nad (f)– dependent dehydrogenase in blood lymphocytes and lymphoid tissue in chronic adenoiditis

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Background

We implemented bioluminescent technique to study the activity of NAD(F) – dependent dehydrogenase in lymphocytes separated from dark blood and lymphoid tissue in chronic adenoiditis.

Methods

55 children aged 3 to 5 years old were examined, with exacerbation of chronic adenoiditis (CA). Laboratory data from 53 conditionally healthy children of the same age range, who were not diagnosed with ENT diseases, were used as controls. Lymphocytes were isolated from adenoid tissue obtained after adenotomy.

Results

When determining the characteristics of metabolism in blood lymphocytes in patients with CA, a decrease in the activity of such enzymes as NADFM-DG, NADFICDG, MDH, NADGDG, NADICDG and LDH, MDG, NADGDG and NADFGDG reverse reactions was found relative to the control range. A comparative analysis of the metabolic activity of lymphocytes isolated from blood and adenoid tissue in patients with CA showed a decrease in G6FDG, G3FDG, LDH and NADFMDG and an increase in the activity of NADICDG in lymphocytes isolated from the tissue of the pharyngeal tonsils.

Conclusions

As a result of comparative analysis we revealed significant lowering of metabolic processes in blood lymphocytes and less expressed changes in adenoid tissue lymphocytes in chronic adenoiditis. We marked the lowering of energy and plastic processes in cell lymphocytes in blood and glucose anaerobic oxidation after their separation from adenoid tissue.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0490
E-Poster Viewing - May 7-10 - E-Poster Hours

Novel Diagnostics

Characterizing management and resource use of febrile illness in immunocompromised children

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[2]London School of Hygiene and Tropical Medicine, Department of Clinical Research- Faculty of Infectious and Tropical Disease, London, United Kingdom
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[4]Erasmus MC, General Paediatrics, Rotterdam, The Netherlands

Background and Aims:

Febrile neutropenia is a common reason for hospital admission in immunocompromised patients. Antibiotics are often given empirically, as no quick reliable test to rule out bacterial infections exists yet. Outpatient management of low-risk febrile neutropenic episodes appears to cost-effective but identification of such episodes is challenging.

The aim of this study is to characterize the management and resource use of febrile immunocompromised children in a tertiary care setting, to investigate the potential added value of a better diagnostic test.

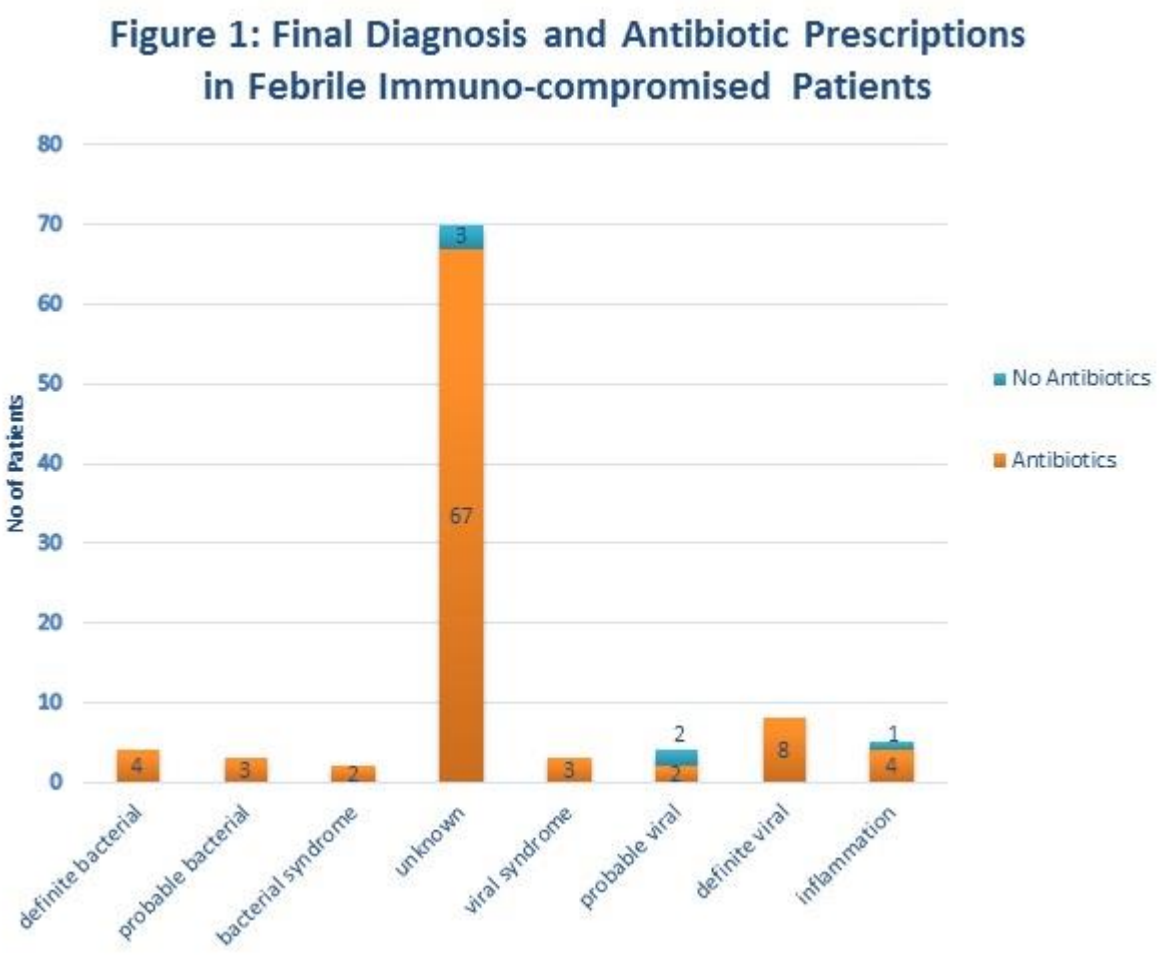
Methods:

Our single centre audit studied primary and secondary immunocompromised patients (<18 years) admitted with febrile illness (>38°C) between 1 April 2017 and 31 March 2018 for 2 weeks/month, at the Great North Children's Hospital, Newcastle upon Tyne. Diagnosis classified according to PERFORM research protocol.

Results:

99 episodes in 73 patients were included. 96% were admitted to the ward bypassing the Emergency Department. 98% had blood tests, 95% blood cultures and 5% imaging within 24 hours of admission.

4% had definite proven bacterial infection and another 5% had probable or possible bacterial infection (Figure 1) yet 95% received antibiotics for an average 2.7 days. In 70% of patients cause of fever was unknown using current available diagnostic tests. The average length of stay was 3.6 days and average costs of diagnostics, antibiotics and admission was £2025/patient.



Conclusions:

The vast majority of immunocompromised patients presenting with a febrile illness were treated with intravenous antibiotics but the minority had any evidence of bacterial infection and most had no causative diagnosis. A better diagnostic test could improve our understanding of the aetiology in this population, as well as reduce unnecessary admissions and antibiotic use with subsequent cost savings and potential reduction of antibiotic resistance and side-effects.

Systematic Review Registration:

N/A

ESPID19-0053
E-Poster Viewing - May 7-10 - E-Poster Hours

Novel Diagnostics

Epstein-barr virus (ebv)-associated myocarditis: a rare cause of acute chest pain in a healthy teenager

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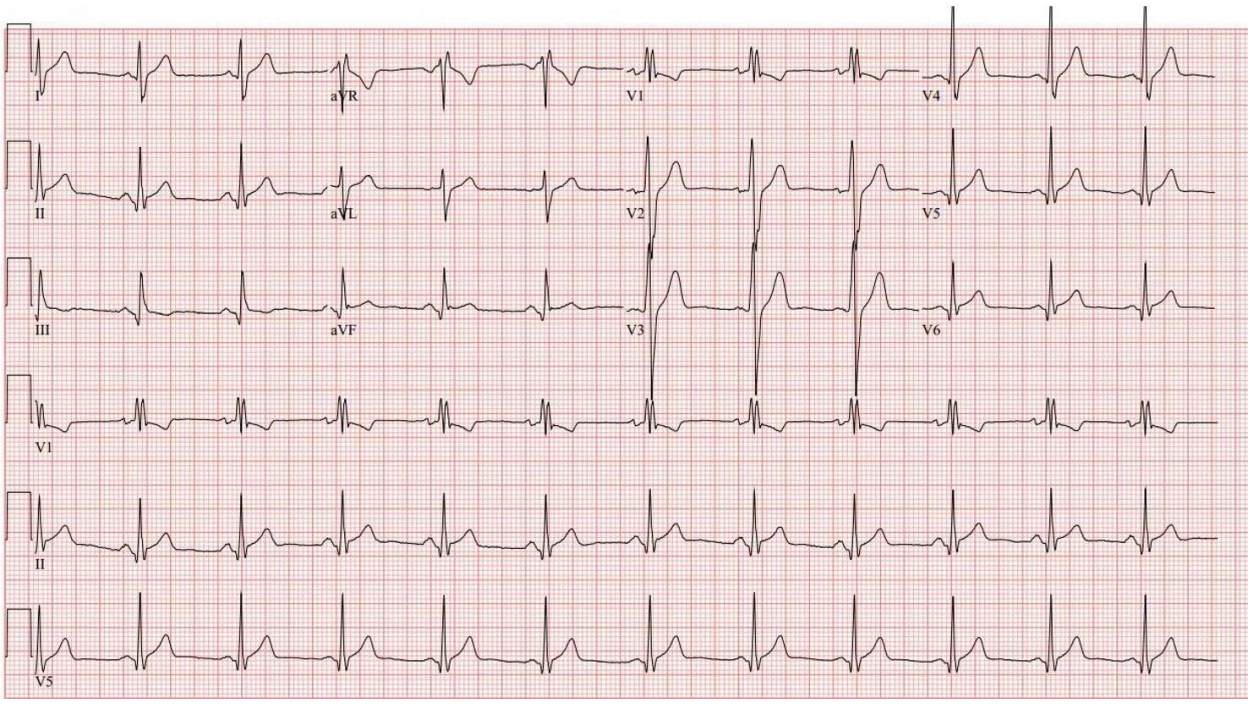
Background

Primary infection with Epstein-Barr virus (EBV) is common in childhood with clinical presentations ranging from asymptomatic infection to serious illness and sometimes death. Acute chest pain secondary to myocarditis is an uncommon presentation of acute EBV infection. Treatment and outcomes of EBV-associated myocarditis are not well described.

Case Presentation Summary

A 17-year-old previously healthy boy presented to the emergency department after awaking from sleep with sudden-onset left sided chest pain following a one week history of headache, sore throat, and malaise. He was afebrile with normal vitals and physical examination, except for bilateral cervical lymphadenopathy. An EKG showed ST elevation in leads II, III and aVF (Figure). Laboratory evaluation revealed elevated Troponin T 1617 ng/L (normal <15) and NT-Pro BNP 570 pg/mL (normal 5-51). Echocardiogram showed abnormal left ventricular relaxation and cardiac MRI showed subepicardial gadolinium enhancement in the walls of the left ventricle, consistent with myocarditis. Respiratory PCR panel was positive for Rhino/Enterovirus. Throat swab viral culture was negative. Plasma Enterovirus, Adenovirus, CMV, and Parvovirus B19 PCRs were negative. CMV IgM/IgG and HIV serology were negative. Plasma EBV PCR was positive (114 IU/mL), IgM positive, IgG VCA/EBNA negative, suggesting primary EBV infection. He was diagnosed with EBV-associated myocarditis. Symptoms resolved with ibuprofen. At a 3-month follow-up visit he was asymptomatic with resolution of EKG, echocardiogram, and laboratory abnormalities.



Learning Points/Discussion

The differential diagnosis for myocarditis in a healthy adolescent with non-specific viral prodromal symptoms includes Enteroviruses (especially Coxsackievirus B), Adenovirus, Parvovirus, Influenza, HIV, EBV and CMV. EBV-associated myocarditis should be considered in children with acute chest pain. Treatment with intravenous immunoglobulin, steroids, and acyclovir has been described in the literature, but is not well studied. Mild cases may be managed symptomatically with good outcomes.

ESPID19-1186
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Two cases with pleuropulmonary blastoma: a rare tumor presenting with pneumothorax and mimicking pneumonia

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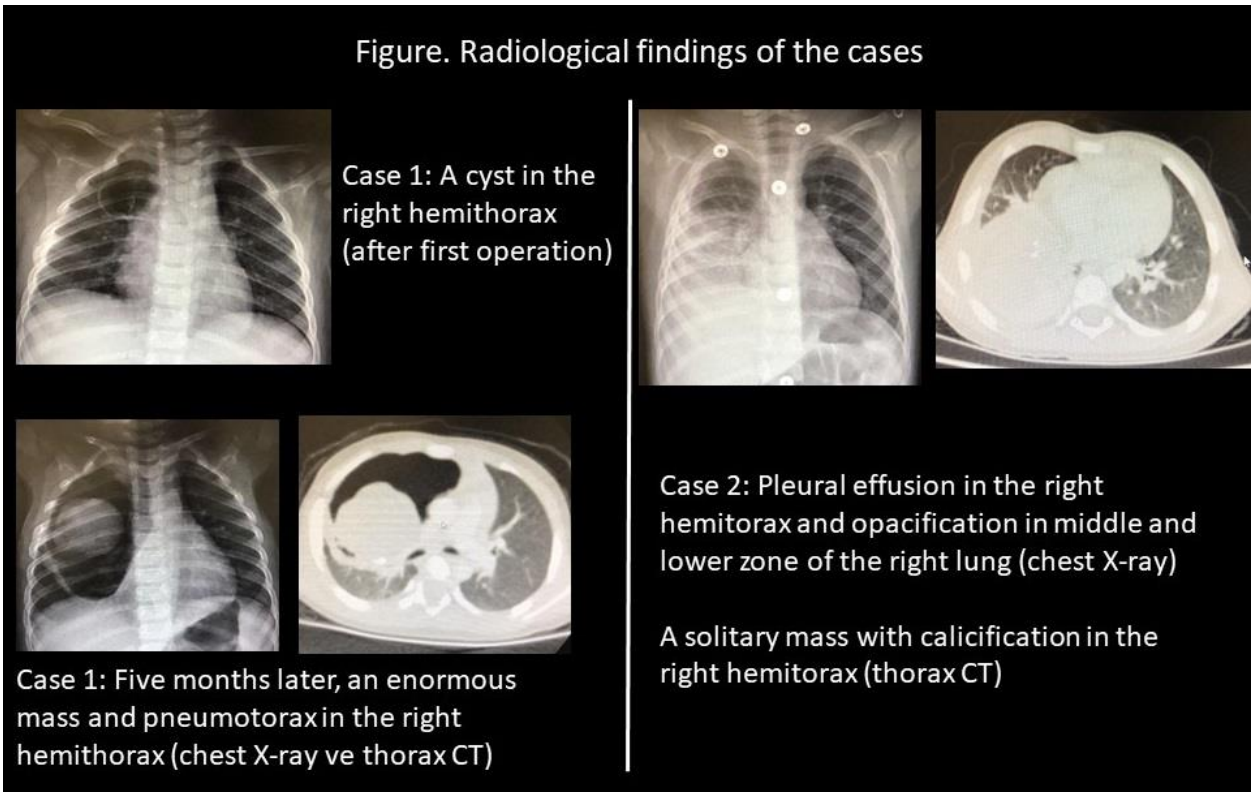
Background

Pleuropulmonary blastoma (PPB) is a rare, pediatric soft-tissue sarcoma that mainly occurs in the pleural cavity or lungs and is usually diagnosed in the pediatric population under the age of five. Patients with PPB present with nonspecific symptoms mimicking pneumonia or other respiratory distress syndromes.

Case Presentation Summary

Case 1: A 1-year-old female infant referred to the pediatric emergency department for acute onset crying and dyspnea. Conventional chest radiography demonstrated an opacification of her right upper hemithorax and pneumothorax. She underwent an operation, and on histological examination of biopsy material there were cystic bronchi and inflammation. After antibiotic treatment, she was discharged without any symptoms. During the follow-up, five months later, an enormous mass detected in the same region of the right upper lung area. Complete surgical resection of the mass was performed, and histological examination diagnosed PPB. Case 2: A 3.5-years-old male child referred to emergency department for acute onset abdominal pain. Pneumothorax was seen and a chest tube inserted. Because of the subpleural pulmonary multiple cystlike blebs in radiological examinations, he operated. The histological examination reported with non-specific cystic changes. Six months later he referred to the hospital with fever, dyspnea, and cough. There were pleural effusion and opacification on his right hemithorax. During the VATS, a solitary mass on the pleural surface and diaphragm was seen, and biopsy revealed

PPB.



Learning Points/Discussion

PPB is a very rare childhood cancer. A chest x-ray, symptoms and signs may look like pneumonia. Because PPB is rare and it may not be suspected when a child has these symptoms. PPB should be included in the differential diagnosis of solid nonhomogeneous thoracic large masses in infants and children.

ESPID19-1129
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Formation of the nordic research network for paediatric infectious diseases (nordpid)

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Background and Aims:

The five Nordic countries (Finland, Sweden, Iceland, Denmark and Norway) have many similarities e.g. in their structure of health care and social security systems, and they all have large national health care-related registers. Despite active research groups in the field of paediatric infectious diseases in all Nordic countries, the level of research collaboration between them has remained low. Improved collaboration between the Nordic countries would be beneficial for everyone.

Methods:

With financial support from ESPID, the inaugural meeting of the Nordic Research Network for Paediatric Infectious Diseases took place in Turku, Finland, on 16-17 September 2018, and a follow-up meeting in Stockholm, Sweden, on 14 January 2019. A total of 13 active research leaders from all Nordic countries presented their own research interests and future plans. Round table discussions ensued to identify common grounds for fruitful collaborative research.

Results:

The national registers and other databases were considered to provide an excellent basis for starting the collaboration and for gathering large amounts of information that could be combined and compared between the Nordic countries. The first topics selected for collaborative research were: epidemiology and disease burden of major respiratory viral infections (influenza and RSV); epidemiology and different approaches to prevention/treatment of group B streptococcus infections in pregnant women and neonates; and early discontinuation of antibiotics in febrile neutropenia.

Conclusions:

All participants agreed that Nordic research collaboration in paediatric infectious diseases holds great promise, and everyone expressed their willingness to continue developing the network further as the need is evident. The group planned to meet regularly, approximately twice a year, to follow up and ascertain the progress of the selected projects and to develop new ones. The next meeting was scheduled for September 2019.

Systematic Review Registration:

N/A

ESPID19-1093
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Bone and joint infections in children due to kingella kingae detected by specific pcr in fez, morocco

K. Moutaouakkil[1], M.A. Afifi[2], K. Atarraf[2], L. Chater[2], S. El Fakir[3], G. El Yahyaoui[4], M. Mahmoud[4], B. Oumokhtar[1]
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[4]bacteriology laboratory, Hassan II University Hospital, Fez, Morocco

Background

Kingella kingae is a fastidious microorganism difficult to grow on routine culture. It may be the reason for the high proportion of negative culture results for bone and joint children's specimens hospitalized for bone and joint infection.

The purpose of this prospective study is to describe the epidemiological, clinical, and laboratory profile of osteoaticular infections in children caused by *Kingella kingae* in Fez, Morocco.

Methods

From December 2016 to December 2017, children admitted in the pediatric surgery department in Hassan II University Hospital in Fez, Morocco with bone and joint infections were included. The bacterium was researched in bone and joint specimens by culture in blood culture flasks (Himedia), on blood agar (Biomerieux) and on chocolate agar (Biomerieux). *Kingella kingae* was confirmed by *Kingella kingae*-specific PCR assay through researching the identification gene *cpn60* encoding the chaperone cpn60 (Invitrogen).

Results

Between 100patients admitted in pediatric surgery department, 14had an osteoarticular infection caused by *Kingella kingae*. It was detected by PCR(100%) but no strains were isolated by culture in joint punctures and surgical drainage in 79% and 21% respectively. The mean age was 34[1-98]months, sex-ratio2.5. The lower limbs were most commonly affected with knee, hip, femur and ankle location of64%, 29%, 21% and7% respectively. Symptoms included pain(100%), fever(86%), swelling(79%), lameness(64%), patellar shock(43%) and inflammation(29%). The mean fever was 38.7[38-39.7]°C. Mean WCC was 13276(Range 69-20490)mm3, CRP 90(Range 20-191)mg/l and ESR 54(Range 17–120)mm/h. The ultrasound showed a soft tissue infiltration(67%) and joint effusion(33%). Median hospitalization was 9.8(3-31)days IV therapy.

Conclusions

The *Kingella kingae* rate was higher in septic arthritis and in male more than female. PCR is needed for detection of *Kingella kingae* and 90% of reported cases occur in children under the age of 5 years.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1085
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Deep neck infections behind the scenes: diagnostic challenges in a retropharyngeal abscess under the veil of pneumonia

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[2]Hospital de Getafe, Pediatric Infectious Diseases, Madrid, Spain

Background

Deep neck infections (DNIs) often have a rapid onset and can progress to life-threatening complications. Their exceptionality and diverse clinical picture can have an impact on the difficulty of its initial diagnosis since it is not commonly suspected in the context of oropharyngeal infections with unfavourable evolution. We here report the case of a children with pneumonia and a DNI as an underlying condition.

Case Presentation Summary

A 3-year-old boy was referred to hospital. He had been suffering from fever of up to 39.6ºC for about 5 days, in association with cervical pain and nasal voice. Initially it was diagnosed as pharyngitis. Blood test: CRP 372 mg/L; PCT: 2.9 ng/Ml; 25060 leukocytes (84.8% N). A chest X-Ray showed a right- upper-lobe pneumonia. Ampicillin was started. Due to the persistence of fever and cervical pain, 36 hours after admission, a cervical ultrasound was performed and amoxicillin-clavulanic was initiated. The US showed a retropharyngeal abscess (from C2 to D4) that was confirmed with a CT scan (that also confirmed the infiltrate in the right–upper-lobe). Cefotaxime and clindamycin were started along with corticosteroids. The abscess was drained and the patient received iv antibiotics for 3 weeks, and 2 weeks with oral amoxicillin-clavulanic, with clinical and radiological improvement. Intraoperative culture was negative, group A *streptococcus* rapid test was positive.

Learning Points/Discussion

DNIs are challenging infections that should be suspected in the presence of typical guide symptoms, such as torticollis. Although pneumonia presenting with torticollis is exceedingly rare, it could be seen, must often in upper lobe pneumonia. Among other complications, DNIs can cause venous thromboembolism. DNIs present a high morbidity and mortality in the absence of treatment, but with a good early infection control, complications can be avoided

ESPID19-1034
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Osteoarticular infections in children in morocco caused by staphylococcus aureus producer of the panton-valentine leucocidin toxin

K. Moutaouakkil[1], M.A. Afifi[2], L. Chater[2], K. Atarraf[2], S. El Fakir[3], G. El Yahyaoui[4], M. Mahmoud[4], B. Oumokhtar[1]
[1]microbiology and molecular biology laboratory, medicine and pharmacy department, Fez, Morocco
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[4]bacteriology laboratory, Hassan II University Hospital, Fez, Morocco

Background

The osteoarticular infections (OAI) of the child pose a real public health problem because the delay of management puts the functional prognosis of the child at stake. The severity of OAI increases with the emergence of the Panton-Valentin toxin (PVL) produced by *S. aureus*, which requires increased vigilance in the daily practice of pediatric emergencies. The aim of this work is to study *S. aureus* producing PVL in children's OAI at Hassan II university hospital in Fez, Morocco.

Methods

From December 2016 to December 2017, patients under the age of 16 admitted in Pediatric Traumatology Orthopedic Unit at Hassan II University Hospital in Fez, Morocco, and appearing to have osteoarticular signs to the detailed examination of the musculoskeletal system have been included.

Puncture or intraoperative specimens were sown in blood culture flasks, to identify the bacteria by biochemical tests (Gram stain, Catalase, Coagulase and ApiStaph), determine the antibacterial susceptibility according to CA-SFM/EUCAST-2017 and detect the presence of the *mecA* gene and the *pvl* gene encoding PVL toxin by multiplex PCR.

Results

In 100 patients with OAI: septic arthritis accounted for 53%, osteomyelitis 43% and spondylodiscitis 4%. The average age was 7 years with a sex ratio of 1.56. Between 76 samples taken, a bacterium was identified in 30% of patients, and *S. aureus* was responsible for OAI in 91% of cases. Resistance to Meticillin was found in 1 isolate. However, 55% of the MSSA carried the gene coding for the PVL toxin.

Conclusions

S. aureus remains the most frequently isolated microorganism in this type of infection with scarcity of Meticillin resistance in Morocco. The majority of PVL+strains are sensitive phenotypes. The presence of PVL is an indicator of the chronicity of the disease.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0861
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Blood stream infection is rare in a cohort of children suspected of serious illness but parameters proving non-serious infection are lacking

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[1]University of Iceland, Faculty of Medicine, Reykjavik, Iceland
[2]Childrens Hospital Reykjavik- Iceland, Immunology, Reykjavik, Iceland
[3]Childrens Hospital Reykjavik- Iceland, Infectious Diseases, Reykjavik, Iceland

Background

It is important to identify febrile children in need of prompt treatment for serious infections but at the same time limit unnecessary interventions, hospitalisations and antimicrobial therapy. Knowledge of epidemiology of severe infections is fundamental for accurate diagnosis and treatment. The aim of this study was to examine the epidemiology of severe infections at the Icelandic Children's Hospital.

Methods

We prospectively recruited children presenting to the emergency department with symptoms of severe infection if febrile and a blood was culture drawn. The study period was 22-months (September 2012-June 2014). The data used was obtained from hospital clinical records. Severe infections were defined as bacterial infection needing intravenous antibiotics and radiologically confirmed pneumonia

Results

Of 196 febrile children that fulfilled the inclusion criteria, 83(42,3%) had severe infection. The likelihood of severe infection was highest among children 1-3 years(55,2%) and 4-12 month infants(53,8%) old. Bloodstream infections were found in 5(2,6%) patients. The most prevalent diagnosis was an unspecified viral infection (n=53). Pneumonia was most common (n=33) among severe infections. No clinical signs or symptoms could discriminate between severe and self-limiting infections, with the exception of oxygen saturation <95%(p=0,015). Elevated C-reactive-protein was the only laboratory investigation associated with higher risk of severe infection. A pathogen was identified in 43(51,8%) children with severe infection and *E. coli* (n=20) was the single most prevalent pathogen isolated.

Conclusions

In concordance with other comparable studies young infants/children are at highest risk of severe infection and no single test can be used to rule out invasive infection. Further profiling of and empiric antimicrobial treatment can be indicated. A 2.6% rate of blood stream infection may justify empiric antimicrobial treatment in selected cases.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0749
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Evaluation of knowledge, behavior and perceptions of the pediatrician in the indication of the hpv vaccine

A.C. Dantas De Assis[1], T.G. Ambrus[1], D. Jarovsky[1], F.J. Almeida[1], M.A. Palazzi Safadi[1], E. Naaman Berezin[1]
[1]Santa Casa de São Paulo, Paediatric Infectious Diseases, São Paulo, Brazil

Background and Aims:

The HPV vaccine is an essential strategy for cervical cancer prevention. The physician is a crucial instrument for disease education and vaccine indication to patients and their families. However, worldwide low vaccination coverage has raised questions about the pediatrician's role in these unsatisfactory numbers.

Methods:

During the year 2018 a questionnaire was applied to pediatricians at a tertiary hospital in São Paulo, Brazil. Knowledge about the disease and vaccine, behavior and perceptions of the physician regarding barriers and strategies for better vaccination coverage were evaluated.

Results:

It were obtained 110 questionnaires. 100% agreed that: (1) HPV is the main factor related to cervical cancer, (2) disease can be asymptomatic, (3) the vaccine should ideally be performed before the onset of sexual life and (4) no severe vaccine-related adverse events were documented. Although 73% always recommend the vaccine and 54% believe to provide strong recommendation, 72% feel that their knowledge is partial or null for proper vaccine orientation, only 19% know the current HPV vaccination schedule, and 1/3 are not aware of the vaccines available in Brazil. Most doctors believe that updating medical professional is an adequate strategy. 52% prefer focusing on HPV vaccination as a cancer prevention strategy rather than STDs and 33% believe the promoting vaccination campaigns in schools is a viable strategy.

Conclusions:

Lack of knowledge can lead to incorrect orientation and not recommendation of the vaccine, therefore contributing to low HPV vaccine coverage.

Systematic Review Registration:

HPV vaccine; vaccination coverage; questionnaire; Pediatrician; vaccination knowledge; health provider attitude; vaccine hesitance

ESPID19-0739
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Dilemmas in the disclosure of HIV infection in children and adolescents

T.G. Ambrus[1], A.C. Dantas de Assis[1], D. Jarovsky[1], M.A. Palazzi Safadi[1], E. Naaman Berezin[1], F.J. Almeida[1]
[1]Santa Casa de São Paulo, Pediatric Infectious Diseases Unit, São Paulo, Brazil

Background and Aims:

The introduction of antiretroviral therapy (ART) significantly reduced morbimortality of HIV, allowing more infected children to achieve late adulthood. The WHO recommends that diagnostic revelation should begin during school age in a gradual, continuous and individualized approach. We aimed to evaluate the knowledge, feelings and difficulties involved diagnostic revelation in a tertiary hospital in São Paulo, Brazil.

Methods:

We prospectively applied a questionnaire for HIV-infected patients with revealed diagnosis, their caregivers and the health professionals involved in their regular care. This ongoing data collection started in September 2018.

Results:

Caregivers (n=14): 71% were mothers, with a mean age of 44.4 years; 57.2% were living with HIV, half of whom had already revealed the disease to their children. Ideal moment for revelation: ±13 years old. Adolescents (n=10): 60% were girls, with mean age of 19 years; 80% acquired infection through vertical transmission - the mean age of revelation was 12.9 years; all were using ART. 90% were ot aware of their disease at revelation; Ideal moment for revelation: 13-17 years - especially when the patient starts questioning the disease; 70% improved adherence after revelation. Health Providers: (n=17). Most are in their second year of pediatric residency, with an average age of 30.1 years. 100% think there is no ideal age for disclosure, and the main reason to do it is to improve auto care; 70.5% were not trained for revelation; Parents (76.5%), physicians (82.3%), and psychologists (23,5%) were cited as key elements for revelation.

Conclusions:

Understanding the challenges involved in HIV revelation can lead to improved approach methods and, ultimately, increased adherence and disease control.

Systematic Review Registration:

HIV revelation; Health providers; Caregivers; HIV; AIDS; questionnaire; adolescent

ESPID19-0705
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Hypopyon in a severely malnourished child with measles

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[1]faculty of medicine Airlangga University, Childhealth Department, Surabaya, Indonesia

Background

Acute measles infection at an early age is associated with increased complications and mortality. Complication are increased by immune deficiency disorders, malnutrition, vitamin A deficiency, intense exposures to measles and the lack of previous measles vaccination. Measles virus may present in the corneal ephitelium and conjunctiva, leading to keratitis, conjunctivitis, corneal ulcer that may worsen sa hypopyon and panophtalmitis and blindness. We report a case of hypopyon in a severely malnourished child with measles

Case Presentation Summary

A 32 month old girl with severe malnutrition came with complaint of a white spot in the right eye for 4 days. Both eyes were hyperemia, non purulent secretion in both eyes. The right eye was discharging pus with a painful sensation, spasm of both palpebrae. Bilateral corneal ulcer (positive fluorescein test 6x4 mm in right and 1 mm in left cornea) and hypopyon was evident in right anterior chamber. The vision was not affected, and no headache. She had hyperpigmented rash after suffering measles 15 days before, and did not get medication. She had not been immunized, except for BCG and Polio and never breastfed and only drank sugar water since 1 year old. Moniliasis was evident in her oral cavity. Laboratory revealed anemia, thrombocytosis, negative HIV and TB screen. High dose of oral vitamin A, nutritional correction, Ampicillin injection, oral nystatin, Moxifloxacin HCL and Homatropine eye drop were given. Hypopyon improved after 9 days treatment leaving a corneal leukoma in both eyes with a normal vision.

Learning Points/Discussion

Hypopyon is rare complication of measles in the era of routine vitamin A suplementation, however it may occur after measles in severe malnourished child, whom never breastfed nor received measles vaccination, and with underlying vitamin A deficiency.

ESPID19-0689
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Factors associated with stunting among under five children in bangladesh-a population based study

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Background and Aims:

Analysis of the risk factors of stunting provides awareness into chances and priorities for prevention, policy, and development of health/nutrition condition among children in a country as well as globally. We aimed to explore the risk/associated factors of stunting among under-five years old children in Bangladesh.

Methods:

This was a case control study. We used the most recent data from the nationally representative Bangladesh Demographic and Health Survey (BDHS) reported in 2014, and applied binary logistic regression to determine the risk/associated factors of childhood stunting.

Results:

Of the 7,173 children studied 2,599 (36.2%) were found stunted. The risk/odds of stunting was found higher if the age of the children was >12 months (OR=5.24), birth interval was <24 months (OR=1.42), had fever during last two weeks (OR=1.32), children were from poor families (OR=1.43), the mother was undernourished (BMI <18.5) (OR=1.26) or stunted (height <1.45 meter) (OR=2.15), mothers education was <5 years (OR=1.33), and fathers education was <5 years (OR=1.42). Moreover, the children having poor sanitation facility had greater chance of stunting (OR=1.28) compared to the children having toilet with flash. However, children suffering from acute respiratory tract infection/pneumonia, diarrhea, mother's age and their mass media access had no significant effect on the nutritional status of children.

Conclusions:

The identified associated/risk factors can be used for designing and targeting preventive programs for stunting in under-five children.

Systematic Review Registration:

Not applicable

ESPID19-0579
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Bartonellosis (cat scratch disease) and sporotrichosis as causes of parinaud oculoglandular syndrome

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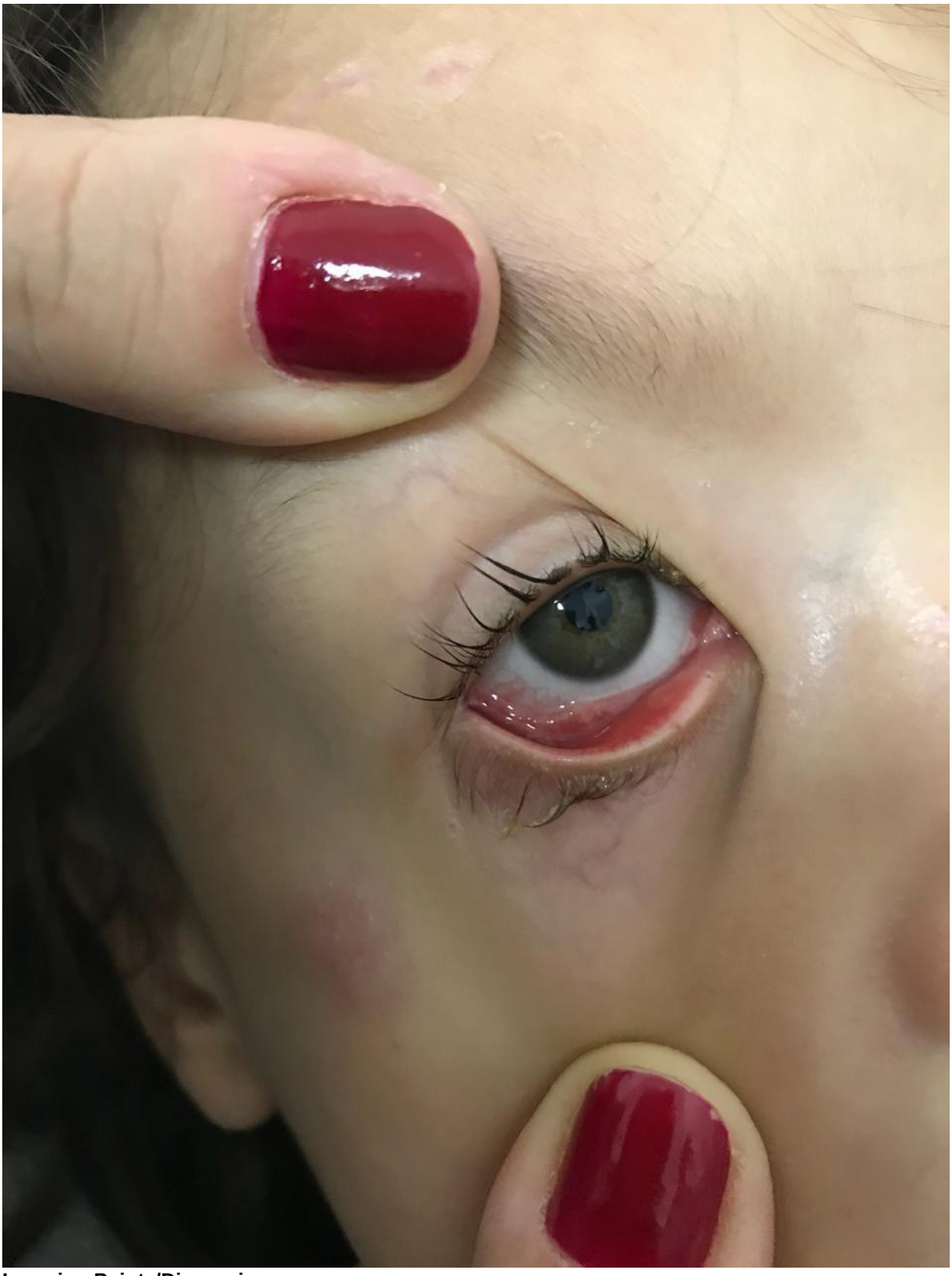
Background

Parinaud Oculoglandular Syndrome (POS) is characterized by unilateral granulomatous conjunctivitis and ipsilateral (pre-auricular or submandibular) lymphadenitis, with variable etiology. Among the most common causes are *Bartonella henselae* and *Sporothrix schenckii.* The diagnosis is based on clinical and epidemiological findings, and serological tests to confirm the causing agent. Here are described two cases of POS, due to infection by these two agents.

Case Presentation Summary

CASE 1: A three-year-old boy, previously healthy, admitted to the ER with hyperemia, edema, pruritus and purulent secretion in the right eye one month before hospitalization. He had ipsilateral nodular lesion in malar region and ipsilateral cervical lymph nodes. There was intimate contact with a cat diagnosed with sporotrichosis recently. The diagnosis of sporotrichosis was confirmed by culture of the nodular lesion biopsy. Initiated treatment with itraconazole 100 mg / kg / day, twice a day, for 6 months, and improvement of symptoms after 2 months of treatment.

CASE 2: A thirteen-year-old boy, previously healthy, was admitted to the ER with hyperemia, edema, pruritus and purulent secretion in the left eye eight days before hospitalization. He also presented ipsilateral cervical, retroauricular and submandibular lymph nodes. He had intimate contact with cats. Diagnosis of bartonellosis was confirmed by positive serology for *Bartonella henselae* and treated with azithromycin for 14 days, with gradual improvement of symptoms.



Learning Points/Discussion

POS is a rare and atypical presentation of several different agents, such as bacteria (Bartonella henselae, Chlamydia trachomatis), mycobacteria (Mycobacterium tuberculosis), fungi (Sporothrix schenkii, Cryptococcus neoformans) and viruses (EBV and herpes simplex 1). The diagnosis must be individualized according to the most probable hypotheses, considering epidemiology and clinical presentation. It is important to keep in mind POS most common causes and guide the clinical investigation accordingly.

ESPID19-0517
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Successful outpatient parenteral antibiotic therapy (p-opat) to treat bone and joint infections in children: a retrospective study from a uk tertiary paediatric centre

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Background and Aims:

Bone and joint infections (BJI) are a heterogeneous group of conditions that include osteomyelitis (OM), septic arthritis (SA) and discitis (D). Paediatric outpatient parenteral antibiotic therapy (p-OPAT) is safe, effective and associated with an improved quality of life, but there is limited evidence for its use in BJI. We sought to ascertain if p-OPAT was suitable to effectively and safely treat BJI.

Methods:

Retrospective case review of children (aged <18 years old) treated for BJI were identified from p-OPAT records between January 2015 and December 2018. Outcome measures were completion of treatment, adverse events and clinical outcome.

Results:

There were 125 children identified with a BJI (SA: 42; OM: 58; D: 6; combined: 19), of which 6 were excluded as they were diagnosed with an inflammatory arthropathy. The median age was 6 years (2 weeks to 16 years) old. Fever at presentation was documented in 66 (55%) children. Positive isolates from 70 children (56%) included *Staphylococcus aureus* (n=37; 53%), group A streptococcus (n=9; 13%), *Kingella kingae* (n=4; 6%). Complex disease (combined SA/OM/D, multifocal, multiple surgical interventions, soft tissue involvement, periosteal abscess or infected metalwork) occurred in 52 (42%) children. Both successful completion of p-OPAT and a good clinical outcome of infection were achieved in 116 (98%) children. Three children had disease relapse or progression whilst receiving p-OPAT; all three were aged less than 2 month old. Reported complications included blocked or dislodged intravenous access (n=12), antibiotic-related reaction (n=10) or possible line or line-site infection (n=3). These children did not require readmission to hospital as a result of their complication.

Conclusions:

We demonstrate that BJI can be safely and effectively managed by p-OPAT in children.

Systematic Review Registration:

N/A

ESPID19-0495
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

An evaluation of pertussis and influenza vaccination in pregnancy within secondary care at princess anne hospital, southampton, uk

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Background

Pertussis and influenza are infections that can result in severe complications for infants during the first few weeks of life. The uptake of maternal pertussis and influenza vaccinations during pregnancy is suboptimal. In 2017, a new midwife-led clinic was set up at Princess Anne Hospital that offers vaccinations alongside other antenatal appointments to try to improve uptake.

The aims were to determine pregnant women's and maternity healthcare professionals' (HCP's) satisfaction with the information provided to them about vaccination in pregnancy, satisfaction with the new service at Princess Anne Hospital and their preferred healthcare site for vaccine administration.**Methods**

Questionnaires were given to pregnant women attending the vaccination clinic at Princess Anne Hospital during October and November 2018. Maternity HCPs were contacted via email with an online questionnaire using iSurvey.

Results

Responses from 100 pregnant women and 47 maternity HCPs were analysed. A total of 82% of pregnant women and 81% of HCPs rated the clinic as either 'Excellent' or 'Good'. The majority of participants were satisfied with the information provided to them about vaccination in pregnancy. Of both pregnant women and maternity HCPs, 58% reported a preference towards vaccine administration taking place in hospital at the time of antenatal clinic appointments. The most common theme for their reasoning was 'efficiency, ease and convenience'. Recommendations for improvement of the service included providing more information about vaccination in pregnancy and more notice with text message reminders about appointments.

Conclusions

The vaccination clinic at Princess Anne Hospital was supported by both pregnant women and maternity HCPs. Implementation of similar midwife-led clinics across the UK may indeed improve the national uptake of pertussis and influenza vaccination in pregnancy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0446
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Trends in the microbiology of acute otitis media in the post- pneumococcal vaccination era (2007-2017) among children in greece

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Background and Aims:

Acute otitis media (AOM) is one of the most common paediatric infections. Pneumococcal vaccination was introduced in the NIP in 2006 (PCV7) and 2011 (PCV13) in Greece. Already since 2007 more than 80% of children<5 years of were vaccinated. The changing microbiology and antimicrobial resistance profile of AOM was studied for the period 2007-2017 for the classic pathogens *Streptococcus pneumoniae* (*Spn*), *Haemophilus influenzae (Hin), Streptococcus pyogenes (Spy), Branhamella catarrhalis (Bca), Turicella otitidis (Tot)*.

Methods:

Data were extracted through LIS. Bilateral and successive AOM episodes within a month were grouped as a single episode. Ear discharge cultures and susceptibility testing were performed with standard methods. MICs for *Spn* were determined by Etest®. Risk ratios (RR) with 95% confidence interval were calculated to evaluate the change in the relative incidence of pathogens.

Results:

2635 cases of AOM were recorded (59.4% boys, median 3ys), ranging from 211 to 304 annually. Isolated pathogens (n=2963) were: *Spy*=29.5%, *Hin*=28.6%, *Spn*=21.8%, *Tot*=16.3%, *Bca*=3.8%. Polymicrobial OM was found in 11% of cases. A decrease in the incidence was observed for *Spn* by 23% and by 14% for *Hin* for the period 2012-2017 compared to 2007-2011 (RR=0.77, 95%CI=0.67-0.88, p=0.003 and RR=0.86, 95%CI=0.76-0.97, p=0.014, respectively). *Tot* incidence increased, while *Spy* and *Bca* remained stable. Non-susceptible *Spn* isolates were: Penicillin 36% (32% MIC_{PEN}0.12 to <2mg/L and 4% MIC_{PEN}≥2 mg/L), amoxycillin 4.9% (MIC_{AMX}>2 mg/L) and cefotaxime 2.3% (MIC_{CTX}>1 mg/L). *Hin* resistant to ampicillin were 9.1%. Resistance to erythromycin and clindamycin was 34.1% and 19.5% for *Spn* and 16.1% and 12.9% for *Spy.*

Conclusions:

S. pneumoniae and secondarily *H. influenzae* are in decline in AOM after PCV13 vaccination. Better identification of Gram(+) bacteria increases *Tot* incidence. Amoxycillin remains superior to macrolides as empirical treatment.

Systematic Review Registration:

none

ESPID19-0160
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Safety in neonates of tramadol hydrochloride versus pethidine used for labour analgesia in university of ilorin teaching hospital

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Background and Aims:

Intramuscular pethidine is routinely used in many Western countries for labour analgesia. Studies have suggested that pethidine has a number of side effects affecting neonate. These include respiratory depression and impaired feeding. Tramadol is an opioid like analgesic which has been tried for labour analgesia in different studies. There are few studies comparing the relative side effects and efficacy of different opioids in labour especially in Nigeria.

Methods:

This is a randomised double-blind controlled trial comparing tramadol hydrochloride and pethidine regarding their side effects to the neonate. Information about the study was given in the ante natal period or in early labour. Consent and recruitment to the study was obtained when the mother requested analgesia. The sample size requirement was 300 women. The neonatal primary outcomes were need for resuscitation and Apgar Score<7.

Results:

There was no statistically significant difference(p=0.997) in the first minute APGAR scores of the three groups. None of the babies in either of the pethidine or tramadol groups required NICU admission, two babies in the placebo group had NICU admission on account of perinatal asphyxia. This was not statistically significant(P=0.135). Two babies required bag-mask ventilation in the tramadol group(2%), three were in the pethidine group(3%) and two in the placebo group(2%). The relationship was not statistically significant(P=0.867).There was no need for naloxone in any of the groups.

Conclusions:

The results of the study demonstrated no statistiacally significant difference in the side effect profile of the neonates when tramadol , pethidine or a placebo is used as labour analgesic in early labour. This is based on the need for resucitation and NICU admission. This concludes that either of the drugs is a safe analgesic alternative for parturients in labour.

Systematic Review Registration:

-

ESPID19-0960
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Lactobacillus sepsis in an immunocompetent host due to improper probiotics administration

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Background

According to the WHO probiotics are live microorganisms that, when administered in adequate amounts, provide health benefits to the host. However, probiotics can cause bacteremia in immunocompromised patients or the ones with severe chronic disorders. There are no publications regarding *Lactobacillus* sepsis after intravenous probiotics administration.

Case Presentation Summary

A 3-year-old boy was admitted to Neurology Department because of facial nerve paralysis and balance disorder. A CT scan of his head as well as examination of cerebrospinal fluid did not reveal any abnormalities. He was diagnosed with otitis media. Intravenous administration of antibiotics, and oral probiotics was recommended. During the first day of treatment the patient received probiotic intravenously by accident. Probiotic was brought to his hospital room in a syringe and boy's parent administered the suspension intravenously. After 30 minutes he started vomiting, developed fever and rash on his legs. He was then transported to Pediatrics Department. We started empiric therapy with piperacillin/tazobactam. In the blood sample collected before the antibiotic treatment we were able to detect *Lactobacillus spp*. bacteria susceptible to β-lactam antibiotics. Producer of this probiotic in the Summary of Product Characteristic declares resistance to many antibiotics, including β-lactam antibiotics. Our therapy was successful, the general condition of the patient rapidly improved and inflammatory markers normalised. We continued therapy for three weeks, without any additional complications.

Learning Points/Discussion

Infections associated with probiotic strains of lactobacilli are rare. *Lactobacillus*, when administered intravenously has the potential to trigger bacteremia and sepsis. Treatment of sepsis caused by probiotics can be problematic due to producers' declaration of lactobacilli resistance to many antibiotics. Improper use of medical equipment and medications can cause a serious threat to patient's health.

ESPID19-0578
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Municipally sponsored human papillomavirus (hpv) vaccination of boys in slovenia: 2014-2018

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Background and Aims:

In Slovenia, human papillomavirus (HPV) vaccination was included in the national vaccination program in the 2009/2010 school year and is state funded. It is recommended for girls attending the sixth grade of elementary school. Despite initiative by paediatricians and school medicine specialists and overwhelming data on importance of gender-neutral vaccination, especially if vaccination coverage of girls is below 50%, boys are not yet included in the national vaccination program.

Methods:

Based on the initiative of a school medicine specialist, Idrija and Cerkno were the first municipalities to offer sponsored HPV vaccination to boys in 2014/2015 school year, showing promising results. Hence, our aim was to evaluate HPV vaccination coverage among boys attending the sixth grade who received municipally sponsored HPV vaccine. Data were collected from corresponding physicians from different municipalities.

Results:

Table 1 presents municipalities that offer municipally sponsored HPV vaccination of boys, total number of eligible boys, and the proportion of HPV vaccinated boys. The number of municipalities that offer sponsored HPV vaccination to boys increased from two in 2014/2015 to 10 in 2017/2018 school year. Although the proportion of vaccinated boys was relatively low during the first years, almost all municipalities reached at least 50 % vaccination coverage rates, which is similar to current HPV vaccination coverage of girls in Slovenia.

Table 1: HPV vaccination coverage of boys in various Slovenian municipalities.

	2014/15 school year		2015/16 school year		2016/17 school year		2017/18 school year	
Municipality	Total no. of boys	No. (proportion) of vaccinated boys	Total no. of boys	No. (proportion) of vaccinated boys	Total no. of boys	No. (proportion) of vaccinated boys	Total no. of boys	No. (proportion) of vaccinated boys
Idrija	57	11 (19 %)	56	12 (21%)	51	29 (57%)	52	30 (55%)
Cerkno	19	4 (21%)	18	6 (33%)	22	8 (40%)	21	7 (37%)
Mislinja	/	/	/	/	20	11 (55%)	19	9 (47%)
Slovenj Gradec	/	/	/	/	87	52 (60%)	88	50 (57%)
Ormož	/	/	/	/	71	19 (27%)	71	49 (69%)
Radenci	/	/	/	/	19	13 (68%)	25	10 (40%)
Sv. Jurij ob Ščavnici	/	/	/	/	16	12 (75%)	13	6 (46%)
Apače	/	/	/	/	10	4 (40%)	/	/
Gornja Radgona	/	/	/	/	/	/	31	11 (36%)
Zagorje ob Savi	/	/	/	/	/	/	79	20 (25%)
Postojna	/	/	/	/	/	/	73	21 (29%)

/ = no municipally sponsored vaccination for boys.

Conclusions:

Unfortunately, the number of municipalities throughout Slovenia that provide free HPV vaccination for boys is low. However, our data show that the outstanding local initiative by several paediatricians and school medicine specialists can result in HPV vaccine coverage rates of boys that are comparable or even higher than those in girls. Thus, we urge governmental authorities to implement gender-neutral HPV vaccination program in Slovenia.

Systematic Review Registration:

Not applicable.

ESPID19-0448
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Overlap between kawasaki disease and group a streptococcal infection: a case report

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Background

Kawasaki disease (KD) is an acute multi- system vasculitis which primarily affects children. Although the etiology remains unknown, it seems that KD is a response to superantigens in genetically susceptible individuals. It was reported that treatment with intravenous immunoglobulin (IVIG) is empirically effective because it inhibits bacterial superantigen induced production of proinflammatory cytocines.

Case Presentation Summary

A six-year-old boy presented with a history of fever for 5 days. Based on a positive strep test and typical red rash he was diagnosed with scarlet fever and was under treatment with amoxicillin. His clinical examination revealed bilateral conjunctival infection without exudate, cracked lips, strawberry tongue, injection of pharyngeal mucosa, maculopapular rash and unilateral cervical lymphadenopathy. Investigations showed increased WBC count, ESR=52mm/hr, CRP=143mg/lt and elevated liver enzymes. The film array test for upper respiratory tract infection was negative. He fulfilled the criteria of KD, so he was started on IVIG and acetylsalicylic acid. He required more than one dose of IVIG in order to demonstrate an effect. On the 13th day periungual peeling of fingers and elevated PLTs appeared. After the therapy administration, eosinophilia was observed . The periodic cardiological evaluation was negative.

Learning Points/Discussion

Features of KD are similar to those found in certain illnesses which are caused by toxin-producing bacteria such as scarlet fever.

Certain patients require more than one dose of IVIG before demonstrating an effect because there is a threshold level of IgG which is necessary to reduce the clinical signs of inflammation.

The identification of causative agents will result in the development of less expensive and more specific therapies.

ESPID19-0190
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Anthropometric characteristics of infants born to hiv-infected mothers

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Background

Taking into account the growth of HIV-infected women in Belarus and despite the availability of antiretroviral therapy, the problem of congenital HIV-infection in children is becoming more urgent.

Purpose. To study anthropometric features and to estimate a condition of the children born to HIV-infected mothers.

Methods

Purpose. To study anthropometric features and to estimate a condition of the children born to HIV-infected mothers.

The material for this study was a retrospective comparative analysis of 35 newborns from HIV-infected women (study group) and 35 newborns from uninfected women (control group). The estimation of anthropometric data, which included: weight, height, head circumference and chest circumference.

Results

Of the 35 children born to HIV-infected women, the birth occurred min in the gestation period 34 weeks, max in the gestation period 40 weeks, the average gestation period was 38 weeks. The number of children born in a satisfactory condition with an Apgar score of 8/9 was 71% and in a state of moderate severity with an Apgar score – 29%.

The medium growth of children in the main group at birth was 50.6 cm (min – 43 max – 56), weight – 3043 g (min – 1980 max – 3940), head circumference – 33.6 cm (min – 31 max – 36), chest circumference – 32 cm (min – 28 max – 35).

The medium height of the control group at birth was 52 cm (min – 47 max – 58), weight – 3317 g (min – 2400 max – 4550), head circumference – 34.7 cm (min – 32 max – 37), chest circumference – 33 cm (min – 30 max – 36).

Conclusions

Children born to HIV-infected women despite the carried-out ARVT lag behind in the physical development.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1177
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Kawasaki disease shock syndrome

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Background

Kawasaki disease (KD) is a systemic vasculitis effecting small and medium-sized arteries, especially the coronaries. It typically occurs between the ages of 6 months and 5 years.

Sporadic cases of Kawasaki Disease Shock Syndrome (KDSS) have been described in the literature and it is recognized that a subgroup of children with KD were admitted to Intensive Care Unit (ICU) in shock, prior to having signs of KD.

Case Presentation Summary

The authors describe a case of a 2-month-old boy who was transferred from another hospital to our ICU with a clinical picture compatible with shock, associated with 3-day fever. Physical examination revealed a maculopapular rash on the torso, palpebral oedema and non-exudative conjunctivitis.

Blood tests on admission revealed anaemia, raised C-reactive protein and a normal leucocyte count. KD was suspected, and an echocardiogram was performed on day 4 of illness, with no significant changes. Based on existent clinical and laboratory findings, the patient was initially treated empirically with antibiotics.

Because he maintained a persistently high fever at 14th day of illness and had rising inflammatory markers, with a maximum erythrocyte sedimentation rate of 16 mm/s, the echocardiogram was repeated revealing a 4.0mm aneurysm in the right coronary artery and a 3.8mm in the left coronary artery. The diagnosis of KD was confirmed and subsequently initiated treatment with Immunoglobulin 2g/kg/day, acetylsalicylic acid 100mg/kg/day and methylprednisolone 2mg/kg/day. Later, a doppler-ultrasound revealed bilateral axillary aneurysms.

Outpatient follow-up 6 months after discharge, the patient had near complete coronary aneurysm regression.

Learning Points/Discussion

KDSS is associated with more severe markers of inflammation and greater risk of coronary artery aneurysms.
Typical signs of KD may not be obvious in the early phase of KDSS making this syndrome challenging to diagnose.

ESPID19-1164
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Pets, children and fever: not so good combination

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Background

Some infectious diseases are related to contact with animal-human at home. Fever and diarrhea are in general due to bacterial infections.

Case Presentation Summary

6 year old girl, first a twin of a double pregnancy who starts fever until 39 º C and bloody stools over 20/day. Despite of a great intake of liquids she were finally admitted due to moderate dehydration. Blood test showed leukopenia, high proinflammatory markers and low sodium . In 36 hours laboratory informed positivity for *Salmonella C* in stool culture. Suddenly, a worsening along with bad appereance and tachicardia forced us to begin empiric therapy with ceftriaxone just in moment when we we´re awared about the growth of *Salmonella C* in hemoculture. Temperature drops dramatically and the little girl went progressively well reaching normal temperature and decreasing stools until 3-4/day in next 24 hours. Three days later we proceed to switch therapy to ampicillin knowing sensitivity profile of sample.

Reinterrogating family, they recognised the presence of turtles at home as companion pets that lived in an aquarium wich water were very dirty according to father´s story, so a culture of aquarium water was performed and the result was the same species of *Salmonella C* tan blood or stools, so the turtles abandoned the familial home.

At 6th day of admission the patient was discharged giving three more days of oral Amoxicilin/Clavulanate with complete clinical recovery in 10 days. No more related cases similar than this were identified.**Learning Points/Discussion**

1. Bacteriemia due to *Salmonella* can be a severe disease recquiring admission in hospital.

2. Turtles are usual reservoirs for *Salmonella*

3. A meticulous anamnesis is mandatory for a proper diagnosis and an adequate management.

ESPID19-1163
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

The microbiological causes of paediatric inpatient deaths in malawi

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Background and Aims:

Microbiological infections are common causes of morbidity and mortality in low middle income countries like Malawi, however performing microbiological cultures is often challenging. The Queen Elizabeth Central (QECH) hospital Blantyre, Malawi, is a large governmental hospital with access to a microbiological laboratory. A prospective descriptive study was performed to determine the microbiological causes of paediatric inpatient deaths and demographics of these patients.

Methods:

Data was collected for every inpatient paediatric death with a blood or cerebrospinal fluid (CSF) culture sent at QECH, from December 2015 until November 2016. Data covered demographics, HIV status, nutritional status, microbiological results and cause of death. The attending clinician filled in a proforma based on their assessment and the written notes. Inborn neonates and those dead on arrival were excluded.

Results:

Organism	Positive Blood cultures (n)	Age (years)			HIV status (NE= Non-exposed, NR= Non-reactive, E = Exposed mum not on treatment, E-Txt =Exposed mum on treatment, R= Reactive)					Nutritional Status (N= Normal, UWFA = Under Weight for Age, M/K = Marasmus and/or Kwashikwor)		
		< 1	1 to 5	>5	NE/NR	E	E- Txt	R-Txt	R	N	UWFA	M/K
K. pneumoniae	12	11	1	0	7	1	4	0	0	8	3	1
E. coli	11	5	2	4	2	0	2	4	0	3	6	1
S. aureus	5	2	1	1	2	1	0	0	1	2	1	0
S. Typhi	4	0	1	3	1	0	1	0	0	1	1	0
S. Typhirium	3	1	2	0	1	0	0	1	0	1	0	2
H. influenzae type B	3	2	1	0	3	0	0	0	0	2	0	0

Of 488 inpatient deaths, 252 blood cultures were sent with 51 positive for pathogenic bacteria. *Klebsiella pneumoniae* (12) and *Escherichia Coli* (11) were the most common organisms, present in younger patients, with a higher burden of HIV and poorer nutritional status (see table). HIV reactivity was similar in the bacteraemia deaths (17%) in comparison to the main cohort (21%).

Eighty-seven children had CSF cultures, 14 were positive for pathogenic bacteria, the most common being *Streptococcus pneumoniae* (7), all of which were over 1 years, 6 who had a normal nutritional status.

Conclusions:

The common microbiological causes of paediatric inpatient deaths in Malawi are *K. pneumonia, S.pneumonia and E.coli,* with very few non-typhi salmonella cases which used to predominate. The under 1s had a higher burden of gram negative sepsis. The older population had a higher burden of gram positive sepsis. Interestingly, HIV was not associated with more bacteraemia deaths.

Systematic Review Registration:

n/a

ESPID19-1150
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Fever and elevated muscle enzymes in a newborn: when myositis is a fake news

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Background

High temperature in newborns provoques concern in pediatrics. It usually depends on infectious causes. Increase of creatin phospokinase (CPK) is related with muscular diseases. If fever myositis is the main reason althought fetal asphyxia or neuromuscular disorders must be ruled out.

Case Presentation Summary

A neonate born by caesarean section started fever (38.1ºC), pain and right thigh redness in first 24 hours of life. Blood test: leukocytosis, increased CPK and proinflammatory markers. Soft tissues ultrasound: Greater thickness of right thigh muscles. Cloxacillin and gentamicin were indicated suspecting myositis. He improved in 4 days. At 7 days of life he began fever again and a hot red plaque in right thight and buttock along with lack of mobility of right lower limb were observed. Thinking about osteoarticular infection of hip an MRI was performed showing hipointensity of fat signal in pelvic girdle muscles, hipercaptation in muscles of right thigh and edema between different calf muscles. In a new ultrasound increased echogenicity in gluteal fat was appreciated suggesting cellulitis switching therapy to cefotaxime and vancomycin An electromyogram was made because of the low mobility of right leg watching moderate axonal neuropathy of sciatic nerve trunk.

Afther those findings Newborn Fat Necrosis was suggested and a skin biopsy confirmed the suspected diagnosis. Antimicrobials were removed and the patient began muscle rehabilitation with a slow recovery in coming months**Learning Points/Discussion**

1. Newborn fat necrosis is unfrequent. It compromises addipose tissue and is located in limbs and back among others

2. Pathogenesis remains unclear and it evolves spontaneously to regression in few weeks.

3. The main complication is hypercalcemia. We must be alert to this situation in next 6 months after diagnosis

ESPID19-1064
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Clinical differences of influenza subtypes in children

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Background and Aims:

Clinical findings, mortality, and morbidity rates may differ among influenza subspecies. The aim of this study was to evaluate the clinical differences of influenza subspecies among children.

Methods:

The children with proven influenza infection by polymerase chain reaction on nasopharyngeal swab specimens, between 2016-2018, were enrolled. The children were divided into 3 groups as Influenza A/ H1N1 (n=53), Influenza A/H3N2 (n=34), and Influenza B (n=45).

Results:

The median age of the children was 3.25 years (IQR 0.44-5.95 years). The most common presenting symptoms were fever (n=113, 85.6%), cough (n=108, 81.8%), runy nose (n=47, 35.6%). The most common non-respiratory findings were gastrointestinal system involvement (n=29), myalgia (n=14). Prolonged fever was significantly more observed in Influenza B group (p=0.035). Respiratory distress was significantly more common in H1N1 group (p=0.029). Neutropenia (n=22, 16.7%) and thrombocytopenia (n=19, 14.4%) were the common pathologic laboratory findings. Neutropenia and thrombocytopenia were not found significant among influenza subspecies (p=0.125, p=0.163 respectively). Twenty two patients were transferred to the intensive care unit with diagnoses of severe pneumonia (n=16), encephalitis (n=4), status epilepticus (n=1) and sepsis (n=1). Three patients died (2/3 H1N1, 1/3 H3N2) secondary to acute respiratory distress syndrome.

Conclusions:

Detection of influenza subtypes will enable prediction of complications.

Systematic Review Registration:

No

ESPID19-1063
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Cervical lymphadenopathy: an atypical diagnosis

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Background

Cervical lymphadenopathy is a common finding in paediatrics. It is frequently due to reactive lymphoid hyperplasia caused by viral or bacterial infection and, rarely by malignant disease.

With unknown prevalence, cat-scratch disease caused by B*artonella henselae* is estimated to be the second most common cause of cervical lymphadenopathy. It has a benign and self-limited course and cultural tests are often negative.

Case Presentation Summary

11-year-old boy, previously healthy, was referred to our emergency department with a 7 day history of painful cervical mass and ultrasound imaging suggestive of lymphoproliferative disorder. Physical examination revealed a right submandibular and periauricular lymphadenopathy and ipsilateral non-purulent conjunctival hyperaemia, not previously mentioned, along with contralateral facial skin excoriation. When questioned, the patient assumed owning several kittens. Diagnostic hypothesis of oculoglandular Parinaud syndrome secondary to cat-scratch disease was suspected. Ophthalmological examination revealed a follicular conjunctivitis with conjunctival granuloma, corroborating the hypothesis.

Serologic tests for *Bartonella spp.* and eye swab culture were performed as well as orbital CT-scan to exclude local complications. Empiric antibiotic treatment with oral and ophthalmic azithromycin were started, with clinical improvement. Eye swab was positive for *Bartonella spp*.

Learning Points/Discussion

Cat-scratch disease is an infectious disease transmitted by the scratch or bite of a cat infected with *Bartonella spp*. Oculoglandular Parinaud syndrome is a rare entity that also occurs secondary to cat-scratch disease presenting with periauricular, submandibular or cervical adenopathy associated with granulomatous conjunctivitis. Treatment is controversial, but if secondary to *Bartonella spp.* infection, azithromycin may be considered. This case reinforces the importance of taking a complete medical history and a meticulous physical examination to avoid unnecessary exams in a benign condition. Cervical lymphadenopathy combined with a kitten contact history should raise suspicion of *Bartonella spp.* infection.

ESPID19-1020
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Pyogenic sacroiliitis in children: three case reports

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Background

Pyogenic sacroiliitis is a rare osteoarticular infection, occurring most frequently in children and young adults. Clinical presentation may be poor and misleading. We present three cases of pyogenic sacroiliitis in children.

Case Presentation Summary

Case 1.
A 11-year-old male, with a history of gluteal trauma two days before, presented with severe pain in the right lumbar region for 15 days. He presented with claudication of the gait and intense pain at the palpation of the right sacroiliac joint. Analytically with leukocytosis with neutrophilia and elevation of C-reactive protein and sedimentation rate. Magnetic resonance demonstrated right sacroiliitis. Intravenous treatment with flucloxacillin was started. Blood culture was positive for *Staphylococcus aureus*.

Case 2.A 13-year-old male, presented with severe pain in the left hip for 2 days. Physical examination showed intense pain of the mobilization of this joint. Analytically with leukocytosis with neutrophilia and elevation of C-reactive protein and sedimentation rate. Magnetic resonance demonstrated left sacroiliitis. Intravenous treatment with flucloxacillin was started. Blood culture was positive for *Staphylococcus aureus*.

Case 3.
A 12-year-old male, presented with severe pain in the lumbar region and hip for 3 weeks associated with fever, asthenia and anorexia. Physical examination showed intense pain at the palpation of the left sacroiliac joint. Analytically with increased C-reactive protein and sedimentation rate. Magnetic resonance demonstrated bilateral sacroiliitis. Polymerase chain reaction was positive for *Brucella Melitensis.* He completed 6 weeks of treatment with doxycycline and rifampin.

Learning Points/Discussion

Pyogenic sacroiliitis is an uncommon disease in children. The key to successful management is early diagnosis. The magnetic resonance findings play a crucial role and blood cultures are useful to identify the pathogen. If the diagnosis is established promptly, most patients can be managed successfully with antimicrobial therapy.

ESPID19-1000
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Narratives medicine a tool to reveal primary bio psycho social needs in children with severe chronic conditions

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Background

We tested the hypothesis that narrative medicine may help implementing a personalized bio-psycho-social model in children with severe conditions, including HIV infection.

Case Presentation Summary

Forty-eight narratives were collected from 12 children (cystic fibrosis, lymphoma, Crohn's disease, autoimmune hepatitis, intestinal failure and AIDS, 2 for each condition), their mothers, physicians and nurses. Narratives were classified based on their prevalent impact as *disease* (corresponding to the biological burden in the bio-psycho-social model), "*illness"* (psychologic burden) or *sickness*, (social burden). Class labelling was based on textual analysis. Classification distribution was evaluated according to storytellers and etiology.

Overall, 61% of text was "illness" class, 28% "disease" and 11% "sickness". In patients and physicians, illness class was 50% and "disease" 40%. Nurses and parents clustered together with "illness" being 70%. "Sickness" was limited to parents. Narratives were also determined by etiology, and "illness" was largely prevalent in all but Crohn's disease and AIDS. The latter had a peculiar class distribution, with high "sickness", related to stigma. Qualitative analysis revealed hidden needs including specific fears in children, misunderstanding when the diagnosis was discussed, and burnout and anxiety among health care personnel. Children coped better than their parents with the problem. Nurses were more empathic than physicians, who focused on clinical processes. Occasionally they revealed fears of being infected from HIV.

Learning Points/Discussion

Narrative approach allows identification of problems that may negatively impact the lives of children with chronic diseases and their parents, whose major needs may be emotional rather than clinical. Similarly, narratives collected by health care personnel show human understanding combined with practical proposals. Children with HIV infection and their families cluster separately from other chronic conditions and require specific bio-psycho social approach.

ESPID19-0999
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Recent measles outbreak in greece: epidemiology of cases at a tertiary care children's hospital

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Background and Aims:

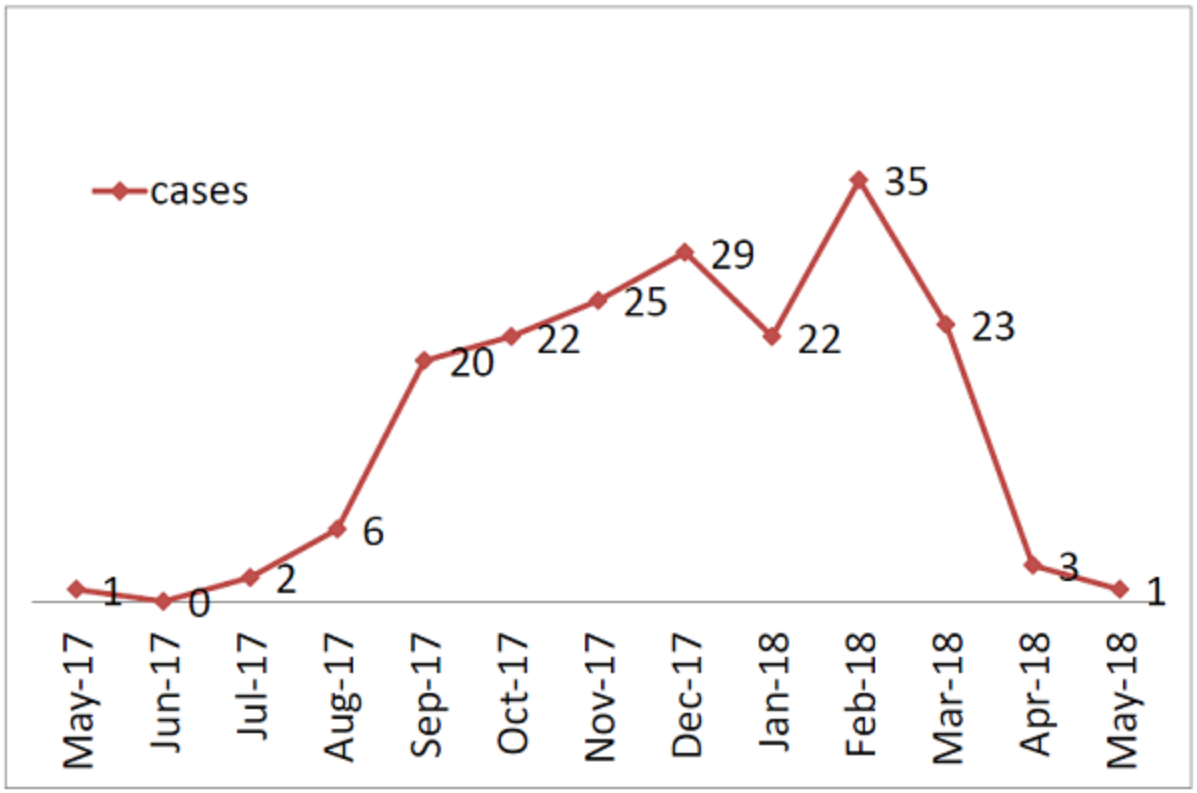
Measles is a highly contagious viral infection that has currently re-emerged in several European countries, including Greece. Between 05/2017-12/2018 Greece registered 3258 measles cases, including 4 deaths according to data provided by the Hellenic Centre for Disease Control and Prevention(KEELPNO).

Methods:

The aim of this study was to describe the epidemiological characteristics of children suffering from measles that presented to our tertiary care Children's hospital. We retrospectively recorded and evaluated children(0-16years) that presented to the Emergency Department(ED) and admitted to the general Paediatric wards during a 13-month period(05/2017-05/2018).

Results:

A total of 189 children with measles visited our ED. Median age was 3 years(range:40 days-15years). The commonest symptom was fever(98.5%), while 20% of cases had no typical rash in the initial evaluation. Close contact with someone who had measles was reported in 57.1%. Hospitalization rate was 41.8%(n=79children) and 52% of hospitalized children were <2 years. Median duration of hospitalization was 4 days(range:1-9days). The main reasons for hospital admission were dehydration/poor feeding(62%). Complications were recorded in 81% of hospitalized children(52% being <2years); the commonest was dehydration(65%) followed by acute otitis media(24%) and pneumonia(18%). Two cases developed encephalitis, confirmed by CSF PCR and two patients were admitted to the PICU while there was no death. Underlying disease was reported in 9.7%. Vaccination MMR status was known in 81%. No case was reported among fully vaccinated children, while 8% of the patients had received only one vaccine dose. Three cases were recorded among health-care workers of our hospital.



Conclusions:

A large number of measles cases were admitted to our hospital during the recent measles epidemic and were associated with considerable morbidity. Young age and underlying disease were predisposing factors for hospital admission and measles complications.

Systematic Review Registration:

ESPID19-0969
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Case of etiotropic treatment of human herpesvirus 6/parvovirus b19 myocarditis in a child with abdominal aortic aneurism and aplasia of kidney

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Background

Over the last 20 years, the spectrum of identified viral pathogens in myocarditis has expanded from only enteroviruses to a large number of other viruses including parvovirus B19 (PVB19) and human herpesvirus 6 (HHV-6).

Case Presentation Summary

A 20-month-old girl presented with a 2 week history of worsening fatigue during feeding after upper respiratory tract infection with exanthema. Physical examination indicated tachycardia (150-160 beats/min; normal for age, 98-140 beats/min), muffled heart tones, arterial hypertension (175/110 mmHg; normal for age, 86-106/42-63 mmHg), hepatomegaly and generalized lymphadenopathy. Laboratory tests indicated slight leukocytosis (16.3), while cardiac troponin and C-reactive protein were normal, electrocardiogram showed sinus tachycardia. Echocardiography indicated an increased left ventricular (LV) dimensions, along with low ejection fraction (EF): LV end-diastolic diameter (LVEDD) - 39 mm; LV end-systolic diameter (LVESD) -36 mm; EF - 21% (normal forchildren is 64–83%). Additionally abdominal aortic aneurysm and aplasia of the left kidney were revealed. Serum screening tests for inborn errors of metabolism and endocrine disorders were negative, real-time qualitative polymerase chain reaction (PCR) DNA test of blood was positive for HHV-6 (88 copies/ml) and PVB19. HHV-6 DNA was also detected in urine (43 copies/ml).

The patient received IV immunoglobulin 1g/kg and IVganciclovir 2.5 mg/kg twice a day (due to glomerular filtration rate decreasing) for 21 days. Treatment with calcium-channel blockers, inotropes anddiuretics was initiated. As a result HHV-6 DNA test in blood became negative.

Despite clinical improvement (increasing of EF to 47%), repeated echocardiograms showed persistent increase of left ventricle. At the time of writing, the patient was under regular observation.

Learning Points/Discussion

Children with clinical myocarditis should be examined for HHV-6 and PVB19. Early etiologically driven treatment might reduce the possibility of development of myocardial injury

ESPID19-0950
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Consequences of an undiagnosed mastoiditis; a case report.

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Background

Cerebral sinus thrombosis is an uncommon and potentially life-threatening complication of mastoiditis.

Case Presentation Summary

A six years old child presented to the Emergency Department with progressive left-sided ear pain, frontal headaches, emesis, diplopia and an history of one month otalgia, treated with Amoxicillin-Clavulanic for five days with partial clinical resolution. No evidence of mastoiditis signs (swelling and postauricular pain). Eye examination showed bilateral papilledema, while the Head-CT reported a left-sided mastoiditis without intracranial abnormalities. Angio-MRI revealed intracranial hypertension (ICH) and partial thrombosis of the transverse left sinus with slow venous flow. Intravenous Vancomycin was started, followed by Amoxicillin-Clavulanic, acetazolamide and enoxaparin.

Even tough he had been discharged thanks to clinical improvement, he was admitted to the hospital two times because of symptoms due to ICH (headache, ocular symptoms such as diplopia and reduced visual acuity). The two angio-MRIs, performed in hospitalization, showed persistence of signs of ICH despite progressive amelioration of the vasculopathy. Three lumbar punctures had been performed but symptoms showed up again, so we decided to perform a ventriculoperitoneal (VP) shunt intervention with a rapid clinical improvement. At the last follow-up the child was in good clinical status**Learning Points/Discussion**

Most patients with sinus thrombosis have history of AOM and have already been treated with antibiotic making the typical mastoiditis signs rare and otoscopy normal. The most common symptom at presentation is headache. Angio-MRI is diagnostic gold standard and allows the distinction between slow venous flow and occlusive thrombosis. Antibiotics and anticoagulants, main treatment of sinus thrombosis, reduce the necessity of surgery interventions, such as serial lumbar punctures and VP derivation, that are still performed in patients with neurological deterioration despite pharmacological therapy.

ESPID19-0920
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

The role of procalcitonin as an inflammation marker in the early postoperative period after cardiac surgery in pediatric patients

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Background and Aims:

Procalcitonin (PCT), an acute phase protein, is a well established infection marker in critically ill pediatric patients. The aim of this study is to evaluate PCT as an index of inflammation severity and its value in predicting outcome during the early postoperative period after pediatric cardiac surgery.

Methods:

We present a prospective observational study of a single Pediatric Cardiac Intensive Care Unit (CICU). Fifty-five (55) children under 18 years old with Congenital Heart Disease (CHD) undergoing cardiac surgery were enrolled. Plasma PCT 24 hours after admission was measured, and patients were categorized into high and low risk group, with a cut-off value of 5 ng/ml, which has sensitivity (100%) and specificity (95%) as the organ failure predictive cutoff values. CPB time, lactate level, Vasoactive Inotropic Score (VIS), major complications, duration of mechanical ventilation and CICU length of stay (LOS) were compared

Results:

PCT levels at 24 hours after admission were influenced by CPB duration (153.5 min vs 96 min, p0.03). Among high-risk patients, we observed significant peak lactate (4.5 vs 2.1, p 0.005) and higher VIS scores (20 vs 12.5, p 0.006). PCT levels correlated with postoperative liver dysfunction (55% in high-risk group vs 28%, p 0.05) and acute kidney injury (40% vs 11.4%, p=0.01). Furthermore, mechanical ventilation and CICU stay were longer in high risk group (5.5 vs 3 days and 10 vs 6 days respectively).

Conclusions:

Procalcitonin levels in the early postoperative period after pediatric cardiac surgery appears as a good index of intraoperative stress and postoperative inflammation severity. Furthermore, they could be used as a predictive marker of postoperative organ dysfunction among pediatric patients with CHD.

Systematic Review Registration:

o

ESPID19-0896
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Hiv- related burkitt's lymphoma - prolonged neutropenia associated with raltegravir: a case report

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Background

HIV infected children are at increased risk of developing cancer, particularly in the later stages of AIDS.The HIV infection itself represents a major risk factor for developing malignancies such as Non-Hodgkin's Lymphoma (NHL) which remains the most frequent cancer in subjects with AIDS.The choice of Antiretroviral treatment in this condition is crucial.

Case Presentation Summary

A 6-year-old girl was admitted for fever and parotid swelling; the latter had appeared three months ago and was treated with intravenous antibiotics, without benefits. Family history included HCV-infected father. The patient underwent an open biopsy of the parotid gland; the biopsy resulted compatible with Burkitt's Lymphoma (BL). According to the Ann Arbor Staging Classification a diagnosis of Stage III BL was made. Standard ELISA serology test and quantitative PCR showed HIV-infection (Viral load > 1000000/ml). CD4+ lymphocytes count was 307/mm3. Patient's mother resulted HIV negative and one of the big sister HIV positive. A modified AIEOP LHN 97 protocol was started, with administration of Rituximab, dexamethasone, cyclophosphamide, vincristine, ifosfamide, high dose methotrexate, high dose cytarabine, etoposide and intrathecal prednisolone, methotrexate and cytarabine. We administrated methotrexate, cytarabine and etoposide at full dosage instead of reduced doses as suggested by the protocol. HAART (including Emtricitabine/TAF and Raltegravir) was also started. The first two methotrexate-including courses provoked liver and skin toxicity, with increased liver enzymes and diffuse erythematous rash then solved. Neutropenia developed and persisted after the end of chemotherapy, requiring G-CSF administration; it resolved after replacing Raltegravir with Dolutegravir .

Learning Points/Discussion

This case report showns that, even though there are no cases described in literature, Raltegravir associated with antiblastic chemotherapy could cause prolonged neutropenia.

ESPID19-0883
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Immunizing pediatric healthcare workers with tdap: does it work?
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Background and Aims:

Pertussis resurgence is evident over the last decades with young infants at risk for severe disease. Given the waning immunity in previously vaccinated individuals and pertussis' contagiousness, healthcare workers (HCWs) may pose a reservoir of infection for susceptible infants. Accordingly, public-health authorities require that HCW, particularly those in close association with young infants be immunized with Tdap. Since little is known regarding the effectiveness of Tdap administered to pediatric HCWs, we sought to study its impact on pertussis toxin antibody levels among such workers over time.

Methods:

The infection control unit manages the HCW immunizations of the hospital employees in accordance with the Israel Ministry of Health guidelines. Although no serological correlate of protection against pertussis is established, 5 IU/mL of ELISA antibodies to Pertussis toxin are considered protective. Subjects were divided into groups depending on whether their ELISA antibodies were above or below this cutoff (EUROIMMUN).

Results:

Eighty-seven pediatric HCW (69 female), vaccinated at mean age of 36 years were sampled in a hospital in Northern Israel, October 2018. Among the females, there were more with protective levels ≥5 IU/mL than with <5 IU/mL, 49/67 (75%) versus 20/20 (100%), p=0.02, respectively. There were no differences between the protected and unprotected group regarding time elapsed between Tdap administration and antibody sampling, 48.5±26.2 versus 57.0±16.8, p= 0.9. All males samples had PT antibody levels ≥5 IU/mL.

Conclusions:

Despite compliance with Tdap immunization, nearly a quarter of the females exhibited insufficient PT antibodies. Notably, Tdap effectiveness did not vary over time among the HCWs studied. Moreover, all male pediatric HCWs exhibited immunity. Further pertussis immunogenicity studies are warranted to evaluate vaccination strategies.

Systematic Review Registration:

N/A

ESPID19-0831
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Osteomyelitis in children: a report of four cases

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Background

Osteomyelitis, defined as a bone infection, is an uncommon but significant disease that can lead to severe sequels if not diagnosed and treated in time. In most cases the lesion is solitary and located in the long bones of the lower extremities. The hallmark of osteomyelitis presentation is localized pain and diminished function but symptoms can be variable and physical findings non-specific.

Case Presentation Summary

We present the four cases of osteomyelitis that occurred in our department between January 1st and December 31st of 2018. First case, 2 months infant presented with an uninterrupted crying and diminished movements of the left lower limb, physical examination revealed decreased spontaneous movement of that limb and pain in mobilization, further investigation revealed osteomyelitis of the left femur. Second case, 2 months infant presented with diminished movements of both upper limbs that was confirmed by physical examination, investigation revealed osteomyelitis of both humerus. Third case, 9 years old girl presented with thigh pain and claudication associated with 24 hours fever, clinical examination revealed selective pain on pubic symphysis palpation and claudication, further investigation revealed osteomyelitis of the pubic symphysis. Forth case, 4 years old boy, presented with four days fever and pain in the right hand, physical examination demonstrated edema of the right hand back and wrist, further investigation revealed osteomyelitis of the metacarpals. All cases completed antibiotic therapy and are sequel free at this time.

Learning Points/Discussion

These cases illustrate different presentations of osteomyelitis, highlighting that a detailed clinical history and careful examination combined with a high index of suspicion followed by laboratory and imaging exams are essential for early diagnosis and treatment in order to avoid future sequels.

ESPID19-0829
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

E. Coli monomicrobial necrotizing soft tissue infection in an iron- overloaded adolescent with congenital dyserythropoietic anemia and ichthyosis vulgaris

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Background

Pediatric necrotizing soft tissue infection (NSTI)/ Necrotizing fasciitis (NF) are rare but severe, life-threatening infections. Gram positive bacteria like Streptococcus *pyogenes* and *Staphylococcus aureus* are the most common causes. *E Coli* is an extremely unusual cause of monomicrobial NSTI/NF of the extremities. Hereby, we report a child with iron overload who developed fulminant *E.coli* NSTI/NF of the leg and had very good outcome with optimal antibiotic coverage and prompt surgical intervention. We want to highlight the importance of covering organisms associated with infections in iron-overloaded patients.

Case Presentation Summary

A 15 yr old adolescent known to have congenital dyserythropoietic anemia and ichthyosis vulgaris presented for routine blood transfusion. He had low grade fever, progressive swelling of left lower limb and severe pain for 2 days following twisting of his left ankle. He underwent investigations to look for infection, deep vein thrombosis and fracture. He had rapid deterioration and developed severe septic shock within few hours of his arrival to the hospital and required 3 inotropic agents to maintain his blood pressure. Urgent surgical exploration revealed necrotic anterior compartment of the left leg. Fasciotomy was done and dead tissue was debrided. Cultures revealed pure growth of *E.coli* from all surgical specimens. He required multiple surgical reviews for debridement and antibiotic therapy for four weeks. Upon discharge, the child was capable of ambulation without aids, having left sided foot drop and mild circumduction gait.

Learning Points/Discussion

Although Gram positive organisms are the most common cause of NSTI/NF in children, we should always cover for Gram negative bacteria in children and we should consider rare organisms in patients with iron-overload. High index of suspicion is needed for NSTI/NF diagnosis, even in the absence of classic clinical signs.

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Other

Randomised prospective step-wedge multicentre study to evaluate the relationship between pneumococcal colonisation density in 2-year-old children and rates of transmission to family contacts: interim results

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Background

Interruption of transmission of vaccine serotypes underlies effectiveness of pneumococcal conjugate vaccine programmes at population level. Nasal colonisation density varies widely between individuals and over time but its relationship to infectiousness is unknown. *Streptococcus pneumoniae* (Sp) nasal colonisation density is increased by upper respiratory viral infections and the live attenuated influenza vaccine (LAIV).

In a multi-centre prospective randomised stepped-wedge trial, we are using LAIV as a probe to increase density of pneumococcal nasal carriage in LAIV-naive 2-year-olds and then assessing the impact on transmission rates to household contacts.

Methods

410 families with an eligible 2-year-old index child were recruited over 2 seasons across 10 sites in the UK. Families were randomised 1:1 for the index child to receive LAIV at visit 1 or visit 3 (4 weeks later); saliva and nasopharyngeal samples (NPS) were collected from participants every two weeks over 2 months. Samples are being analysed for Sp using real-time quantitative PCR (lytA). Samples are considered positive when the threshold cycle (Ct) value is less than or equal to 35.

Results

Table 1. Season 1 mean values of Sp carriage density in the NP of index children before and after vaccination with LAIV

Study Arm	Week from vaccine	Gene copies/ml (Mean)	Proportion of pre vaccine
Vaccine at Visit 1	PreVaccine	9019	1
	2	10450	1.16
	4	23683	2.6
	6	9669	1.09
	8	12979	1.44
Vaccine at Visit 3	PreVaccine	13021	1
	2	18452	1.42
	4	61242	4.7

Conclusions

This study exemplifies novel use of live attenuated vaccines as experimental probes in human challenge experiments to elucidate the biology of colonisation and transmission.

In season 1 carriage density data (30% of total dataset), an increase in the density of carriage was observed in index children for Sp, which was maximal four weeks after the administration of LAIV (table 1). Season 2 sample analysis is on-going and is required to assess whether changes in carriage density result in changes in Sp transmission.

Clinical Trial Registration (Please input N/A if not registered)

N/A

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Other

Approach to the recurrent meningitis with a case report

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Background

Acute bacterial meningitis is a life-threatening infection of the cranial and spinal leptomeninges. Recurrent attacks are rare. In the presence of recurrent meningitis, extensive research is needed to define the cause. Here we present a childwith recurrent meningitis due to the history of head trauma 3 years ago.

Case Presentation Summary

An 11-year-old male who had a history of skull base fracture due to falling from a tree three years ago, presented to the external center with fever, severe headache and altered consciousness.He was then referred to our pediatric intensive care unit. Physical examination revealed signs of positive meningeal irritation and lumbar puncturewas performed. When his historywas deepened, it was learned that he was hospitalized with the diagnosis of meningitis one year ago and was discharged after treatment and no vaccine was administered. Cerebrospinal fluid (CSF) analysis yielded numerousleukocytes, immeasurably low glucose and high protein level. He was started on vancomycin and meropenem. Paranasal sinus computerized tomography revealed communication between right frontal sinus and right ethmoid sinus with anterior cranial fossa (Fig-1). Control lumbar puncture performed on the 7th day of the treatment. There was no leukocytes in the microscopic examination. CSF culture remained sterile. Elective surgery for patch placement was planned by otolaryngologydepartment. Meningococcal and pneumococcal immunizationswere performed. The patient was discharged after 21 days of treatment.

Learning Points/Discussion

Skull base defects are important causes of recurrent meningitis. The most important point to remember is that, in addition to surgical repair correct immunization strategy is essential to avoid recurrence.

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Other

Acute disseminated encephalomyelitis associated with kawasaki disease.

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Background

Acute disseminated encephalomyelitis (ADEM), also known as post infectious encephalomyelitis. ADEM is often preceded by a viral or bacterial infection and vaccination history. The pathogenesis of ADEM is incompletely understood. Previously, there is no report showing ADEM and Kawasaki diseases association. Herein we presented a 3,5 years old girl diagnosed kawasaki diseases and ADEM together.

Case Presentation Summary

A previously healthy 3 and half years old girl was admitted to our hospital with a 10 day history of fever (up to 39.4°C). Her initial physical examination revealed only a high fever. Her laboratory test results was a leukocyte count of 15×10^9/L, hemoglobin level of 11.4 g/dL, and a platelet count of 770 000/ mL. His C-reactive protein was 8.3 mg/L; procalcitonin level 0.11 ng/mL, erythrocyte sedimantation rate 103 mm/hr, AST of 34 IU/L, ALT of 37 IU/L. Her echocardiography revealed a normal ejection fraction, but perivascular echo brightness of the right coranary coronary artery with a 4 mm diameter. She was diagnosed with an incomplete Kawasaki Disease because of prolonged fever (10 days), thrombocytosis, and echocardiography findings. Intravenous immunoglobulin (IVIG, 2 g/kg/dose), and oral aspirin (50 mg/kg/day) were administered. His temperature returned to normal soon after the IVIG therapy. She developed cerebellar ataxia and speech problems 24 hours after IVIG infusion. Her cranial MRI showed that bilateral patch hyperintense lesions in the cerebellum, thalamus, subcortical area in the frontaparietal region. She was diagnosed as ADEM and followed by clinically since she previously received IVIG and her clinical conditions was gradually improving and she was discharged.

Learning Points/Discussion

This is the first report shown an association of ADEM and Kawasaki Diseases. The etiology of both of the diseases unknown and may be linked to post-infecitous event.

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Other

Heck's disease: a rare entity caused by hpv 13

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Background

Heck's disease, or focal epithelial hyperplasia, is a rare form ofhuman papillomavirus (HPV) infection, mainly caused by 13 and 32 subtypes. Its diagnosis is important in order to make a differential between oral lesions including the suspicious ones related with child abuse. Herein we report a 6 year old child who was diagnosed with HPV 13 associated focal epithelial hyperplasia.

Case Presentation Summary

Previously healthy a 6-year old boy was presented with multiple recurrent lesions in the oral cavity since he was 2 years of age. His physical examination was unremarkable other than the lesions in the oral cavity. There were several flat papules ranging 2-5 mm,mainly localized on the inner aspect of both lips and buccal mucosa (Fig-1). There was no history or a suspicious finding regarding sexual abuse and his anogenital examination was normal. In laboratory evaluation, complet blood count, immunoglobulin levels and lymphocyte subset analysis were appropriate for his age. He was negative for human immune deficiency virus (HIV) infection. An excisional biopsy showed epithelial acanthosis and mild subepithelial inflammation. P16 was negative. For HPV detection, Viral DNA extraction from biopsy material was performed and HPV 13 was found positive in the tissue sample.

Learning Points/Discussion

Heck's disease usually shows spontaneous regression in time. Besides, enhancing local oral hygiene, cryotherapy and vitamin A supplementation have also been recommended in the literature. We trained our patient about oral hygiene and decided to follow-up him closely. The aim of this report was to draw attention to HPV related benign oral lesions that can be observed in children.

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Other

Higher dosage of vitamin d3 supplementation does not affect circulating antibody levels to capsular polysaccharides of streptococcus pneumoniae in vaccinated 2-years old children

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Background

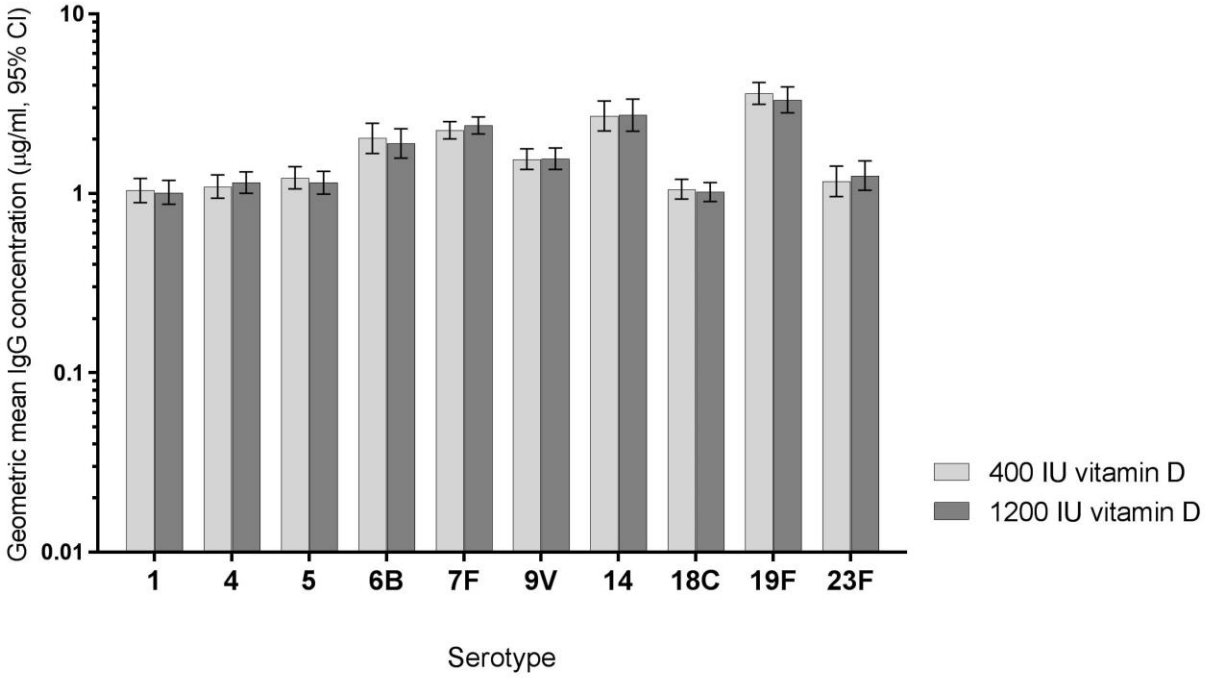
Vitamin D is mainly known for its role in bone homeostasis, but is also a potent modulator of both innate and adaptive immunity. The influence of vitamin D on humoral immunity is, however, unclear. This study aimed to compare humoral immunity to 10-valent pneumococcal conjugate vaccine (PCV10) in 2-years-old children randomized to receive a daily dose of 400 or 1200 IU of vitamin D_3 supplement.

Methods

This was a sub-study of a randomized, double-blind, clinical trial of vitamin D intervention conducted between 2013 and 2016 in Finland. Infants were randomized (1:1) to receive daily vitamin D_3 supplementation of 400 or 1200 IU from age 2 weeks to 24 months. All the participating infants (N=343; 176 in 400, and 167 in 1200 IU –groups, respectively; 50% girls) received PCV10 at 3, 5 and 12 months of age. Serum IgG antibody concentrations to vaccine type capsular polysaccharides were analyzed by multiplexed immunoassay from blood taken at 24 months of age. Serum 25-hydroxyvitamin D (25-(OH) D) -concentration was measured at 12 and 24 months of age by automated immunoassay.

Results

Mean pneumococcal antibody concentrations at 24 months did not differ between 400 and 1200 IU – vitamin D groups for any serotype. At 12 and 24 months of age 99% of children had serum 25(OH)D) – concentrations above 50 nmol/l, which is considered to indicate a sufficient level. Antibody concentrations at 24 months of age did not correlate with serum 25(OH)D) –concentrations (range 47-213 nmol/l) at 12 or 24 months of age.



Conclusions

Higher dosage of supplemental vitamin D_3 does not affect IgG antibody levels to PCV10 at 24 months suggesting that in vitamin D-sufficient children additional vitamin D provides no further benefit for humoral pneumococcal immunity.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.govIdentifier:NCT01723852

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Other

Higher dosage of vitamin d3 supplementation does not affect circulating antibody levels to tetanus, dipthteria and haemophilus influenzae type b in vaccinated 2-years old children

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Background

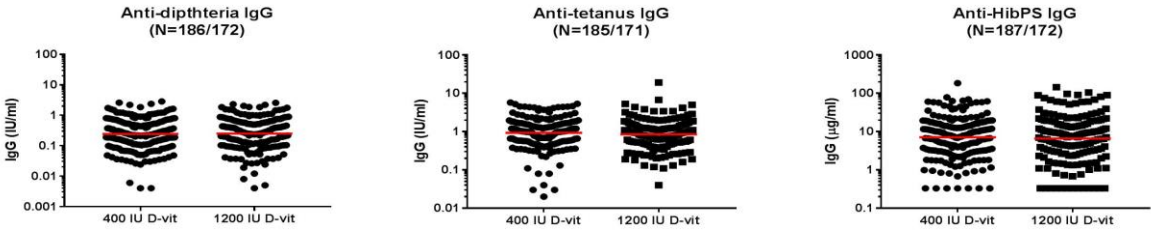
Vitamin D is mainly known for its role in bone homeostasis, but is also a potent modulator of both innate and adaptive immunity. The influence of vitamin D on humoral immunity is, however, unclear. This study aimed to compare humoral immunity to 3 vaccine antigens in 2-years-old children randomized to receive a daily dose of 400 or 1200 IU of vitamin D_3 supplement.

Methods

This was a sub-study of a randomized, double-blind, clinical trial of vitamin D intervention conducted between 2013-2016 in Finland. Infants were randomized (1:1) to receive daily vitamin D_3 supplementation of 400 or 1200 IU from age 2 weeks to 24 months. Infants (N=359; 187 in 400, and 172 in 1200 IU –groups, respectively; 50% girls) received the DTaP-IPV-Hib vaccine at 3, 5 and 12 months of age. Serum IgG antibody concentrations to tetanus and dipthteria toxoids and the capsular polysaccharide (PS) of *Haemophilus Influenza* type b (Hib) were analyzed by multiplexed immunoassay from blood taken at 24 months of age. Serum 25-hydroxyvitamin D (25-(OH) D) -concentration was measured at 12 and 24 months of age by automated immunoassay.

Results

Geometric mean antibody concentrations at 24 months did not differ between 400 and 1200 IU –groups. At 12 and 24 months of age 99% of children had serum 25(OH)D) –concentrations above 50 nmol/l, which is considered to indicate a sufficient level. Antibody concentrations at 24 months of age did not correlate with serum 25(OH)D) –concentrations at 12 or 24 months of age.



Conclusions

Higher dose of vitamin D_3 supplement does not affect mean antibody levels to dipthteria, tetanus and Hib at 24 months suggesting that in vitamin D-sufficient children additional vitamin D provides no further benefit for humoral immunity.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.govIdentifier:NCT01723852

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Other

The therapeutic effect of hydrocolloidal oatmeal extract for molluscum contagiosum; a pilot study

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Background

Molluscum contagiosum (MC) is a common viral infection presented as an umbilicated pale pearly papules. To date, there is no consensus for the optimal treatment of MC. Hydrocolloidal oatmeal has an inhibitory effect on arachidonic acid metabolism which is important for replication of poxviruses, but its therapeutic effect on MC is unknown

Methods

Twenty one pediatric patients with MC were enrolled. The study was scheduled with 8 weeks of active treatment and 4 weeks of follow-up. Patients and their parents were instructed to apply the hydrocolloidal oatmeal extract on the MC lesions 3 times a day. We counted the number of remaining MC lesions and evaluated adverse events at the end of week 1, 4, 8 and 12.

Results

Treatment with hydrocolloidal oatmeal extract decreased the mean MC lesion counts from 15.1 to 10.3 at the end of week 12. The proportion of patients whose lesions > 50% disappeared was 48%. For the patients associated with atopic dermatitis (AD) the mean MC lesion counts was decreased from15.4 to 3.2 at the end of week 12. The proportion of patients with AD whose MC lesions > 50% disappeared was 60%. No serious adverse event was noted, and most parents were satisfied with the treatment outcome as a whole.

Conclusions

Our results suggest that topical application of hydrocolloidal oatmeal extract can be considered an effective and safe option in the treatment of MC, especially associated with AD.

Clinical Trial Registration (Please input N/A if not registered)

n/a

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Other

A rare case of measles-associated hemophagocytic lymphohistiocytosis (hlh) in a 4-month old male infant

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Background

HLH is a potentially fatal hyperinflammatory syndrome, either familial, primarily among infants, or secondary, triggered by autoimmune diseases, malignancies or infections, although rarely associated with measles so far. We describe a case of a 4-month-old male infant with measles-associated HLH.

Case Presentation Summary

On admission, our patient presented with severe respiratory distress due to measles-associated pneumonitis and a possible bacterial coinfection treated with i.v. cefotaxime. On Day 5th, he still had fever, developed liver dysfunction and splenomegaly, while laboratory tests revealed hypofibrinogenemia(134mg%), hyperferritinemia(9243ng/ml) and bone marrow haemophagocytosis. Fulfilling 5/8 criteria for HLH diagnosis (HLH2004 protocol), he was treated with IVIG and dexamethasone. Hypotriglyceridemia and a drop in all blood cells presented later in the course of his illness. He progressively recovered and is currently on the 15th month of the initial therapy with no signs of relapse. Secondary HLH is our most likely diagnosis due to the absence of positive family history, the rapid response to treatment and the fact that natural killer cell activity was normal. However, primary HLH cannot be excluded especially in the context of a possible re-activation.

Learning Points/Discussion

To our knowledge, this is the first case of measles-associated HLH in an infant with no history of familial HLH, consanguineous parents or sudden death of a sibling. Amidst a period of measles outbreaks across Europe due to suboptimum vaccination coverage, increased awareness of a possible measles-related HLH, together with early recognition and initiation of appropriate treatment is crucial to prevent a cytokine storm progressing to multi-organ failure.

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Other

A rare case of severe thrombocytopenia associated with epstein-barr virus infection

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Background

Epstein-Barr virus (EBV) infection generally follows an auto-limited and benign course, but, rarely, moderate to severe hematological, neurological, hepatic, respiratory and/or psychological complications can occur.

Case Presentation Summary

We report a case of an 9-year-old male, previously healthy, with a 2-day history of petechiae and hematuria without fever. On physical examination, petechiae and small ecchymoses, were noticed in soft-palate, cervical region, thorax and lower limbs. Laboratory tests revealed lymphocytosis, severe thrombocytopenia (platelet count 4 $x10^9$/L) and elevation of liver enzymes. A peripheral blood smear showed numerous reactive lymphocytes and confirmed the presence of thrombocytopenia. He was hospitalized and intravenous immunoglobulin (IgIV) was started. Initially, he presented progression of petechiae and ecchymoses, hematuria and recurrent persistent epistaxis, which required chemical cauterization. After administration of two doses of IgIV, there was an increase in platelet counts with resolution of epistaxis, an improvement in hematuria and a regression in petechiae and bruises. An acute EBV infection was serologically confirmed. Serological tests for HIV, HBV, HCV, CMV, Parvovirus B19, Toxoplasmose, HSV 1 and 2 as well as autoimmunity tests were all negative. Complement C3 and C4 fractions and immunoglobulins levels were within normal ranges. After seven days of hospitalization, the patient had clinical improvement with platelet count of 69 $x10^9$/L, was discharged and evaluated as an outpatient.

Learning Points/Discussion

Although a mild-to-moderate thrombocytopenia occurs in 25-50% of uncomplicated EBV infections, severe thrombocytopenia (platelet count <20 $x10^9$/L) is extremely rare and has only been reported sporadically. In our case, the child presented severe thrombocytopenia with persistent hemorrhagic complications, requiring IgIV treatment (more than one perfusion). Thus, the authors state the importance of considering EBV infection in the differential diagnosis of patients with acute thrombocytopenia even with very low counts.

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Other

Challenges in diagnosis and treatment of septic arthritis of the sacroiliac joint - a case report

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Background

Septic arthritis of the sacroiliac joint only represents 1%–2% of septic arthritis in children. This condition remains a diagnostic challenge, but its prompt recognition and treatment are crucial to avoid long-term morbidity.

Case Presentation Summary

A previously healthy 6-year-old boy presented with a 6-day history of fever and progressive hip/lower back pain with irradiation to the left lower limb with noturnal awakenings and 1-day history of limp. Physical examination revealed left hip pain with the left hip joint's passive and active flexion and right positive FABER test. Laboratory evaluation: WBC count 8920 cells/uL (73,9% neutrophils), CRP 71,4 mg/L, CK 79 U/L. Blood culture, oropharyngeal swab PCR for *K. kingae* and *M. tuberculosis* IGRA were negative. Hip and lumbosacral spine radiographs and ultrasonography were normal. MRI revealed a left sacroiliac joint and bone signal alteration, slight joint space enlargement and periarticular soft tissue enhancement, without significant joint effusion or periarticular/intraosseous liquid collections. Based on clinical and MRI findings, septic arthritis of the left sacroiliac joint was diagnosed. In conjunction with Orthopedic Surgery and Interventional Radiology, a conservative approach, without drainage, was established. He was admitted and empiric intravenous flucloxacillin started. After 3 days of therapy, he showed no clinical improvement, so intravenous clindamycin and cefuroxime were associated. After a 10-day course of flucloxacillin and a 21-day course of clindamycin and cefuroxime, he became asymptomatic and was discharged on oral cefuroxime.

Learning Points/Discussion

Joint fluid drainage and antimicrobial therapy are cornerstones of treatment for septic arthritis. Empiric therapy for children ≥3 months should be directed toward *S. aureus* and other gram-positive organisms. Our patient showed no clinical improvement with flucloxacillin alone and, without any drainage procedure or organism isolation, a combined empiric antimicrobial therapy resolved the symptoms.

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Other

Fairytale syndromes by infectious factors

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Background and Objective

There are neurological and psychiatric syndromes, named after fairytales that are possibly related with infectious factors.

Methods

Our effort was to find, by systematic study of the literature, fairytale syndromes caused by infectious factors.

Learning Points Discussion

The syndrome of "Sleeping Beauty" or Kleine Levin Syndrome (KLS) is a rare disorder that appears with a frequency of 1/1,000,000. In 75% of the cases it manifests as a result of a viral infection. The viruses that are probably involved are Epstein Barr Virus, Varricella-Herpes zoster Virus (HSV3), subtypes of Influenza Virus type A and adenoviruses. The syndrome is related to Charles Perraults' famous same-titled fairytale, which was published in 1697, based on the older version of the fairytale by Giambatista Basile. Alice in Wonderland Syndrome (AIWS) or Todd's syndrome (named after psychiatrist John Todd) or liliputian hallucinations is a neurological condition that affects the human perception. It is about a very rare syndrome for which only 169 cases have been formally recorded since 1955. In 50% of cases, the cause of the syndrome is unknown. In the rest of the cases it is usually related to infections that provoke encephalopathy. The most frequent reason is encephalitis caused by Epstein Barr Virus. Other reasons of the syndrome are the H1N1, Coxsackie B, Varricella viruses, as well as Borrelia. Its name is inspired by the homonymous fairytale of Lewis Carrol, which was published in 1865.

ESPID19-0590
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Clinical features of children with deep neck infections: a single center experience

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Background and Aims:

The aim of this study is to determine the clinical characteristics, radiological findings, reasons for delayed diagnosis, treatment details and complications of children with deep neck infections.

Methods:

The study was conducted on 76 patients with deep neck infection between ages 1 month and 18 years in Ankara, Turkey between 2000 and 2016. The data of the patients were evaluated retrospectively. Deep neck infections were divided into 3 subgroups as peritonsillar abscess (PTA), retropharyngeal abscess (RPA) and parapharyngeal abscess (PPA) according to the location of involvement. The demographic information of each patient, the initial symptoms and findings, the history of previous antibiotic usage, the time between the onset of symptoms and diagnosis, laboratory, culture and radiological results, the duration and groups of antibiotics and surgical interventions were examined.

Results:

The mean age of the patients was 7.4±4.4 years. The median ages of patients with PPA, PTA and RFA were 4.7, 10.5 and 5.5 years, respectively. The most common subgroup of infection was PPA (42.1%) followed by PTA (40.7%) and RPA (17.1%). Fever (92.1%), cervical lymphadenopathy (89.5%), sore throat (65.8), swelling on neck (65.8%) and restriction of neck movement (63.1%) were the most common complaints and symptoms. The most frequently isolated microorganism from the throat and abscess was *Streptococcus pyogenes*. 51 patients (67.1%) recovered only with antibiotics and 25 patients (32.9%) underwent abscess drainage with antibiotics. No complication, relapse or death occured.

Conclusions:

As a result of the surgical approach decision due to the response of the antibiotics administered within the first 48-72 hours in the case of PPA and RPA, regardless of the radiological findings, our rate of surgical application is lower than the most other centers.

Systematic Review Registration:

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ESPID19-0365
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Recurrent kawasaki disease complicated by intravenous immunoglobulin-related hemolytic anemia in a child: a case report

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Background

Kawasaki disease (KD) is an acute febrile vasculitis, characterized by prolonged fever, bulbar conjunctivitis, oral changes, polymorphous exanthema, extremity changes, and cervical lymphadenopathy. To treat KD, high-dose intravenous immunoglobulin (IVIG; 2 g/kg as a single infusion) and aspirin are administered to significantly reduce the risk of sequelae such as coronary artery aneurysm (CAA). However, IVIG treatment can produce serious complications, including hypertension, anaphylaxis, thrombosis, renal failure, and Stevens–Johnson syndrome.

Case Presentation Summary

The 6-year-5-month-old girl with Kawasaki disease history on 3-month-old was brought to the emergency department, presenting with a 3-day ongoing fever and a tender right neck soft 3 × 4 cm mass. Laboratory data showed leukocytosis (white blood cell count = 21,240/μL) with elevated C-reactive protein (CRP) level. The echocardiogram indicated a new onset right coronary artery dilatation (diameter = 3.4 mm), which confirmed recurrent KD. During hospital course, she had complication of hemolytic anemia that was observed after the second course of IVIG. The anemia recovered spontaneously without transfusion. The patient was discharged with a low-dose aspirin prescription (4 mg/kg/day) for 6 months. Her coronary dilatation subsided and no aneurysm formation was observed at the 13-month follow-up.

Learning Points/Discussion

Among the hematologic complications of IVIG, hemolytic anemia is a particularly serious side effect. This case of pediatric recurrent KD complicated by hemolytic anemia that became refractory during the second episode, but was salvaged through repeated dosing with IVIG. For patients who possess the risk factors of refractory KD, additional consideration is critical; in these cases, we suggest a baseline study of hemoglobin levels before administering IVIG and close monitoring of hemoglobin levels after completing the IVIG dosage, especially if repeated IVIG infusion is to be performed.

ESPID19-0361
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Actinomycosis in singapore children- a 15-year retrospective review

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Background

Actinomycosis is a rare subacute-to-chronic infection caused by filamentous Gram positive bacteria from the Actinomyceteceae family. This study aims to describe the epidemiology of Actinomycosis in children.

Case Presentation Summary

A retrospective medical review of all children admitted with Actinomycosis to KK Women's and Children's Hospital, Singapore, from 1 Jan 2004 to 1 Jan 2019, identified from the inpatient registry of the Paediatric Infectious Disease Service. There were 7 patients in the study, mostly female (4, 57.1%). Median age of first presentation was 9.8 (range 4.7 to 15.7) years. Sites of Actinomycosis included orocervicofacial (5, 71.4%), pulmonary (1, 14.3%), and cervical spine (1, 14.3%). Risk factors included dental infection (4, 57.1%), of which 1 patient also had a pyriform sinus tract, recent dental procedure (1, 14.3%), and cholesteatoma (1, 14.3%). Five cases had histopathological-confirmed diagnosis, while 3 were microbiologically confirmed-*Actinomyces odontolyticus* (2, 66.7%) and *Actinomyces israelii* (1, 33.3%). Six cases had concomitant organisms including anaerobes such as *Fusobacterium necrophorum*, *Fusobacterium nucleatum*, *Prevotella oris*, *Bacteroides* species, *Propionibacterium acnes*, Gram-positive organisms such as *Streptococcus milleri*, *Streptococcus constellatus* and Gram-negative organisms such as *Pseudomonas aeruginosa*, and *Aggregatibacter actinomycetemcomitans*. All patients received Ampicillin/Augmentin or other beta-lactams, for a median of 7.2 (range 1.5 to 8.8) months. Six patients underwent surgical procedures, such as incisional drainage and excision biopsy. Complications included recurrent neck abscesses (1, 14.3%), and intracranial extension (1, 14.3%). All patients had complete resolution after treatment.

Learning Points/Discussion

Actinomycosis in children is rare, and can occur in immunocompetent patients, with risk factors that include dental caries, recent dental procedures, presence of pyriform sinus tract and cholesteatoma. The prognosis is excellent, after surgical intervention and appropriate antimicrobial therapy.

ESPID19-0328
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Could consider spain, as an endemic country for strongyloidiasis?

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Background

Strongyloides stercoralis, is intestinal parasitic nematode endemic in tropical and subtropical areas. Strongyloidiasis frequently can be asymptomatic but can progress to potentially fatal hyperinfection, especially among immunocompromised patients. Recently, autochthonous cases of Strongyloidiasis has been describing among adult population in Spanish mediterranean coast. Objective: to describe characteristics of children <18 years diagnosed with Strongyloidiasis who were born in Spain and no history of previous travel abroad, in Spanish Tropical Pathology Reference unit.

Case Presentation Summary

Five children were included, mean age 7 years (rank 5-10), 3 male and 2 female. All spent summer holidays in Spanish Mediterranean coast. Medical background: bronchial hyperreactivity 2/5, dermatitis 1/5, one case of Noonan syndrome and one recipient of multivisceral transplant. At diagnosis, 3/5 referred skin disorders, 1/5 gastrointestinal symptoms, 1/5 asymptomatic. Four patients showed moderate eosinophilia (mean:1.678mm3(rank 1720-2400)). All showed positive serology for *S. stercoralis* and stool-test and serologies for others parasites negative. Initially four patients received two cycles of ivermectin, and the remaining one albendazole. Clinical evolution was satisfactory in three cases, with normalization of eosinophils and serology. Patient with Noonan Syndrome required four cycles. Patient with multivisceral transplant required 5cycles of combined treatment with ivermectin and albendazole without resolution of symptoms, was diagnosed with chronic Strongyloidiasis and started on prophylaxis with ivermectin.

Learning Points/Discussion

Autochthonous acquisition of *Strongyloides stercoralis* infection is possible among children spending holidays in the east cost of Spain. Eradication of this parasite in the immunocompromised patient is a challenge, therefore screening should be included in all programs before immunosuppressive therapy. Due to the presence of *Strongyloides* on Mediterranean coast of Spain and the potentially severity of the pathology, we have to always consider Strongyloidiasis wthin the possible differential diagnosis of parasitosis in Spain.

ESPID19-0322
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Analysis of the etiology of fever in infants aged ≤90 days using multiplex real-time pcr and 16s rrna gene amplicon sequencing

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Background and Aims:

Fever is frequently the only sign of infection in young infants, complicating the clinical identification of the underlying cause. The aim of this study was to document the etiology of fever in infants aged ≤90 days.

Methods:

The present study retrospectively analyzed the nasopharyngeal fluid, blood plasma, and laboratory findings of febrile young infants (temperature ≥ 38℃) at three emergency departments in Japan from June 2017 to October 2018. In total, 53 infants (median age, 47 days; 56.6% boys) were enrolled. Pathogen diagnosis was performed by multiplex real-time PCR using nasopharyngeal fluid and sequencing analyses of 16S ribosomal RNA gene amplicons in blood.

Results:

One or more viruses were detected in 39 (73.6%) cases. Rhinovirus was most commonly observed [14 (26.4%)] followed by enterovirus [10 (18.9%)], coronavirus [5 (9.4%)], and respiratory syncytial virus [4 (7.5%)]. Eighteen (34.0%) cases were identified as having severe bacterial infections with urinary tract infections (UTIs). Among these, viruses were detected in 11 (61.1%) cases. Moreover, 5 (45.5%) of the 11 cases exhibited upper respiratory infection symptoms. Notably, only one case was positive for *Streptococcus pneumoniae* based on the blood sequencing analyses, and the case patient was co-infected with respiratory syncytial virus. White blood cell and neutrophil counts were significantly higher in the UTI cases than in the non-UTI cases (Student's *t*-test; $p < 0.05$).

Conclusions:

Because the etiology of fever in young infants cannot be determined based only on symptoms, it may be necessary for clinicians to actively verify laboratory findings.

Systematic Review Registration:

Case series study

ESPID19-0291
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Varicella hospitalizations, and methicillin-resistant staphylococcus aureus as leading bacterial complication, in children from a mexican hospital on the mexico –usa border: seven years active surveillance

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Background and Aims:

In Mexico, vaccination against Varicella is not part of the National Immunization Program. A few Mexican studies have shown that is highly prevalent, and vaccination cost-effective. This is the first prospective study of children hospitalized with Varicella in Mexico.The Tijuana, Mexico – San Diego, USA border is the highest transited globally.

Methods:

From January-2012 to December-2018, active surveillance for children < 16 years of age admitted with Varicella at the Tijuana, General Hospital, was performed. Diagnosis of Varicella was based on the CDC-1999-clinical case definition. All captured data were descriptively analyzed.

Results:

A total of 40 patients were enrolled. Median age at admission was 20.5 months (1-190), with 29 (72.5%) < 5 years. All but 4 (10%) were previously healthy children. None were vaccinated against Varicella. Clinical presentations were: Cellulitis (20=50%), from which 15 progressed to abscess formation, and 10 needed surgical drainage (Methicillin-Resistant *S. aureus* (MRSA) isolated in 7, *S. pyogenes* in 3); Encephalitis/Meningitis (13=32.5%), among which 8 presented seizures; Sepsis (10=25%), blood isolation was confirmed in seven (3 MRSA, 2 *S. pyogenes,* 1 *S. pneumoniae,* 1 *E. coli*); Hemorragic Varicella (5=12.5%); Anicteric hepatitis (4=10%); Pneumonia with Pleural Empyema (1=2.5%), caused by *S. pneumoniae* serotype 18C. All but one received intravenous (IV) Acyclovir, and 29 (72.5%) IV Antibiotics and other medications. Median hospitalization days was 8 (1-62), and two patients died (5%, both of septic shock). Following three months of discharge, 5 patients had sequelae (3 neurological and 2 with severe skin scars).

Conclusions:

Hospitalizations by Varicella in our Hospital are not uncommon, and associated with high morbidity, hospitalization days and treatment, with relatively low mortality. Our data, in accordance to other Mexican National publications, strongly suggest Universal Vaccination.

Systematic Review Registration:

N/A

ESPID19-0224
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

The roles of oxidative stress in streptococcus pyogenes infection

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Background

Streptococcus pyogenes (Group A *Streptococcus*, GAS) is an important human pathogen that leads to life-threatening invasive diseases. Oxygen-derived free radicals, collectively termed reactive oxygen species (ROS), play important roles in host defenses. The key producers of ROS in cells are the family of NADPH oxidases (NOX), which could regulate host defense, cellular signaling and gene expression. However, excess ROS are lethal to cells. In this study, correlation between oxidative stress and severity of GAS disease and the protective role of antioxidant against severe GAS infections were explored.

Methods

The population consisted of patients who were treated for GAS infection from National Cheng Kung University Hospital. Patients were subdivided into those with invasive or noninvasive infections. Human microvascular endothelial cells (HMEC-1) were used as GAS infection-induced oxidative stress and anti-oxidant treatments in *vitro* study

Results

Clinical results showed that serum levels of thioredxoin (Trx) in GAS patients including non-invasive and invasive symptoms were significantly higher than the healthy control. Tissue sections from GAS infected-patients with necrotizing fasciitis revealed that cyclooxygenase-2 (COX-2) expressed in vascular. We further studied the roles of GAS infection-induced oxidative stress in *vitro*, GAS infection effectively caused abundant ROS production followed by NF-kB activation and increased expression of COX-2. Treatments with apocynin (APO), dextromethorphan (DM) and recombinant Trx notably attenuated ROS production in GAS-infected cells and inhibited NF-kB activation. The expression of endothelial activation marker and iNOS decreased after these anti-oxidant treatments. Recombinant Trx also attenuated the expression of COX-2 in GAS infected-cells.

Conclusions

Oxidative stress was associated with severity of GAS disease. NOX inhibitor, DM and Trx could inhibit the oxidative stress in GAS-infected cells and reduce the inflammation to serve as anti-inflammatory modulators.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0202
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Kawasaki disease associated with scarlet fever (group a streptococcal infection).

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Background

Early recognition and distinction of Kawasaki disease (KD) from other febrile infectious diseases is one of the biggest challenges in pediatric clinics. Herein we report a incomplete KD associated with Scarlet Fever.

Case Presentation Summary

A 4 years old boy was admitted to our hospital with a 3 day history of fever and rash. His physical examination showed that a irritable acutely ill boy with a high fever and scarlatiniform rash that was noted on the trunk, spreading to involve the limbs and face, and stawberry tongue. His initial laboratory test results was a leukocyte count of 12×10^9/L, hemoglobin level of 11.7 g/dL, and a platelet count of 385 000/ mL. His C-reactive protein was 400 mg/L; erythrocyte sedimantation rate 103 mm/hr, procalcitonin level 3.8 ng/mL, AST 111 IU/L, ALT 217 IU/L. His rapid throat swap assay was positive for *Streptococcus pyogenes* antigen and later his initial throat culture revealed Group A beta-hemolytic *Streptococcus pyogenes*. His fever was continued even cefotaxime treatment. His abdominal ultasound showed a hydropic gallbladder, his echocardiography revealed a normal ejection fraction, but perivascular echo brightness of the left coranary coronary artery with a 2.3 mm diameter. Given that his clinical symptoms did not fulfill the diagnostic criteria for classic KD, therefore, intravenous immunoglobulin (IVIG, 2 g/kg/dose), and oral aspirin (50 mg/kg/day) were administered on the 7h day of illness. His temperature returned to normal soon after the IVIG therapy was completed. During the his follow-up his platelet count increased to 987000/mL at 2 weeks of diagnosis of KD.

Learning Points/Discussion

It may be difficult to distinguish streptococcal infection and Kawasaki disease. It is possible that some cases of Kawasaki disease are precipitated by streptococcal infection.

ESPID19-0168
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Incidence and significance of klebsiella oxytoca infections in a japanese pediatric hospital

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Background

Klebsiella oxytoca is Gram negative bacillus which belongs to Enterobacteriaceae, and is known as a commensal of human intestinal tract and other sites. It may cause, however, severe infections such as pyelonephritis or bacteremia. There are scarce data about its clinical epidemiology in pediatric populations.

Case Presentation Summary

We collected the culture data and reviewed medical charts of both inpatients and outpatients from whom Klebsiella oxytoca were isolated in Nagano Children's Hospital, from January 2013 to November 2018.

During the study period, Klebsiella oxytoca were isolated from 138 patients, and 108 (78.3%) of them were colonization. Among colonized patients, 56(40.6%) were from neonatal ward. The number of the patients with Klebsiella oxytoca isolation was 13-33 per year (mean 23). Although there had been sporadic outbreaks in specific wards, there found no significant fluctuations of total number of the patients with Klebsiella oxytoca.

There had been 53 clinical episodes of Klebsiella oxytoca infections: 34 urinary tract infections, 9 blood stream infections, 7 respiratory tract infections (ventilator-associated pneumonia), 1 hip abscess, 1 appendicitis and 1 surgical site infection. There was no case of antibiotic-related hemorrhagic colitis. In most of the cases, the prognoses of infections were excellent.

The proportion of ESBL producer was 10-20% of all Klebsiella oxytoca isolates, and there had been no apparent increase during the study period.

Learning Points/Discussion

Klebsiella oxytoca is one of commonest pathogen in pediatric tertiary care settings, and it may cause severe infections. Although most of the Klebsiella oxytoca infections seem to have good prognoses, more attention should be necessary to this pathogen.

ESPID19-0164
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Incomplete kawasaki disease associated with entamoeba histolytica gastroenteritis

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Background

Kawasaki disease (KD) is an acute febrile multisystem vasculitis with unknown etiology. Previously many reports presented an association of KD and viral and bacterial infections but herein we report an incomplete KD associated with *Entamoeba histolytica* infection that was not reported previously.

Case Presentation Summary

A previously well 6 months old boy was addmitted to our clinic because of fever for 4 days, his physical examination revealed bilateral conjunctival hyperemia and redness of BCG vaccine scar. His initial laboratory test results was a leukocyte count of 11×10^9/L, hemoglobin level of 11.7 g/dL, and a platelet count of 328 000/ mm^3. The patient's erythrocyte sedimentation rate 34 mm/h, his C-reactive protein was 49 mg/L; aspartate aminotransferase of 25 IU/L, alanine aminotransferase of 8 IU/L. His urinalysis showed leukocyturia without any bacteria. Meanwhile he developed diarrhea, and his stool examination revealed few white blood cells and red blood cells on direct microscopy and negative for adenovirus antigen, norovirus antigen and rotavirus antigens but positive for *Entamoebea histolytica* antigen. His echocardiography revealed a normal ejection fraction, but perivascular echo brightness of the left coranary coronary artery with a 3 mm diameter. Given that his clinical symptoms did not fulfill the diagnostic criteria for classic KD, he was diagnosed with an incomplete KD because of prolonged fever (7 days), bilateral conjunctival hyperemia, BCG scar redness, and echocardiography findings. Therefore, intravenous immunoglobulin (IVIG, 2 g/kg/dose), and oral aspirin (50 mg/kg/day) were administered on the 7h day of illness. His temperature returned to normal soon after the IVIG therapy was completed.

Learning Points/Discussion

Gastrointestinal symptoms and findings in children with prolonged fever should be evaluated carefully in order to keeping a high index of suspicion of KD.

ESPID19-0115
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Kawasaki disease and concomitant adenovirus infection

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Background

Kawasaki Disease (KD) is the leading cause of acquired heart disease in children and hence, requires prompt recognition and treatment. KD shares clinical features with many viral infections, including Adenovirus infections, which share the most similar clinical and laboratory characteristics with KD. As shown in recent studies, KD and Adenovirus infection can co-exist in the same patient, making the diagnosis clinically challenging. However, little has been described of the clinical characteristics and management of patients with both diseases.

Case Presentation Summary

Methods

From 1st June 2013 to 11th March 2018, 1240 patients with Adenovirus infection and 791 with KD were admitted to our institution. Cases with KD and concomitant Adenovirus infection were identified from the inpatient registry of the Paediatrics Infectious Disease Service. An Adenovirus infection is confirmed in patients with a positive nasopharyngeal aspirate for Adenovirus on immunofluorescence or polymerase chain reaction. Patient demographics, clinical characteristics, treatment and outcomes were extracted from electronic medical records and case notes. Laboratory indices between patients with coronary artery dilatation and those without were compared with the Mann-Whitney U test.

Results

There were 16 cases identified, with a median age of 27 months (range: 7 to 73 months). All patients were treated with intravenous immunoglobulin (IVIg). One patient had a very high Adenovirus viral load, and received 2 doses of IVIg as well as intravenous cidofivir, with good response to the combined therapy. Analysis of laboratory characteristics showed both highest white blood cell counts and highest absolute neutrophil counts were predictors of coronary artery dilatation.

Learning Points/Discussion

Conclusions

It is important to manage both KD and Adenovirus infections when they co-exist in patients. Further studies would be beneficial in exploring better management of such patients.

ESPID19-0096
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Predominant role of haemophilus influenzae in pediatric conjunctivitis-otitis media syndrome

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Background and Aims:

Acute purulent conjunctivitis and acute otitis media were first denominated as conjunctivitis-otitis media syndrome in 1982. According to previous studies, *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* are predominant pathogens. The purpose of this study is to investigate etiologies and clinical manifestations of conjunctivitis-otitis media syndrome in children and to assess the epidemiologic feature in modern times.

Methods:

Children younger than 18 years old with a diagnosis of conjunctivitis-otitis media syndrome during 2009 and 2018 were included. Biological data, clinical manifestations, bacterial culture results, and treatment were reviewed retrospectively. Student t test or Mann-Whitney test was used to examine differences among continuous variables. Chi-square test was used for category variables. All statistical analysis via SPSS version 22 is two-tailed and $p < 0.05$ is considered statistically significant.

Results:

A total of 77 children were recruited. The mean age was 33.7 months old and 61% patients were younger than three years old. The male-to-female ratio was 1.85. 45.5% children had bilateral conjunctivitis and otitis media. The three most common pathogens were *Haemophilus influenzae* (69.7%), *Moraxella catarrhalis* (19.7%) and *Staphylococcus aureus* (7.6%). Spring and summer were the prevalent circulation seasons. Clusters in household was observed in 31% of patients. Only two children needed hospitalization. Amoxicillin-clavulanate resistance rate of *Haemophilus influenza*e increased gradually. Girls were prone to have a higher resistant rate ($p < 0.05$).

Conclusions:

Conjunctivitis-otitis media syndrome is a unique infectious disease entity in children. The presence of this syndrome give hints to offending pathogens and such an information may be important for the choice of empiric antibiotics.

Systematic Review Registration:

N/A

ESPID19-0071
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Mucocutaneous leishmaniasis in slovenia: a case report

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Background

Only sporadic imported cases of leishmaniasis are reported in Slovenia. This is the first reported case of mucocutaneous leishmaniasis in our country.

Leishmaniasis is caused by *Leishmania* spp., flagellate protozoa transmitted by the bite of an infected female sandfly. Reservoirs are represented by a wide range of mammals, the main ones are dogs. Human leishmaniasis can be divided into three disease manifestations: most common cutaneous, mucocutaneous and visceral leishmaniasis, it is found in parts of the tropics, subtropics, Middle East and Mediterranean area.

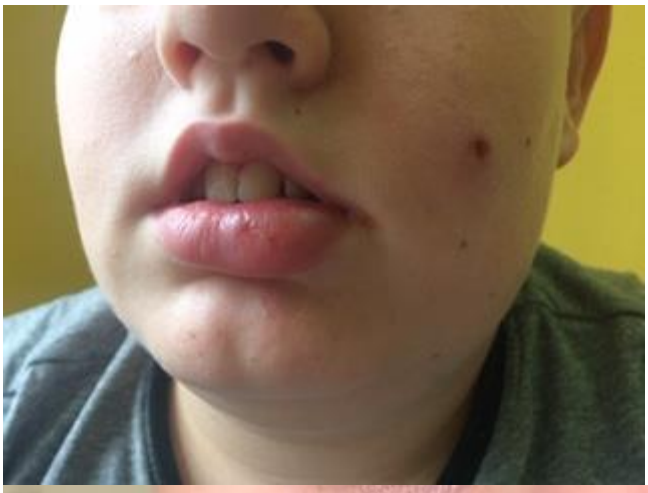
Case Presentation Summary

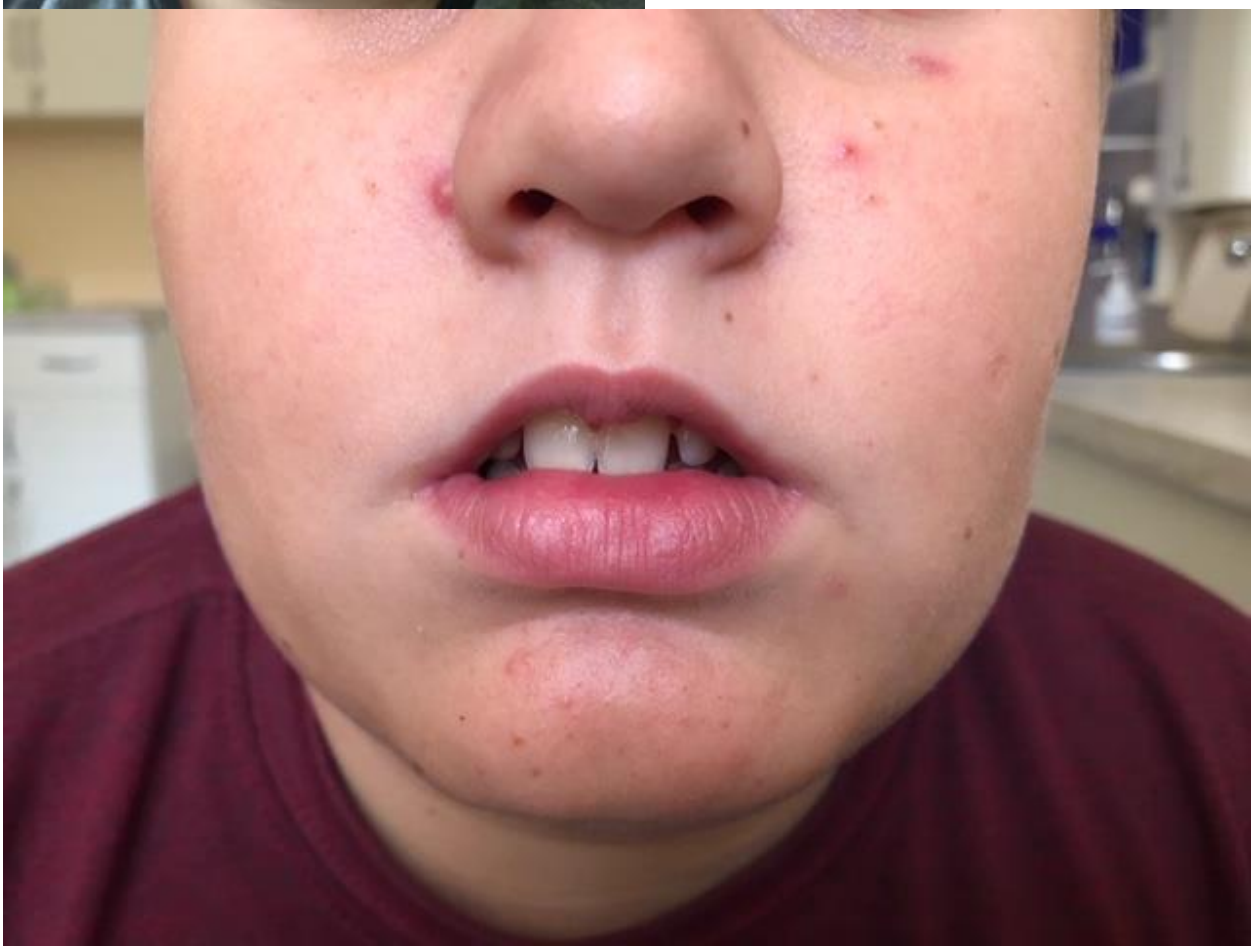
A 12-year-old boy presented in February 2018 with one month history of papule on the left cheek that progressed into ulceration and persistent swelling of the left side of the lower lip (Figure 1).

On physical examination solitary ulcer of 5 millimeter in diameter on the left cheek and edematous lower lip with firm consistency were observed.

Because of unclear clinical appearance biopsy of the lip was performed. Histopathological examination showed granulomatous inflammation and in some macrophages amastigotes-like structures were seen. Real-time PCR identified the parasite as *Leishmania spp.* Presence of anti-Leishmania spp. antibodies was confirmed with western blot.

The boy was on vacation on the Croatia coast in the summer 2017, where leishmaniasis is (hypo)endemic. The patient was treated with liposomal amphotericin B, total dose of 20 mg/kg. Both lesions completly resolved after 5 months of therapy (Figure 2).





Learning Points/Discussion

Lip leishmaniasis lesions can be challenging to diagnose since lip involvement is very rare and can be confused with other diseases. This unusual clinical presentation of leishmaniasis should be considered in differential diagnosis of macrocheilitis also in non-endemic regions, such as Slovenia, due to increasing rate of traveling and global warming.

ESPID19-0854
E-Poster Viewing - May 7-10 - E-Poster Hours

Other

Arthritis secondary to invasive meningococcal disease: a case series

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Background

Arthritis 2nd to invasive meningococcal disease (IMD) is a known complication of immune complex phenomena. Compared to septic arthritis, clinical onset of IMD is delayed and synovial fluid is sterile. We present 6 children with immune-mediated meningococcal arthritis from our hospital since 2010.

Case Presentation Summary

Between 2010 and 2018, 6 children (5/6 girls), mean age 1.5 years old (6mo-9y) with immune-mediated arthritis were identified. Basic immunology work-up including complement studies was normal. Diagnosis was sepsis (n=3), meningitis (n=2) and bacteremia (n=1). In 3/6 children fever reoccurred with joint symptoms; arthritis manifested 7.8 (4-17) days after the onset of the IMD. One joint was affected in 4/6 patients, 2/6 had multiple joints involved and included wrist (n=2), hip (n=2), ankle (n=3) and fingers (n=1).

No other immune-mediated manifestation was observed. *N. meningitidis* isolated serogroups were B (n=4), Y (n=1) and not determined (n=1). All children correctly received either MenC or Men ACWY according to the Spanish vaccine program

Arthrocentesis was performed in 4/6 patients with no isolation of *N. meningitidis*. Synovial fluid characteristics were similar in all the patients (table). All patients received antibiotics and 4/6 adjuvant

corticosteroid therapy. One patient suffered from osteonecrosis as sequelae.

Summary of clinical and laboratory parameters of patients with arthritis 2nd to IMD (n=6)

	Mean	Range
Age (years)	2.8	6 mo - 9 y
Days until joint symptoms	7.8	4 - 17
Fever (days)	4.5	1-8
SERUM		
CRP max. (mg/l)	283.7	131.8 - 347.1
Leucocytes max (cell/mcl)	29875	9480 - 70190
SYNOVIAL FLUID		
Cells/mm3	90852.5	45260 - 135440
Protein (g/l)	57.95	48.2 - 64.2
Glucose (g/l)	0.16	0.01 - 0.6
Corticosteroids treatment (days)	7	0 - 20
Antibiotic treatment (days)	14.1	7 - 25

Learning Points/Discussion

Arthritis 2nd to meningococcal disease is a complication occurring days after initial clinical presentation and is characterized by fever recurrence and increase of inflammatory markers. Synovial fluids are typically sterile and management is based on NSAIDs and/or corticosteroids.
Awareness can potentially reduce unnecessary procedures and therapies.

ESPID19-1068
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Association between the epidemiology of acute childhood myositis and type of influenza in the community during a 10-year period (2007-2017)

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[3]"Aghia Sophia" Children's Hospital, 3. Department of Clinical Biochemistry, Athens, Greece
[4]"Aghia Sophia" Children's Hospital, 3. Department of Clinical Biochemistry, Athens, Greece

Background and Aims:

Acute Childhood Myositis (ACM) is a clinical syndrome usually accompanying acute viral infections, mostly influenza, which occurs both sporadically and epidemically. Because ACM is usually para-infectious or post-infectious, it is not always feasible to detect the aetiologic viral agent. The aim of the study was to evaluate the association of the epidemiology of ACM in a tertiary pediatric hospital with the type of influenza in the community.

Methods:

A retrospective analysis of children's records who were hospitalized at the largest Greek tertiary Children's Hospital with the diagnosis of ACM during the years 2007-2017 was performed. Surveillance data regarding activity and type of influenza were retrieved from the Hellenic Center for Disease Control & Prevention (HCDCP) data to define periods of different type influenza activity.

Results:

During the study period, 726 children were hospitalized due to ACM which accounts for 13,9 cases/10000 patient-days. The highest incidence rate of ACM was 36 cases/10000 patient-days in 2017, followed by 21 cases/10000 patient-days in 2016 while the lowest incidence rate was estimated in 2013 with 5 cases/10000 patient-days. From January-March were recorded 450/726 (61.8%) of ACM cases. According to the surveillance data from HCDCP the highest percentage of Influenza type A cases was 99.98% (H1N1:77.75%) during the 2009-2010 season and of Influenza B cases was 71.2% during the 2017-2018 season. A positive, although non-statistically significant association was found with the ACM cases and the presence of influenza B in the community (Spearman's rho: 0.552, *P*-value: 0.09).

Conclusions:

Although there is variation in the incidence of ACM each year, the maximum incidence is detected during the influenza activity season, with limited effect of the influenza type that is circulating in the community.

Systematic Review Registration:

ESPID19-0955
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Vaccination status of patients with chronic renal disease and their close contacts

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Background and Aims:

Chronic kidney disease (CKD) and renal transplant patients are particularly vulnerable to vaccine-preventable infections. Immunization of these vulnerable populations as well as of close contacts can substantially contribute to their protection. We evaluated the immunization status of CKD/renal transplant patients and their close contacts.

Methods:

Immunization status of haemodialysed/renal transplant adult patients and children with CKD and of their household contacts was prospectively investigated in three hospitals in Crete, Greece through interview and vaccination records.

Results:

The study included 285 patients (213 dialysed adults, 45 adult renal transplants and 20 children with CKD) and 317 contacts (213 adults, 104 children). Dialysed adults were well vaccinated for HepB (98.6%) but less for other recommended vaccines: influenza 79.5%, pneumococcal 58.6%, TdaP 35%, herpes zoster 29.6% and measles 29.4% (92.2% reported natural infection). Adult transplant patients were the least adequately vaccinated (influenza 31.1%, pneumococcal 13.3%, TdaP 2%). The paediatric CKD patients were fully vaccinated for HepB and DTap (100%) and 85% for hepatitis A but less for other recommended vaccines (influenza 35%, pneumococcal 59%, TdaP 20%, varicella 75%, measles 70%). High vaccination rates were recorded for children contacts for recommended vaccines, except for influenza (7.5%) and Tdap (63.4%). However, the rates of adult contacts were suboptimal for all recommended vaccines (influenza 24.9%, pneumococcal 10.3%, TdaP 0%).

Conclusions:

Vaccination coverage among CKD/transplant patients is suboptimal. Targeted cocooning policies could motivate vaccination among families, protect these vulnerable groups and address the weaning of vaccination adherence after childhood.

Acknowledgements: Departments of Nephrology and Renal Dialysis Units of Heraklion University Hospital, Rethymnon General Hospital, Chania General Hospital

Systematic Review Registration:

N/A

ESPID19-0881
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Invasive pneumococcal disease before and after the pneumococcal vaccination pcv13 in a paediatric tertiary hospital in greece (2007-2017)

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Background and Aims:

Invasive pneumococcal disease (IPD) is a major cause of morbidity and mortality among children. Pneumococcal vaccination was introduced in the NIP in 2006 (PCV7) and 2011 (PCV13) in Greece. Already since 2007 more than 80% of children <5 years were vaccinated. The epidemiology, serotyping and antimicrobial resistance of IPD was studied for the period 2007-2017.

Methods:

All IPD cases hospitalized in our hospital during the study period were analyzed retrospectively, using the medical archives. Clinical specimen cultures and susceptibility testing were performed with standard methods. For blood cultures BACTEC 9240 system (BD) was used. MICs for *Spn* were determined by Etest®. Pneumococcal serotyping was performed on 88 available strains with latex agglutination test and Quellung reaction test. Risk ratios (RR) with 95% confidence interval were calculated to evaluate changes before and after PCV13 implementation.

Results:

104 cases of IPD were recorded (56% boys, aged from 1m to 13y, median 2y). IPD was more common during October to March (69%). Of these cases, 64 (61.5%) had a focal infection (pneumonia 42 [66%], meningitis 12 [19%], orbital cellulitis 4 [6.2%]) and 40 (38.5%) occult bacteraemia. Two deaths occurred due to meningitis. A decrease in the incidence of IPD was observed by 64% (RR=0.36, 95%CI=0.24-0.53, p=0.001) during the post PCV13 period. Nineteen different serotypes were found, with 19A (26%) and 7F (24%) being the most common (figure). Non-susceptible *Spn* isolates were for penicillin: 16.6% for meningitis strains (MIC_{PEN}≥0.06mg/dl), 0% for non-meningitis; cefotaxime: none for meningitis, 3% for non-meningitis (MIC_{CTX}>1 mg/l). Resistance to clindamycin and erythromycin was 17.3% and 27%.

Conclusions:

IPD incidence was significantly reduced among children in the post PCV-13 period. Third-generation cephalosporins remain the treatment of choice.

Systematic Review Registration:

none

ESPID19-0824
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Analyzing two groups of children with type a and type b influenza infection from clinical and paraclinical point of view

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[2]*Faculty of Medicine - Transilvania University, Paediatrics, Brasov, Romania*

Background and Aims:

Flu vaccination coverage for 2017-2018 season in Romania was under 20%.There are no published data for the pediatric population. This study determines correlations between socio-demographic statuses, flu associated symptoms, lab results, for children with positive rapid test for *Influenza* typeA or B in a ER department of a country where Flu vaccination is not mandatory.

Methods:

Observational-retrospective study on 479 Flu positive children detected at the ER department between January-April and November-December 2018.For the first period we enrolled 231 patients while for the second part 248.

Results:

Strains distribution was different. For the first months of the year-57% presented with *Influenza* typeB while 99% of the patients from the last moths of the year had *Influenza* typeA. Boys were predominant in both groups (56% vs 57%), while the average age was 64 months for the first part of the year while 58 months for the rest. 40% of the children came from rural areas in first group while 37% in the second, with no significant statistical differences between weight for the 2 studied groups. In the first group 15% had already started an antibiotic at home, 7 children had a CRP above 1 mg/dL compared with 11 children in the second group. Normal white blood cells value was predominant in both groups (67% and 57%), leucocitosis(7% vs13%), leucopenia more predominant among *Influenza* typeA(5%>2%).The average days of symptoms before the ER consultation was similar 2 vs 3 days. Overall more than 50% of the patients had URTI associated symptoms, while fever was mentioned in every case.

Conclusions:

1.There are more cases of Influenza between November-December than January-April with different strain distributions.
2.In Romania, the irrational use of antibiotics remains high among the pediatric population

Systematic Review Registration:

N/A

ESPID19-0609
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Human herpes virus 6 severe infections in immunocompetent pediatric patients: case series and review of the literature

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Background and Objective

Human Herpes Virus 6 (HHV-6) is the causative agent of exanthema subitum, a benign and self-limiting febrile disease of infancy. Infections in immunocompromised hosts can be severe. Less frequently, complications can occur also in immunocompetent (IC) children, with cerebral, hepatic, cardiac and hematological involvement. The rate of sequelae and the best therapeutic approach in these patients is not clearly reported in the literature.

Methods

A review of the Literature was conducted to analyze the current knowledge about therapeutic management of HHV-6 severe infections in IC children. An observational retrospective study on IC children with a CNS infection caused by HHV6 admitted to the “Bambino Gesù” Children’s Hospital (OPBG) in Rome from June 2007 to July 2018 was also conducted in order to compare data from the literature with the strategies adopted in our hospital.

Learning Points Discussion

The review of the literature identified 88 papers,reporting 339 pediatric IC patients with HHV6 severe infections.The main complication was CNS involvement: 63% of patients had seizures; among them, 23% reported permanent neurological damage. Antiviral therapy, intravenous immunoglobulins, steroids or combinations of them were the most common approaches. None of these therapies appeared to be significantly associated with prevention of sequelae. These data were confirmed by reviewing the 28 IC children with a CNS infection caused by HHV6 admitted to OPBG in the study period. The rate of sequelae was 25%. No correlation was found between administered therapy and outcome.
Learning points:
1) Therapeutic management of HHV-6 severe infection is not clear
2) Currently used therapies don’t seem to impact on the outcome
3) Further studies are needed to identify new markers involved into the pathogenesis of the HHV6 infection that could be used as potential therapeutic targets in the future.

ESPID19-0399
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

B part of it study –implementation of a large cluster randomised controlled trial using a school immunisation program

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Background

Carriage studies are logistically challenging due to the large sample size required. We describe the processes of conducting a cluster randomised controlled trial in high school students to assess the impact of a meningococcal B vaccine on carriage of *Neisseria meningitidis* in adolescents (B Part of It study).

Methods

In South Australia (SA) adolescent vaccination is managed through the State health department and delivered though a School Immunisation Program (SIP). The SIP is delivered by a variety of service providers including local councils, general practice, community health services and private health agencies. The study utilised the SIP protocols and engaged the community to participate in the B Part of It study in 2017. A description of engagement and collaboration with key stakeholders and logistical challenges of implementing the study will be provided.

Results

Of the 253 high schools in SA, 238 (94%) agreed to participate in the study, representing a cohort of approximately 58,900 eligible Year 10,11 and 12 students (15-17 years of age). The study trained over 250 personnel across metropolitan, regional and remote communities. In 2017, over 37,330 students consented to the study (63% uptake) resulting in 34,489 students (58%) participating and 34,467 oropharyngeal swabs being collected over a 3 month period (April-June 2017). A further 20,886 followup 12 month swabs (2018) were collected during the same period. Over 58,634 doses of Bexsero were administered (92% receiving 2 doses) in 2017-2018 by nurses conducting school visits; 79% (10026/12746) of students in 2017 received the vaccines with an interval of 45-86 days between doses.

Conclusions

Intersectoral collaboration and utilisation of the existing systems resulted in successful achievement of the large sample size required to meet the primary objectives of the study.

Clinical Trial Registration (Please input N/A if not registered)

NCT03089086

ESPID19-0367
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiology of cmv infection in pediatric residents

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[3]Doce de Octubre University Hospital, Infectious Diseases, Madrid, Spain
[4]La Paz University Hospital, Gynecology and Obstetrics, Madrid, Spain

Background and Aims:

CMV excretion is common among toddlers and preschoolers. Pediatric residents (R) could be at elevated occupational risk of acquiring this infection. The aims of this study are: to describe serological status, to analyze risk factors for CMV infection, and to evaluate knowlegde of congenital CMV among pediatric residents.

Methods:

Online anonymous survey among R from 3 different hospitals in Madrid, Spain (La Paz, Doce de Octubre, Severo Ochoa) in autumn 2018.

Results:

Sample size was 77R (85% women, mean age 27y), 19 first-year (R1), 21 R2, 20 R3 and 17 R4. Thirty-two R (42%) had no serology test performed or did not know its result. Among the remaining 45, 23 were CMV-seropositive (51%). There were no differences in seropositive rates regarding sex (19/39 vs 4/6; p=0.41), being born in Spain (21/41 vs 2/3; p=0.57) and residency year (15/25 R1-R2 vs 8/20 R3-R4; p=0.18), nor between seropositive and seronegative R among day-care attendance during childhood (13/23 vs 8/22; p=0.19), treating patients diagnosed with CMV (10/23 vs 11/22; p=0.66) or having experienced mononucleosis symptoms (7/23 vs 2/22; p=0.074).

Ninety-seven percent of respondents consider pediatric residency as a risk factor for CMV infection. Nineteen percent (67% R1-R2) wrongly believe that CMV is routinely tested during pregnancy, and 4% (all R1) that there is universal newborn screening for CMV. A high number (84%) are aware that CMV is the most common congenital infection, and 87% (70% R3-R4) know that asymptomatic newborns may develop late-onset hearing loss.

Conclusions:

Half of pediatric residents are not CMV-infected, although 40% do not know their serological status. The rate of seropositivity does not increase during residency, suggesting there are other risk factors. Knowledge of congenital CMV is accurate, and increases during residency.

Systematic Review Registration:

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ESPID19-0316
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Risk factors for meningococcal disease in children and adolescents: a systematic review and meta-analysis

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Background

Invasive Meningococcal Disease (IMD) is a serious bacterial infection caused by the gram-negative bacterium *Neisseria Meningitidis* (NM). IMD remains nowadays a major cause of mortality and morbidity in children worldwide. Thus, identifying children at risk for IMD is of paramount importance.

Methods

2 databases (PubMed and Cochrane Controlled Trials Register) were systematically reviewed for articles on risk factors for IMD in children and adolescents published during a ten-year period (19/09/1998 to 19/09/2018). Inclusion and exclusion criteria were established and applied. The data were meta-analyzed using fixed-effect model and the results were presented on forest plots separately for each risk factor.

Results

We identified 12,397 studies after duplicates were removed. Titles, abstracts and full texts were screened and finally seven studies (6 case-control and 1 cohort study) were included in qualitative synthesis and 6 in meta-analysis. 563 cases and 284,646 controls were included in the analysis. The most common meningococcal serogroup was serogroup B (178, 31.6%) followed by W (66, 11.7%) and C (51, 9%) while 9.9% (56) cases were confirmed but non groupable. The mean age of MD cases was 78.8 months. Household crowding, smoking exposure and close relationships like intimate kissing conferred a nearly 2-fold risk for MD in exposed individuals compared to controls [overcrowded living: OR 1.60 (1.20-2.14), exposure to smoking OR 1.53 (1.18-2.00) and kissing OR 1.85 (1.15-2.96)]. Male gender, contact with MD and chronic disease were not shown to be significant risk factors for MD.

Conclusions

Our review highlights the importance of individual characteristics as risk factors for MD in childhood. Preventive policies may consider individual as well as social and environmental characteristics to target individuals at risk.

Systematic Review Registration (Please input N/A if not registered)

n/a

ESPID19-0187
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Adverse event following immunization during the outbreak response immunization against diphtheria in east java 2018

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[2]East Java Provincial Health Office, Immunization, Surabaya, Indonesia

Background and Aims:

The government of the Republic of Indonesia performed a three-round outbreak response immunization (ORI) to tackle continuous high-number of the diphtheria cases in East Java Province (total population of 35 million people). These ORI targeted 1-19-year-old children in 38 districts. During this activity, the record and report of the adverse event following immunization (AEFI) was monitored. The aim was to report a surveillance study of AEFI during the three-round of ORI against diphtheria in East Java Province in 2018

Methods:

: The reports were collected from 38 districts on daily, weekly, and monthly basis. Descriptive calculation and reports include the type of AEFI, the vaccines, the demography data include name, age, sex, and the address, and also the health officers involved. For each incident, the short chronological story was also recorded. The AEFI experts then decided the classification of the AEFI.

Results:

For the whole year period the coverage of three ORIs was 30,703,416 children doses. There were 2007 cases of AEFI (0.007%). Only twenty-four cases were classified as serious AEFI and involved seven among 38 districts in the province. Bangkalan was the most prominent district with 1314 reports. This district also had one of the highest numbers of diphtheria cases. In two incidents, the large numbers of children were involved, one with food poisoning and the second with mass hysteria. All serious cases were not related to the vaccines.

Conclusions:

The AEFI numbers during the ORI program in East Java province in Indonesia was very low. Only 2007 cases were reported. None of the cases has related to the vaccine.

Systematic Review Registration:

None
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ESPID19-0023
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Comparison of immunization status of children of rural and urban areas of ludhiana,punjab,india

D. Bhat[1], A. Kaur[1], G. Dhooria[1]
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Background and Aims:

In India vaccines are provided free of cost under Universal immunization programme (UIP) through all the public health facilities across the country, disparities in coverage exist for different population groups. Despite several programmatic initiatives, urban-rural difference in child immunization pose a challenge to India's public health agenda. Through this study the differences in rural and urban immunization and the various social determinants affecting routine immunization programs are explored.

Methods:

This was a community based cross sectional study in which a total of 1000 school going children were studied, 500 each from rural and urban schools of Ludhiana district of the sdtate of Punjab. Data was collected in two visits to each selected school, on a self structured performa .

Results:

Full immunization was seen in 81.8% children in urban area and 78.4% children in rural area. After the administration of BCG and OPV at birth, the frequency of administration of other vaccines goes on decreasing. Males were more immunized in urban area. Immunization status of children went on significantly improving as their mother's and fathers education level increased. Immunization status of children was found directly related to their socioeconomic class and inversely to birth order. This study also suggested poor awareness of parents about optional vaccines and adolescent immunization. Amongst the various reasons for not immunizing the child, the most common in both rural and urban area was unawareness for the need of vaccination.

Conclusions:

To improve immunization coverage, improvement in female literacy is necessary. Similarly improvement in socioeconomic status, limiting the family size and increasing hospital deliveries will lead to improvement in immunization coverage status of children.

Systematic Review Registration:

not done yet

ESPID19-0872
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Incidence of imd in children & adolescent/young adults' population in europe: results from a systematic literature review

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Background

Invasive meningococcal disease (IMD) is a public health concern due to its epidemic potential, high mortality, and sequelae. Throughout the world, IMD rates peak specially among infants and adolescents/young adults (0-24 years old), who represent the greatest burden. The aim of this review was to determine IMD burden by European country, age and serogroup.

Methods

A systematic review of PubMed, EMBASE and Cochrane Library databases was conducted (publication date 2000 to January 2018) to characterize the burden of IMD in EU-27 countries. Here we report the results on incidence in the 0-24 years old population, overall, by serogroup and by age.

Results

Out of 73 included papers with IMD incidence data, 37 presented data in the 0-24 years' old population from 9 EU countries. Data reported covered the period from 1974 to 2016. Overall, IMD incidence rates ranged from 0 to 82 per 100,000 for all serogroups and age groups. As expected, the highest incidence of IMD is typically reported in infants <1 year old, with a secondary lower peak occurring in adolescent/young adults (15-24yrs). The most incident serogroups observed were B (1.97-60.3 per 100,000 in <1 year and 0.08-20.8 in ≥1 year) and C (0-20.8 in <1 year and 0-21.1 in ≥1 year). Although there were few W & Y cases (<4 and <1 per 100,000 respectively) during this review period, several EU countries recently reported increasing trends for W and Y.

Conclusions

We observed the circulation of meningococcal serogroups B, C, W and Y causing disease in children & adolescent/young adults in Europe. Continuous and strong epidemiological surveillance is key to set up and adapt country vaccination policies to evolving epidemiology and the most impacted population.

Systematic Review Registration (Please input N/A if not registered)

CRD42018084136

ESPID19-0817
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiology of hospitalizations due to meningococcal infection in spain (1997-2015)

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Background and Aims:

Meningococcal disease remains a major health problem worldwide that affects individuals of all ages, especially children. Its appearance in sporadic cases and/or clusters of cases originates great concern and alarm in communities. An important proportion of those who survive have sequelae. This epidemiological survey estimates the burden of meningococcal infection in general population in Spain during a nineteen-year period (1997-2015)

Methods:

Retrospective survey by reviewing data of the Spanish Surveillance System for Hospital Data including more than 98% of Spanish hospitals and 99.5% of the country population. Data base contains data about admission and discharge date, age, sex, geographical region, diagnosis and discharge status for all hospitalizations in the country. All hospitalizations due to meningococcal infection in general population, reported during 1997-2015 period, were analyzed. Codes were selected by using the ICD-9-CM codes 036

Results:

A total of 14,650 hospital discharges for meningococcal infection were reported during the study period. The annual hospitalization rate was 1.79 cases per 100,000 population and the mean age was 17.10 years old. Almost one half of the cases (n= 6,857) occurred in children up to 5 years old, reaching a hospitalization rate of 16.84 hospitalizations per 100,000. Hospitalization rate decreased during the study period. A total of 1,081 deaths occurred in the period 1997-2015, with a case-fatality rate of 7.4% that increased significantly with age.

Conclusions:

Although an important decrease in meningococcal infections related morbidity and mortality has occurred in the last years in Spain, they still continue being major causes of hospitalization and death, especially, but not only, in children up to 5 years old. Future preventive measures, such as vaccination with vaccines covering new serogroups, could improve population health and reduce the disease burden

Systematic Review Registration:

NA

ESPID19-0804
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Bias in epidemiological studies assessing the impact of rotavirus vaccines on seizures-hospitalizations

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Background and Aims:

Observational studies of vaccine effectiveness or impact may be subject to multiple biases. There is higher risk of bias when studying non-funded vaccines (i.e. rotavirus vaccines in Spain), since socioeconomic status (SES) is different between vaccinated and unvaccinated. These differences become more significant when estimating the possible impact of these vaccines on low incidence extra intestinal manifestations such as seizures-hospitalizations (2-7% of RV-hospitalizations). These biases can be mitigated adjusting by covariates in multivariate models. However, most of the published studies in this context have not been adjusted for proper covariates. We estimate the influence of SES in studies assessing the impact of non-funded rotavirus vaccines on seizure-related hospitalizations.

Methods:

A retrospective analysis using linked population-based administrative databases, among Valencia Region's children <3 years old, during 2008 - 2018. We compared the rotavirus vaccination status on seizures-related hospitalizations (780.3* ICD-9-MC code) between the largest tertiary public hospital of the Region and private hospitals.

Results:

Since RV vaccines licensure in 2007, its coverage increased up to around 50% in the Valencia Region. A total of 615 seizure hospitalizations were recorded in the public hospital in the period studied. Among them, the percentage of admissions previously vaccinated with at least one dose of RV vaccine increased from 7.1 to 51.0% (similarly to vaccination coverage). The percentage of vaccinated in the private hospitals (95-100%) remained unchanged during the years studied.

Conclusions:

Although 95-98% of the Spanish population is covered by the public health system, higher SES families who can usually afford the purchase of non-funded vaccines, also have private insurance. Thus, unadjusted socioeconomic bias analysis (i.e. public vs. private - hospitalizations) may result in an overestimation of the impact or effectiveness of non-funded vaccines.

Systematic Review Registration:

N/A

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Population studies and surveillance

The burden of human papillomavirus-related diseases in males in europe: results from a systematic literature review

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Background

Current clinical data, along with real world evidence studies, confirm HPV vaccine effectiveness not only in females but also in males. Despite the regulatory indication for male HPV vaccination, only a few European countries recommend gender-neutral vaccination. To capture the disease burden of HPV disease in males, this study reviewed the incidence and prevalence rates of HPV-related diseases in European males.

Methods

This systematic literature review was performed following PRISMA guidelines, utilizing MEDLINE and EMBASE databases. Publications were included if they evaluated incidence and prevalence rates of HPV-related anal, penile, head and neck cancers (HNC), genital warts (GW) and recurrent respiratory papillomatosis (RRP) in males from European countries. Only studies published in English from January 2008 to March 2018 were included.

Results

Sixty-five publications from 17 European countries were identified on HPV-related diseases in males: anal cancer (n=20), penile cancer (n=11), HNC (n=18), GW (n=25), and none on RRP. Prevalence rates of up to 1% were reported for anal cancer, 4.2% for penile cancer and 56% for GW. The incidence rate of anal cancers in the UK increased from 0.79/100,000 in 1962 to 1.06/100,000 in 2002. Similarly, oropharyngeal cancer rates among men in several European countries increased from 1.1/100,000 in 1983-1987 to 13.7/100,000 in 1998-2002. Penile cancer and GW trends remained stable over time. Disease rates varied across age groups, peaking in early life for GW, and with higher incidence rates in older ages for penile cancers and HNC.

Conclusions

The data identified in this systematic literature review demonstrates the existing burden of HPV-related diseases in European males. This burden of HPV and its associated diseases might be prevented with prophylactic intervention such as gender-neutral HPV vaccination.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESPID19-0422
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Molecular and biological properties of influenza b viruses in 2017-2018 epidemic season in almaty region of the republic of kazakhstan

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Background

The continuous antigenic changes of influenza viruses mainly in the haemagglutinin molecule are reasons for continuous circulation of these pathogens among the population. Influenza viruses do not have a natural reservoir and they are not capable of reassortment with animal influenza viruses and do not cause pandemics, and their successful survival occurs due to the alternation of representatives of two evolutionary branches B/Victoria and B/Yamagata, as well as the occurrence of reassortants between them.

Methods

The study of antigenic and molecular biological properties of influenza B viruses in the territory of Almaty region in the epidemic season of 2017-2018 and identification of variability in representatives of the two evolutionary branches. During the study were analyzed 314 smears from patients with ARVI symptoms. Laboratory tests for identification of viral RNA performed with molecular genetics and virological methods.

Results

The structure of subtype strains positive for influenza is: A (H1N1) pdm09 - 35% (n = 25), A (H3N2) - 32% (n = 23), B - 33% (n = 24). In 24 samples which positive for the influenza B virus, the B/Yamagata viruses prevailed (95.8%).

Phylogenetic analysis of influenza B virus strains demonstrated, that 9 out of 10 strains belonged to Yamagata line and were similar to reference strain B/Phuket/3073/2013. This strain recommended by WHO for including in tetravalent vaccines for the season 2018-2019 for the northern hemisphere. Meanwhile, one sample was similar to the vaccine strain B/Brisbane//60/2008.**Conclusions**

The results of research demonstrated a dominance of B/Yamagata line among influenza B viruses, which did not include to the composition of a trivalent vaccine for 2017-2018 epidemiological season in Northern Hemisphere. Assumed that recommended by WHO a tetravalent vaccines could be acceptable for Influenza prevention in Kazakhstan.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0411
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Surveillance of severe influenza in the czech republic during three influenza seasons 2015-16, 2016-17 and 2017-18

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Background and Aims:

Influenza infection varies from mild to severe and life-threatening. Severe influenza (SARI) is defined as laboratory confirmed acute respiratory infection that requires hospitalization at intensive care unit. The objective of our study was to analyse SARI cases during influenza seasons 2015-16, 2016-17 and 2017-18 in the Czech Republic (CZ). Due to unpredictable influenza B lineages circulation we also investigated circulation of influenza viruses in order to evaluate the importance of a quadrivalent influenza vaccine usage.

Methods:

The epidemiological and virological surveillance system of influenza in CZ is active through the year and uses EU case definition for influenza. SARI surveillance has been established as national surveillance in all 14 regions from all hospital‘s ICUs. Case-based data were analysed.

Results:

248, 337 and 667 SARI cases (of which 85, 115 and 261 deaths) were reported during 2015-16, 2016-17 and 2017-18 seasons in CZ. Mean age of SARI patient was 56.2 years (age range 0-91) during 2015-16 season, 69.2 years (0-96) during 2016-17 season and 61.3 years (0-97) during 2017-18 season. Most patients had at least one risk factor for severe influenza infection. Influenza B was positive in 7.7% (19/248), 4.2% (14/337) and 56.8% (379/667) of cases during individual seasons.

Among children and adolescents up to 18 years, 10 SARI cases (1 death), 12 SARI cases (0 death) and 43 SARI cases (5 deaths) were reporting during the mentioned seasons.**Conclusions:**

Influenza epidemics differ in duration and magnitude and the circulating A subtypes/B lineages. The severity of some seasonal epidemic is comparable with the pandemic in 2009-10. Quadrivalent influenza vaccine should be used in order to address the uncertainties of influenza B strain circulation, and to offer direct protection against co-circulating two B lineages simultaneously.

Systematic Review Registration:

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Tick-borne encephalitis in the west bohemian region (czech republic) between 1960 and 2018

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Background and Aims:

West Bohemian Region (currently Pilsen and Karlovy Vary Regions) is a high tick-borne encephalitis (TBE) endemic region in the Czech Republic. Between 1960 and 2018, 2,478 cases of TBE were confirmed by laboratory testing in West Bohemian Region, i.e. 4.9 per 100,000 inhabitants p.a.

Methods:

During this period, the laboratory diagnostics were predominantly performed by the Department of Virology of the University Hospital in Pilsen. The records of all laboratory confirmed infections are enabling us to analyze the morbidity trends as well as other selected epidemiological characteristics between 1960 and 2018.

Results:

From 1960 to 1969, children and adolescents comprised 37.5% of the total incidence, and 13.3% of the total incidence between 2010 and 2018. Of the total of 2,478 sick persons, 2,288 (92.3%) were probably infected within the WBR. Seven infections contracted abroad were reported.

Of all the reported cases, twenty cases were fatal (0.8%). Tick bite was reported from 1,543 patients (62.3%). In 4.3% of cases, patient's history showed data on the consumption of non-pasteurized milk. As a result of the gradual infection season prolongation, the transmission can currently occur anytime between March and December. The highest incidence of TBE was among adults in Juni and July, among children and adolescents in July and August – at the time of summer holidays. The proportion of infections occurring from October to December has gradually increased to 10.2% in the last observed period 2010-2018.

During the monitored period there was the altitude shift of infection transmission occurring in the higher altitudes. Based on available data, 27.9% of the Pilsen Region´s young population, and 12.0% adults has been vaccinated.**Conclusions:**

The low vaccination coverage may hardly influence the unfavorable tick-borne encephalitis epidemiological situation.

Systematic Review Registration:

Tick-borne encephalitis

ESPID19-0106
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Pneumococcal vaccination in russia: first results

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Background and Aims:

Pneumococcal vaccination was included in the national immunization schedule of the Russian Federation in 2014. It is carried out for children from 2 months. The aim of our work was to analyze the coverage and timeliness of immunization and evaluate its effectiveness in the first three years.

Methods:

We have used Federal statistical observation forms №5 and №6 to get information about vaccination coverage. The official statistics on the incidence of acute otitis media, pneumococcal meningitis, community-acquired pneumonia and mortality from it were analyzed.

Results:

The coverage of primary series of pneumococcal vaccination (V1 and V2) was 87.7% in 2017. 55% of children received complete vaccination course (with revaccination). However, 73.4% of infants began to be vaccinated at the age of 6 months, that is, later than in scheme. 8% of children under one year old were not vaccinated due to medical contraindication for vaccination and refusals to vaccinate in 2017.

The introduction of vaccination resulted in 11% reduction of children acute otitis media incidence, and in decrease of pneumococcal meningitis incidence in children under 4 years old. We didn`t found any decrease in the incidence of pneumococcal community-acquired pneumonia in children. However, there is a decrease in pneumonia mortality rate among infants under 1 year old (by 49% compared with the period before beginning of vaccination) and by 35% in children 1–2 years old.

Conclusions:

High level of primary series of pneumococcal vaccination coverage was reached. The coverage of complete vaccination series is low, immunization of children Is carried out untimely. A decrease of incidence of acute otitis media, pneumococcal meningitis, and mortality from pneumonia in children was shown.

Systematic Review Registration:

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiology of acute appendicitis in children hospitalized in rambam medical center in haifa, israel between the years 2007-2017

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Background and Aims:

Acute appendicitis is an emergency in children. Treatment mostly consists of surgery and antibiotics. Antibiotics usually were deescalated according to microbiology data. We aimed to study the epidemiology and microbiology of acute appendicitis (AA) among children treated in our medical center

Methods:

Included children were diagnosed with AA, admitted to a tertiary referral hospital during the years 2007-2017. Demographic data, perioperative antibiotics, surgical procedures, length of stay, rehospitalization within 3 months, pathology and microbiology data were collected.

Results:

Among 1941 cases screened, microbiology samples were available for 708 patients. In 203/708 (28.6%) patients 395 isolates were identified.
Gram negative (G-), Gram positives (G+), and anaerobic bacteria were revealed in 67.6%, 21.5% and 10.9% of the specimens, respectively. Among G-, *E. coli* was revealed in 60.3%, Pseudomonas sp. 16.9% and Klebsiella sp. 10.1%. G+ included; Milleri Group Streptococci (MGS) (44.7%), and Enterococci (24.7%). Of 267 G- isolates were resistant to: gentamicin (6.9%), amikacin (0.7%), piperacillin-tazobactam (1.2%), ciprofloxacin (7.4%), and amoxi-clavulanate (29.1%). all isolates were susceptible to carbapenems

Conclusions:

A prominent increase in the isolation of G+ bacteria, dominated by MGS and a corresponding decrease in the isolation of G- bacteria from peritoneal fluid was observed. This could be partially attributed to the deduction of ampicillin from the empiric treatment used until the end of 2008

Systematic Review Registration:

N/A

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E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Tick-borne encephalitis (tbe) prevention: effect of online education among pediatrician and general practitioner knowledge and confidence

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Background and Aims:

To assist in decreasing tick-borne encephalitis (TBE) infection in persons of all ages, clinicians should remain up to date on evidence-based data supporting TBE immunization. We sought to determine if online continuing medical education (CME) could improve the knowledge and confidence of primary care physicians and pediatricians related to the use of TBE vaccine.

Methods:

The educational intervention consisted of an online video-based CME case history with accompanying expert commentary which was analyzed to determine efficacy of education on clinician learners after the educational intervention. Educational themes selected for the activity addressed knowledge gaps related to the burden of TBE, available vaccines and communication with patients. Educational effect was determined via a repeated pairs pre-/post-assessment study that compared responses to 4 identical pre- and post-assessment questions. A chi-square test identified differences between responses. Cramer's V was used to calculate the impact of education.

Results:

For primary care physicians (n=112) and pediatricians (n=37), the data showed statistically significant increases in correct responses from pre- to post-assessment related to:
Severe long-lasting sequelae of TBE (primary care pre 14% to post 73%; pediatricians pre 8% to post 81%)
Strategies for preventing TBE (primary care pre 76% to post 90%; pediatricians pre 97% to post 100%)
TBE vaccine recommendations (primary care pre 93% to post 99%; pediatricians pre 97% to post 100%)
Post assessment, there was a large effect of education (V=0.303 for primary care physicians and V=0.331 for pediatricians)

Conclusions:

The results indicate that participation in a video-based online educational clinical case review was effective in improving knowledge and confidence of primary care physicians and pediatricians regarding strategies for improving appropriate use of TBE vaccine.

Systematic Review Registration:

N/A

ESPID19-1192
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Human rotavirus g8p[8] gastroenteritis in vaccinated children in south korea

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Background

Rotavirus is the most common cause of gastroenteritis worldwide under 5 years-old. After the introduction of two global rotavirus vaccines, RotaTeq in 2007 and Rotarix in 2008 in South Korea, both vaccines significantly reduced hospitalizations of rotavirus infection. However, an emergence of G8P[8] rotavirus gastroenteritis is reported in vaccinated children.

Case Presentation Summary

Of 254 children hospitalized with acute gastroenteritis at Chung-Ang University Hospital in Seoul, South Korea between 2017 and 2018, 97 cases (38.2%) were found positive for rotaviruses. Interestingly, six cases of G8P[8] rotavirus-infected children were detected after vaccination of Rotarix or RotaTeq. Among them, CAU17L-79 case was detected from 27-month-old girl after Rotarix vaccination with severe symptoms; vomit, diarrhea, high fever, and severe inflammatory signs (WBC, CRP, and ANC). Genetic analysis revealed that these viruses showed evidence of re-assortment events of human-to-animal rotaviruses.

Learning Points/Discussion

Our results suggest that the emergence of rotavirus G8P[8] strain might continuously outbreak in the post-vaccination era in South Korea.

ESPID19-1166
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Hospitalisation due to varicella- preliminary results from active surveillance

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Background

In countries where varicella vaccination is not routine, chickenpox is an almost universal disease of childhood. Data regarding hospitalisation are sparse and may represent only the severest cases. However, such information is needed to permit accurate cost-benefit assessment regarding universal varicella vaccination in childhood.

Methods

All patients admitted to Bristol Children's Hospital, from February 2018 ongoing, are asked about their contact with chickenpox. Children identified as being in recent contact with, or having recent chickenpox, are assessed to see if their admission is related to chickenpox. Data are collected on all varicella related admissions. Annual crude age-specific rates were calculated using mid-year population (0-5 years) estimates as the denominator and are expressed as rates per 100,000 0-5 years population.

Results

From May to December 2018, 68 children were admitted with recent exposure to chickenpox of whom in 41 the presenting complaint was directly attributable to varicella. The median age at admission was 2 years (range 0-6 years). 20 children had soft tissue infection of whom four had periorbital involvement, 8 severe primary varicella (5 of whom were under 1 year old), 2 presented as possible sepsis, 4 had neurological disease and 2 had severe shingles. The annual varicella hospitalisation rate is estimated at 48.5 per 100,000 0- 5 years population.

Conclusions

Complications of varicella severe enough to warrant admission to hospital are common, costly and burdensome to families. The annual admission rate does not include the peak season so is likely to be significantly higher than this estimate. We discuss the secondary health care utilisation associated with admissions due to varicella.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1134
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Identifying and adressing vaccine hesitancy among brazilian doctors.

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Background and Aims:

Vaccine coverage in Brazil has declined in recent years, but there is little local data on vaccine hesitancy. The objective of this study was to know how doctors are facing vaccine hesitancy or refusal

Methods:

Prospective, multicenter study. Brazilian physicians respond to an online questionnaire, after reading and approving the informed consent form.The study was approved by Institutional Ethics Committee.

Results:

800 Brazilian doctors participated in the study, 72% of them female. The respondents' ages ranged from 25 to 73 years. The majority of professionals work in private services (74.4%) and 48.5% in Medical Schools. 90% reported having a vaccine card and 2.5% did not remember the last vaccine received; 89.2% received influenza vaccine in the last seasonr. 82.4% reported having had the opportunity to update their knowledge about vaccines in the last 12 months and 89% reported that they often discuss aspects related to vaccines with their patients. 61% of respondents have attended to families who refuse vaccines and more than half believe that this population is increasing. Were considered possible causes for vaccine hesitancy or refusal: fear of adverse events (68.5%), disclosure of negative information (64.7%), concerns about vaccine safety (48.6%). The respondents feel well prepared (47%) and reasonably prepared (45.5%) to face this question. Doubts about efficacy and safety of some vaccines were reported by 32.9% of the physicians interviewed.

Conclusions:

It is necessary to prepare doctors to face vaccine hesitancy or refusal. Even mentioning opportunities to update their knowledge about vaccines, 10% of participants did not receive influenza vaccine and 32.9% of them had questions about the efficacy and safety of some products. By increasing confidence in vaccines among Brazilian physicians we can better adress this problem.

Systematic Review Registration:

none

ESPID19-1131
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

A case report of a pulmonary tuberculosis

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Background

Tuberculosis (TB) is an important cause of morbidity and mortality in children worldwide. The most common form of TB disease in childhood is pulmonary disease followed by extrapulmonary infection, most frequently lymph node or central nervous system disease. Common symptoms of pulmonary TB include cough, fever, weight loss or failure to thrive. A diagnosis of pediatric TB is often based on the presence of the classic triad: recent close contact with an infectious case, a positive tuberculin skin test or interferon-gamma release assay and suggestive findings on chest radiograph or physical examination.

Case Presentation Summary

A previously healthy 3-month-old male infant was brought to the emergency department (ER) because of fever with 5 days of evolution and productive cough. The physical examination was normal. The blood analysis revealed a positive C-reactive protein and treatment with ceftriaxone was started. Cultural studies were negative. The child was discharged after 8 days with clinical improvement. Five day later the patient reiniciated fever and the father was diagnosed with pulmonary tuberculosis. He was readmitted for further studies. A chest radiography revealed a density in the left lower lobe. Gastric aspirate culture and PCR amplification for Mycobacterium Tuberculosis Complex were positive. Tuberculin skin test and Interferon-γ release assay were also positive. Pulmonary disease was confirmed, and treatment with isoniazid, rifampin, ethambutol and pyrazinamide (HRZE) was started. The child was discharged and the clinical outcome was positive.

Learning Points/Discussion

Clinical presentation of TB disease is varied especially on this age group. Comprehensive awareness and knowledge of these manifestations can help to early diagnose and start an appropriate treatment, increasing the probability of a clinical and microbiologic cure.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Infection by enterovirus, what we now? What we have?

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Background and Aims:

Enterovirus infection is a common cause of fever, with several clinical expression.
In 2016, an outbreak of rhomboencephalitis due to enterovirus was reported, causing severe injuries in affected children.

In this study, we will describe the epidemiological and clinical characteristics of children with Enterovirus infection in our centre.

Methods:

Inclusion: all the patients from 0 to 15 years with positive RNA-PCR test of Enterovirus in CSF, nasopharyngeal frotis or fecal sample detected in our centre, a regional Hospital in Osona (Barcelona), from 2016 to 2018.

Results:

45 patients were included (M62.3%, F37.7%), with an age average of 24.5 months. A 77.7% of cases were detected in summer (May-July).
The 100% had fever on the clinical onset, finding cutaneous rash in 31.1%, vomits-diarrhea on 42.2%, and tremor in 17.7%. The 75.5% had <48h of clinical evolution.

Performed laboratory test were: blood test: 93.3% (40% leukocytosis with neutrophilia. Main CRP 21.5 mg/L). Blood culture: 80% (all negative). Lumbar puncture: 62.2% (pathological CSF 11%). Urine analysis: 34% (all negative). The origin of the Enterovirus-test samples were: CSF: 37.5%, nasofaringeal: 17.7%, fecal: 44%.
Final diagnoses: 44.4% meningitis, 22.2% sepsis-like illnes, 17.7% romboencephalitis, 11.1% gastroenteritis, peripheal facial palsy (1case).

The admission rate was 93.3% (stayment-average: 3.6 days), transferring the 8.8% to P-ICU.

The 26.6% received antibioteraphy. Not long-term complications were found.

Conclusions:

Enterovirus infection is present in our environment, with a broad spectrum of severity.

The unespecific clinical behavior leads to perform multiple invasive test and preventive admissions.

A few rate of our patients got severe complications o need critical care.

The addition of a quick detection test in the first line study could be useful in cases of clinical suspicion to reduce unnecessary interventions.

Systematic Review Registration:

Enterovirus infection

ESPID19-1117
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Increase and high variability in consumption of antimicrobial agents for systemic use in the paediatric population in northern spain. Time period 2005-2015

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Background and Aims:

Antimicrobial consumption in Spain has increased in recent years despite the introduction of several surveillance strategies.

Methods:

Observational descriptive and retrospective study about consumption (expressed as defined daily doses per 1000 inhabitants per day, DID) of antimicrobial agents for systemic use (J01C group of the Anatomical Therapeutic Chemical Classification System) in paediatric outpatients in a region in Northern Spain (100,000 children population, belonging to eight health areas) between 2005 and 2015.

Results:

Mean consumption: 19.32 DID; increase in 29.1% along the study period. The most consumed therapeutic groups were: J01C (β-lactam antibacterials penicillins; 15.92 DID, 82.39%), J01F (macrolides, lincosamides and streptogramins; 9.38%) and J01D (other β-lactams antibacterials; 7.03%). Antimicrobial consumption increased in all the health areas, with a high variability among them (maximum 17.1 DID in 2011).

Both amoxicillin and amoxicillin-clavulanate consumption reached nearly 80% of the global consumption; amoxicillin consumption increased more than that of amoxicillin-clavulanate in all the areas; however, amoxicillin-clavulanate consumption was still higher than that of amoxicillin in four of the eight areas in 2015.

Azithromycin and clarithromycin were the most frequently macrolides consumed. Azithromycin consumption increased significantly over the time period (maximum 406%) with large variation among health areas.

J01M group (quinolones) consumption was scarce (0.07%), but 14.2 times higher in the area with the highest consumption compared to the area with the lowest.

J01_B/N quality indicator (ratio broad-spectrum to narrow-spectrum antimicrobials) was fluctuating, with the highest difference among areas (71.44 points) in 2006.

Conclusions:

Antimicrobial consumption in the paediatric population in Northern Spain has increased along 2005-2015, more than previously reported in the general population in Spain along this time period. Areas with the highest antimicrobial consumption showed the poorest quality indicators.

Systematic Review Registration:

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ESPID19-1105
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Effect of e-education on pediatrician knowledge and confidence: the case of immunization against varicella

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Background and Aims:

E-Education tools can be very powerful in continuing medical education (CME). We sought to determine if online CME could improve the knowledge and confidence of pediatricians related to the use of varicella vaccine. The program aimed to update viewers on evidence-based data supporting varicella immunization.

Methods:

The educational initiative consisted of an online video-based CME discussion between two internationally respected experts. Educational themes selected for the activity included the prevalence and burden of varicella infection worldwide, the efficacy and safety of available vaccines for the prevention of varicella-related disease and strategies to improve vaccine coverage rates. Educational effect was determined via a repeated pairs pre-/post-assessment study that compared responses to 4 identical pre- and post-assessment questions. A chi-square test identified differences between pre- and post-assessment responses ($P<.05$ significance level). Cramer's *V* was used to calculate the impact of education on the outcomes. Data from the participants were collected between June 27 and July 31, 2017.

Results:

For pediatricians (n=358), the data showed statistically significant increases in correct responses from pre- to post-assessment ($P<.05$) related to:

- · Burden of illness due to varicella (pre 32% to post 77%)
- · Effectiveness data for the varicella vaccine (pre 73% to post 85%)
- · Safety data for the varicella vaccine (pre 56% to post 66%)
- · Post-assessment, there was a considerable educational impact (V=0.234), including a noticeable (V=.15) increase in knowledge of the efficacy of varicella vaccine
- · 49% increased confidence (3.5/5 pre to 4.2/5 post) in evidence-based choices

Conclusions:

The results indicate that participation in video-based online educational discussionbetween 2 experts was effective in improving the knowledgeand confidence of pediatricians regarding strategies for improving appropriate use of varicella vaccine.

Systematic Review Registration:

n.a.

ESPID19-1066
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Clinical presentation and follow up of infants with congenital zika infection in salvador, brazil

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Background

In 2015, an unprecedented outbreak of newborns with microcephaly raised in major cities at northeastern Brazil. Lately, the association of microcephaly and Congenital Zika Infection (CZI) was confirmed.

Case Presentation Summary

We enrolled 62 infants with CZI in a prospective follow up study. All of them were born during de 2015-2016 Zika outbreak in Salvador, Brazil. The majority (86%) of their mothers reported Zika virus symptoms, mainly skin rash (92%), during pregnancy (78% at first trimester). Of the infants, 53.2% are female and 78.6% were black or mulatto. Based on gestational age and head circumference (HC) at time of birth, 31% were classified as microcephaly and 54.8% as severe microcephaly by the Intergrowth-21 criteria. There are 6 cases of arthrogryposis and 9 cases with hearing loss by Brainstem Evoked Response Audiometry evaluation. Brain image was abnormal in all cases, with ventriculomegaly and calcifications as the main findings. All infants are being followed in medical and physiotherapy care and 17 of them needed hospital admission for orthopedic surgery or clinical complications. One of them died due to respiratory tract infection.

Learning Points/Discussion

As a new clinical syndrome, CZI cases need to be followed closely for the understanding of the clinical spectrum of the disease and its complications. Moreover, long-term follow-up is necessary to identify complications and prognostic factors.

ESPID19-1045
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Unexpected changes in seasonality and size of the annual epidemic of rotavirus acute gastroenteritis (rvag) in the context of low coverage vaccine usage

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Background and Aims:

Two RV vaccines have been used in Portugal on the private market since 2006, with estimated combined coverage rising from 16 to ~45% between 2007 and 2018. A very high effectiveness was shown in a case control study done in this population. Our aim is to describe the annual epidemics over the last 7 years.

Methods:

From January 2012 to December 2018, children aged ≤36M attending the ER with symptoms of AG, defined as ≥2 watery or looser than normal stools within a 24H hour period with or without vomiting, were included if they had a stool sample tested for RV using a rapid test based on immunochromatography.

Results:

Each year, 30-36% of the children with AG had a stool sample available for testing. Following several years with slight variations in the size of the annual epidemic (~20% of all AG), there was an increase in 2016 (30%) followed by an important decrease in 2017 (11%), going back to previous values in 2018. The proportion of admissions has been stable. Over the years we observed varying seasonality, with the peak happening in the first semester, but no progressive trend towards delay. An unexpected and unusually large number of cases occurred in Oct-Dec 2016 and in Jan 2017, followed by a very small number in the rest of that year.

Conclusions:

Despite the high effectiveness of the vaccine in this population, there isn't an overall downward trend probably due the low vaccine use. This unusual seasonality in 2016-17 could be explained by the accumulation of a pool of non-vaccinated susceptible children or introduction of a novel RV strain into this community.

Systematic Review Registration:

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ESPID19-1038
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Emergence of serogroup w meningococcal disease in santa catarina, southern region, brazil

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Background

In Latin America, the incidence of meningococcal disease (MD) varies from < 0.1 to 2.0 cases per 100.000 inhabitants, with higher rates in Brazil and Southern Cone countries (Argentina, Chile, and Uruguay).

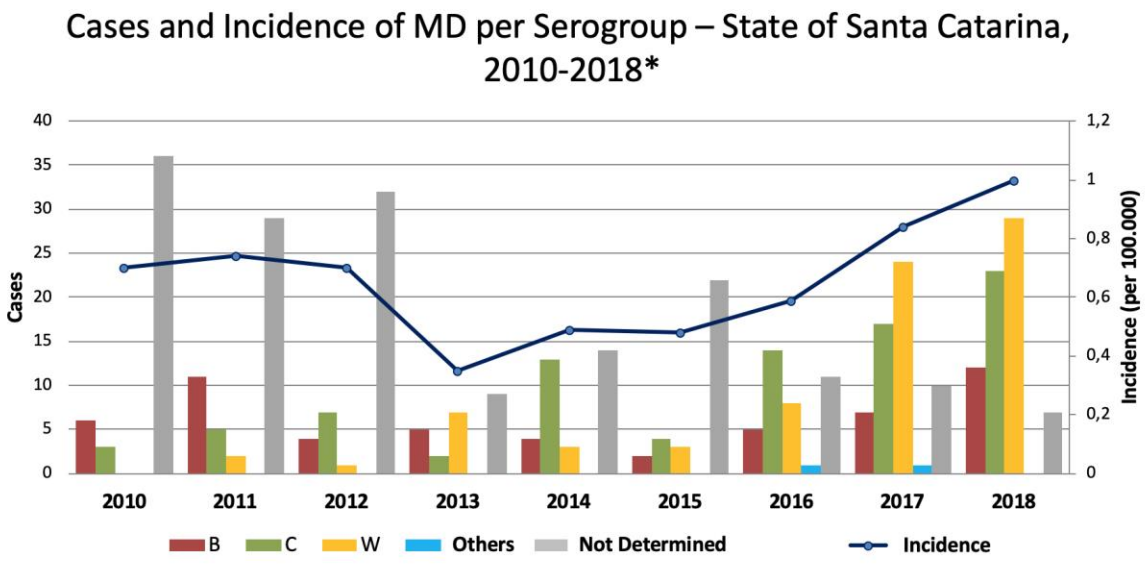
In Brazil, MD is endemic and had rates of 1.5-2.0 cases per 100.000 inhabitants before 2009. Since meningococcal C was the most frequent serogroup, Brazil included in 2010 meningococcal C conjugate vaccine into the National Immunization Program for children < 2 years old reporting a reduction on the incidence rate (0,6 cases per 100.000).

Case Presentation Summary

In 2017, serogroup C was the most prevalent (30%), followed by serogroup B (12%) and W (4%).

Brazil's southern region is composed by three states (PR, SC and RS) which are geographically next to the Southern Cone Countries and that, since 2016 have been presenting a significant increase of serogroup W. In 2017, serogroup C corresponded to 34%, followed by W (16%) and B (8%) in this region.

The state of Santa Catarina (SC), in 2018, reported incidences of MD of 1.0 per 100.000 inhabitants (71 cases). Serogroup W was responsible for 41% of the cases, affecting mainly < 5 years old with lethality of 17% (5 deaths in 29 cases), followed by serogroup C (32%) e B (17%).



Source: SINAN/Health Ministery Brazil/MS (2010- 2016)
Source: DIVE/SC Health Surveillance (2017-2018) – updated at 31.10.2018

Learning Points/Discussion

It is imperative that health officials stay vigilant in order to monitor changes in circulating strains over time. The emergence of serogroup W in Southern Region of Brazil must be a warning for health authorities to improve meningococcal surveillance in the region and develop the diagnostic methodology, also considering the geographical characteristics and discussing recommendations for quadrivalent (ACWY) conjugate vaccines.

ESPID19-1028
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Health related quality of life (hrqol) lost for children and their families due to rotavirus acute gastroenteritis (rvag) in portugal

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Background and Aims:

Rotavirus is the leading cause of gastroenteritis. Rotavirus vaccines are safe and effective. In countries with low mortality due to rotavirus, an important component to assess cost-effectiveness is to quantify the HRQoL lost due to RVAG evaluating quality adjusted life years(QALYs) lost. Previous studies reported QALYs lost per thousand children of 3,1-3,5(United Kingdom) and 2,2(Canada).

Methods:

In this prospective, observational study, children with RVAG aged <=6Y were recruited from the ER in 2017-18. The severity was assessed using the Vesikari scale(0-20 points). Children's HRQoL were assessed using the *Health Utilities Index 2*(HUI2) with visual analogue scale(VAS) for children, and the EQ-5D-5L and visual analogue scale(VAS) for adults(primary carer). Families completed a symptom diary on days 1, 7 and 14 after observation to assess time to recovery.

Results:

81 children were included, with a median age of 22M (23D-6Y). The mean Vesikari score on attendance was 7,2(20% severe); 17% required hospital admission; the mean duration of symptoms was 5D. 61% of the cohabitants had symptoms and 60% of the parents missed work, 3 days on average. The children's mean HRQoL on admission were HUI2=84% and VAS=65%; the carers' were EQ5D=91% and VAS=96%. The mean number of QALYs lost per thousand children was 2,4 for children and 2,2 for caregivers. At the time of presentation, the main affected domains in children were pain(78%) and emotion(57%) and in adults was anxiety(60%).

Conclusions:

This is the first study in Portugal using QALY losses to assess the impact of RVAG in children and their families. It shows the same impact as the study conducted in Canada and lower impact than in the UK. This information will be important in the evaluation of the cost-effectiveness of rotavirus vaccines.

Systematic Review Registration:

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ESPID19-1017
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Respiratory syncytial virus (rsv) may not be the most important cause of respiratory hospitalization in infants from remote/isolated northern communities in quebec, canada

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Background and Aims:

Very high rates of respiratory infections are reported in young Inuit children living in remote/isolated Northern communities, with limited data on their etiology. As part of evaluation of a new immunoprophylaxis program with palivizumab, we estimated the burden/etiology of respiratory hospitalizations in <12-month-old infants in Nunavik (Northern region of Québec, Canada), during 5 years (retrospective, 2014-2016, and prospective, 2017-2018).

Methods:

Medical charts of Nunavik infants admitted between November 2013 and June 2018 with respiratory diagnoses to 2 Nunavik hospitals and to one tertiary hospital in Montreal have been reviewed. During the retrospective period, local rapid antigenic tests and occasional PCR testing (at referral center) were done upon physician request. During the prospective period, all infants were to have a nasopharyngeal specimen tested by multiplex PCR at Quebec public health laboratory(LSPQ).

Results:

Among ≈380 annual live births in this population, >20% were admitted for a respiratory infection (≈5% for a RSV-associated infection) during their first year of life. During the retrospective period at least one test was done in 88% (23% PCR). During the 2 prospective seasons, >90% admitted infants were tested (>50% PCR).

Among the 72 infants admitted during the prospective period tested by multiplex PCR, 97% had at least one virus detected: 13% RSV mono-infection, 21% co-infections with RSV and other respiratory viruses (ORV), and 64% infections with at least one ORV without RSV (rhino/enterovirus, human metapneumovirus, adenovirus, parainfluenzavirus, coronavirus, influenza, bocavirus). Up to 4 viruses were detected simultaneously in one infant.

Important challenges associated with limited resources and complexity of healthcare logistics in this population were faced.

Conclusions:

Other respiratory viruses were more frequent than RSV in Nunavik infants hospitalized with respiratory infections.

Systematic Review Registration:

N/A

ESPID19-0990
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Prevalence of mental health alterations in vertically hiv-infected children and youths in spain

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Background and Aims:

There is increasing awareness that long-term survivors with perinatal HIV infection (PHIV) are at high risk for mental health problems, given genetic, biomedical, familiar and environmental risk. These problems are also associated with risk behaviour and treatment non-adherence. The aim of this work is to describe the prevalence of mental health problems in a cohort of children, adolescents and young adults followed-up in a tertiary Hospital in Spain.

Methods:

All vertically HIV-infected patients that were under follow-up in December 2017 were included in the study. Medical records were reviewed retrospectively from first visit. Prevalence of psychiatric disorders was defined according to the variables: mental health diagnosis, referral for psychiatric evaluation, use of psychiatric medication and/or psychotherapy.

Results:

From 72 patients, 43 (60%) had been transferred to adult units. Mean age was 21 years (SD 7.9). All were on ART and most were virologically suppressed (89%); 23% C stage. Behavioral problems were present in 44.8%. School failure was reported in 38% and bullying in 10%. A 32% of patients had been referred to mental health services (only 12.5% had a formal diagnosis); In patients under pediatric follow up: 45% (13.7% with diagnosis). A background of family breakdown was present in 75% of patients the referred patients vs 25% in those without symptoms (p=0.06). Adherence issues had been present in a 62% of patients.

Conclusions:

The prevalence of mental health disorders and behavioural health challenges was high among PHIV youths in our study. They appear to be influenced by psychosocial adversity. Care systems need to pay greater attention to how mental health and social support is integrated, with a multidisciplinary approach, into the care management for HIV, particularly throughout lifespan changes

Systematic Review Registration:

N/A

ESPID19-0972
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Active tuberculosis and latent tuberculosis infection screening of migrants children in emilia romagna, italy

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Background and Aims:

In Emilia-Romagna all children 0-14ys recently arrived in Italy (asylum seekers, refugees and legal immigrants) are screened for Tuberculosis after their arrival or before school admission. First step of the screening program is based on TST (Tuberculin-Skin-Test)

Methods:

Children with TST≥10 mm and children who had contact with active TB are referred to our dedicated service (St.Orsola-Malpighi Hospital, Bologna). We perform medical examination, TST, blood sample (including Quantiferon), and chest X-ray.

Results:

From January 2013 to August 2018, we visited 233 children: 64 had positive TST, 150 had recent contact with pulmonary TB, 15 with suspected pulmonary TB. 109 patients were born abroad and 124 were born in Italy with foreign families. 122 males and 111 females; average age 6,4 years (22% 0-2 ys, 26% 2-6 ys, 52% >6 ys). 43 patients were surely vaccinated for TB in their native Country. We diagnosed: 123 children exposed to a TB case (without signs and symptoms of infection/disease), 18 children with positive TST for BCG vaccination, 67 children with LTBI, 22 children with pulmonary active TB (8 coming from screening program before admission to school, 6 coming from contact tracing, 8 sent to our service for suspected TB). All affected patients completed the treatment without developing resistances and side effects. Children with LTBI were treated with isoniazid for 6 months without side effects and signs of TB disease at 2 years follow up.

Conclusions:

Our TB screening program proved to be effective in discriminating between TB disease, LTBI and previous immunization. This model, based on TST as first step, limits the use of chest X-Ray to TST positive patients. In patients with positive TST, QFT is essential to discriminate between vaccinated children and LTBI.

Systematic Review Registration:

N/A

ESPID19-0961
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Parental perceptions of childhood immunization in greece: a study in the context of the national health examination survey emeno

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Background and Aims:

The widespread availability and use of vaccines have significantly reduced morbidity, mortality and healthcare costs associated with infectious diseases, worldwide. Nevertheless, parental concerns on the safety and benefits of vaccination have increased recently. We aimed to assess parental perceptions on childhood immunization and possible correlations in Greece, where vaccines in the National Immunization Program are mandatory and provided free of charge.

Methods:

This study was conducted during 2014-2017 as part of the National Health Examination Survey EMENO which aimed to assess morbidity of chronic diseases and its associated risk factors. Participants were selected by applying multistage, stratified random sampling on 2011 Census. All participating households that included children (<18years) were eligible for this study. Parental beliefs and perceptions were recorded using an interviewed-administered, structured questionnaire. 437 questionnaires were collected in total

Results:

Although 95.9% agreed that “vaccinations are necessary for their children”, 87.5% of the participants were skeptical about vaccinations (i.e. confused or suspicious) and 26.3% “have great fear that vaccines may harm their child”. Notably, while 62.2% of parents had an absolutely positive attitude, only 1.14% had an absolutely negative attitude towards immunization.

32.5% reported that a vaccine/dose might have been missed/omitted. For 17.6% of them the reason was uncertainty of its safety/usefulness. Parental perceptions were not significantly associated with the parent’s gender or educational level

Conclusions:

Although parents in Greece seem to acknowlegde the necessity of childhood vaccination, they are also skeptical towards them. This is an important issue that could affect current and future vaccination coverage. Therefore, doctors and public health officials should strive more to adequately inform and educate parents in order to fight against unjustified vaccine safety concerns and general misconceptions about vaccines

Systematic Review Registration:

N/A

ESPID19-0946
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Impact of recent changes in invasive pneumococcal disease epidemiology in young children on decision making for the vaccine choice for the vaccination programme in flanders

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Background and Aims:

In 2007 pneumococcal vaccination to prevent Invasive Pneumococcal Disease (IPD) was added to the vaccination programme in Flanders with the 7-valent vaccine (PCV7). Based upon circulating strains in IPD, the National Immunisation Technical Advisory Group (NITAG) adapted its recommendations for pneumococcal vaccination in children. This resulted in changes in the vaccine of choice for the vaccination programme. From July 2011 to June 2015 the 13-valent vaccine (PCV13) was used. Since July 2015 it was replaced by the 10-valent vaccine (PCV10).

Methods:

Data on capsular types of IPD cases in children younger than 2 years, provided by the reference laboratory were analysed together with the available vaccination data to see the impact on IPD causing serotypes (ST), with special attention to ST 19A.

Results:

Cases of IPD caused by ST 19A decreased from 38% of IPD isolates in 2011 to <2% 4 years after introduction of PCV13. Two years after the switch to PCV10, we started to observe an increase of this type. In 2018 about 30% of cases of IPD in children younger than 2 years in Flanders were caused by ST 19A. As far as vaccination data could be obtained, all children with IPD were vaccinated with at least 2 doses PCV10.

Conclusions:

Despite the almost disappearance of ST 19A before the switch from PCV13 to PCV10 and a sustained high pneumococcal vaccination coverage, IPD epidemiology revealed a progressive reemergence of type 19A only 2 years after PCV10 introduction. As this serotype has now become the dominant ST causing IPD in young children in Flanders, the NITAG recommended a switch back to PCV13 in the vaccination programme as this seems the best option to counter this evolution.

Systematic Review Registration:

no

ESPID19-0927
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Acute flaccid paralysis surveillance after the regional certification in indonesia: fighting the complacency

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Background and Aims:

Indonesia had been free from polio after a mass National Immunization Days (NID) in 1995. The surveillance then developed and strengthened to the whole country and endured the social and some provincial social unrest. Most of the province (73.5%) in Indonesia was in high-risk level classified by WHO risk assessment tools. This study aimed to describe the situation in Indonesia, based on the acute flaccid paralyze (AFP) surveillance, especially after the WHO certification.

Methods:

The data was collected from the district and provincial health offices of Indonesia on weekly and monthly basis. The central committee in Jakarta analyze all reported AFP cases and made final decisions.

Results:

Reinfection break-in (2005), with a total of 351 cases including 46 vaccine-derived poliovirus (VDPV) cases. Indonesia remains polio-free up to the SEARO declaration March 2014. Unfortunately the biological problem and heterogeneous level of governance halt the declaration. Years afterward the hospital surveillance went down to 50% in 2018 and most of the 10 indicators for surveillance are not met. The non-polio AFP rate is declining from 2.81 (2009) to 1.85 (2018). The environmental surveillance added, without significant result. Sequential eradication pathways offered to be a solution, from region to region, from strain to strain, from wild to VDPV, but surveillance weakens and burns down. In the most densely populated province, East Jawa, the non-polio AFP rate only reached 76,5% of all district in 2018, other surveillance indicator decreasing.

Conclusions:

Most parameters of the AFP surveillance in Indonesia recently were not good. Revitalizing the active hospital surveillance, retraining of personal and additional rewards are planned.

Systematic Review Registration:

None

ESPID19-0877
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

A decade of s. Aureus (sa) invasive infection
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Background and Aims:

Sa is responsible for a large number of paediatric infections. Our aim was to describe Sa invasive infection in a paediatric hospital in the last decade.

Methods:

Retrospective review of all cases of Sa invasive infection (Sa in a normally sterile product or in a surgically drained abscess) from 2008 to 2017. Demographic and clinical data were collected. Risk factors for invasive disease including chronic disease with recurrent hospital visits, living in an institution, dialysis, long-term catheter, hospitalisation in the previous 12 months, surgery in the previous 6 months and antibiotic use in the last month prior to sample collection were analysed.

Results:

232 cases were included, 121 (52%) h*ealthcare-associated infection* (HAI) and 111 (48%) community-acquired infections (CAI). 36 (16%) were MRSA (31 HAI and 5 CAI). Median age was 3Y (1D-17Y) and median number of cases/year was 24,5 (16 in 2016, 27 in 2009 and 2012). Sa was detected in blood (110, 45%), abscess (96, 39%), peritoneal fluid (12, 5%), pleural fluid and joint fluid (10, 4% each) and bone biopsy (6, 3%). In 12 (5%) cases there was detection in more than one biological product. Diagnoses were: 94 (40,5%) abscess, 38 (16,4%) bacteraemia, 37 (15,9%) arthritis/osteomyelitis, 32 (13,8%) central venous catheter infection, 15 (6,5%) intra-abdominal infection, 10 (4,3%) pneumonia and 6 (2,6%) sepsis. 168 (80%) required hospitalisation. All received antibiotic and 116 (50%) surgical treatment. 6 (3%) died, all with HAI: 4 had cancer, 4 had MSSA and 2 MRSA.

Conclusions:

Sa invasive infections have remained fairly stable in the last decade, with predominance of soft tissue infections and bacteraemia. Sa was mostly identified in blood. Half of the patients had risk factors. Outcome was favourable in most cases.

Systematic Review Registration:

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ESPID19-0870
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Methicilin-resistant (mrsa) and methicilin-susceptible staphylococcus aureus (mssa) invasive infection – is there a difference?

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Background and Aims:

MRSA is a problem in many countries, not only in healthcare-associated infections (HAI) but also in community-acquired infections (CAI). The aim of this study was to analyse whether there are differences between MRSA and MSSA invasive infection in a paediatric hospital.

Methods:

Retrospective review of all *S. aureus* (Sa) invasive infections (Sa in a normally sterile biologic sample or from a surgically drained abscess) from 2008 to 2017. Demographic and clinical data were collected. Risk factors for invasive disease including chronic disease with recurrent hospital visits, living in an institution, dialysis, long-term catheter, hospitalisation in the previous 12 months, surgery in the previous 6 months and antibiotic use in the last month prior to sample collection were analysed. Results were considered statistically significant if $p<0,05$.

Results:

232 cases of Sa invasive disease were included: 36 (16%) MRSA and 196 (84%) MSSA. Comparison between both groups is presented in the table.

	SaMR: 36 (16%)	SaMS: 196 (84%)	p
Median cases/year (max-min)	3 (1 in 2008 – 9 in 2013)	19,5 (13 in 2016 – 24 in 2012)	
Median age	3Y (4d-16Y)	2Y (1d-17Y)	0,751
Hospitalisation	89%	79%	0,15
HAI	86,1%	45,9%	< 0,05
Risk factor	83,3%	37,2%	< 0,05
Abscess	22,2%	43,9%	0,015
CVC infection	25%	11,2%	0,026
Bacteraemia	22,2%	15,8%	0,153
Arthritis/Osteomyelitis	8,3%	17,3%	0,175
Pneumonia	11,1%	3,1%	0,029
Intra-abdominal infection	5,6%	6,6%	0,809
Sepsis	2,8%	2,6%	0,937
Surgical treatment	30,6%	53,6%	0,011
Complications	13,9%	6,6%	0,158
Mortality	5,6%	2,1%	0,243

Conclusions:

MRSA and MSSA invasive infections remained relatively stable throughout the study period. The MRSA group was more frequently associated with HAI and presence of risk factors. In CVC infection, pneumonia and bacteraemia, MRSA was more frequently identified. Surgical treatment was more frequent in the MSSA group, where abscesses were more common. There was no difference in age, hospitalisation, death and complications.

Systematic Review Registration:

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ESPID19-0856
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Seasonal trends of common viral respiratory tract infections in a children's hospital of northern taiwan

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Background

Respiratory tract infection (RTIs) is the leading causes of medical visits for children. The study aimed to realize seasonal trends of viruses of RTIs in a children's hospital in northern Taiwan.

Methods

The point-of-care tests of respiratory syncytial virus (RSV), adenovirus (Adv) and Influenza virus (Flu) were done in patients with RTIs who visited the emergency room, outpatient clinics and hospitalization in a children's hospital. We retrospectively analyzed the results of patients ≤ 5 years-old from March 2017 to December 2018. We calculated weekly percent positive (PP) of each virus and defined season onset as >2 consecutive weeks when PP exceeded the annual mean for the respective year.

Results

Among 16326 tests were identified, 956 (19.8%) of 4826 were positive for RSV, 857 (14.6%) of 5878 were positive for AdV, and 581 (10.3%) of 5622 were positive for Flu. RSV activity began in week 27 (July), ended in week 43 (October), peak in week 37 and 17 weeks in duration. Flu activity had 2 seasonal trends, one began in week 51 (December), ended in week 10 next year (March), peak in week 4 and 12 weeks in duration and the other season was in week 25-27 (July). AdV had no obvious trend during the study period. As compared with the off-season, the epidemic-season showed significantly higher PP for RSV (29.8% vs. 11.9%, OR: 3.2; 95% CI: 2.7-3.7; *P*<.0001) and significantly higher PP for Flu (18.3% vs. 8.0%, OR: 2.6; 95% CI: 2.1-3.1; *P*<.0001), respectively.

Conclusions

This study suggests that RSV season began in July and ended in October, Flu circulated in winter season and July, and AdV occurred throughout the year with no obvious season in Northern Taiwan.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0846
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Effects of 9 years of immunization with higher-valent pneumococcal conjugate vaccines on children in germany and coverage of future vaccine formulations

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Background and Aims:

A general recommendation for the pneumococcal conjugate vaccine (PCV) was issued for children ≤2 years in Germany in 2006. In 2009, two higher-valent PCVs (PCV10, PCV13) were licensed. Here, we present data on invasive pneumococcal disease (IPD) cases following PCV program onset.

Methods:

Pneumococcal isolates from children with IPD were serotyped at the GNRCS using the Neufeld-Quellung reaction.

Results:

From July 2017 to June 2018, the GNRCS received 94 IPD isolates from children <2 years, of which 18 had PCV13 serotypes. Five of these were from unvaccinated children, three from incompletely vaccinated children.

The 94 isolates represent a reduction of 39% compared to 2005/2006 (before vaccination; n=154), but an increase since 2011-2012 (n=75). Even though the total amount of cases has increased since 2011-2012, the PCV13 proportion has decreased from 88% before vaccine introduction to 69% at the introduction of higher-valent vaccines to 19% in 2017/2018.

Residual PCV13 serotypes in 2017/2018 were 1 (n=1), 6B (n=1), 19F (n=2), 19A (n=3) and 3 (n=11). Among children 2-4 and 5-15 years of age, serotype 19A persisted and serotype 3 increased.

Among children <2 years, coverage of PCV13 was 19%. Future vaccines PCV15 (28%) and PCV20 (52%) would increase coverage considerably. Among the serotypes not in these new formulations, 24F (n=10) and 15C (n=6) were the most prevalent.**Conclusions:**

More than nine years after the introduction of higher-valent vaccines, PCV13 serotypes have been reduced among children, but serotypes 3 and 19A persist. Future vaccine formulation would considerably increase serotype coverage.

Systematic Review Registration:

N.A.

ESPID19-0840
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Axillary lymphadenitis and other rare manifestations from bcg vaccination

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Background and Aims:

The most frequent complication associated with BCG vaccine is axillary lymphadenitis. However, other clinical manifestations may occur, sometimes posing diagnostic challenges. Our aim was to assess BCG adverse reactions in a 10 year period.

Methods:

Retrospective review of all cases diagnosed as BCG adverse reactions in a paediatric center during 2009-2018. Until May 2015, BCG vaccine was given to all newborns in Portugal, and since then only in defined risk groups.

Results:

100 children were diagnosed with BCG adverse reactions. 90% had lymphadenitis: 72% axillary, 8% supraclavicular and 7% axillary+supraclavicular. 10 presented with rare clinical manifestations: 6 osteomyelitis/arthritis (femur, knee, hand, foot, shoulder, radius), 3 soft tissue infections (thigh, scapular and submentonian regions) and 1 disseminated infection. Median age of appearance was 4M(15d-7Y), in 34% <3M and in 4% >2Y. In 53% there was spontaneous drainage, on average 3M(0-28M) after the first symptoms. Red flags for primary immunodeficiency were present in 10 cases: 1 child with disseminated disease and family history of death in childhood was diagnosed with CGD. In 64% some investigation was done: 36% complete blood count, 29% ultrasound and 18% immunodeficiency screening. There was microbiological confirmation in 4 cases and epithelioid granulomas present in histology in 4. 91% did not receive treatment. 7 cases with atypical location were treated with TB drugs, 5 had surgical drainage and 2 lymph node excision. Average time to resolution was 9M(1-38M).

Conclusions:

Although usually occurring in the first months of life, BCG adverse reactions may have late presentation. Spontaneous drainage is frequent. Most cases resolved without treatment, but some with very slow progression. Axillary lymphadenitis was the most common manifestation, however there may be atypical locations, even in the absence of primary immunodeficiency.

Systematic Review Registration:

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ESPID19-0809
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Risk factors associated with severe rsv lrti in the first year of life in lyon (france): a hospital-based cohort study

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Background and Aims:

As reported by the WHO 33.8 million episodes of RSV LRTI occur annually in children, with 3.4 million hospitalizations. The aim of this study was to identify, from recent RSV seasons, in a catchment population, prognostic factors associated with severe RSV LRTI-infected patients.

Methods:

From November 2016 to February 2017, were prospectively included all patients from Lyon Metropole (catchment population 265 kids < 1 year) admitted to city academic children hospital with microbiologically confirmed RSV infection. . Bronchiolitis severity was defined as requiring respiratory support, associated with blood acidosis (pH < 7.35, PCO_2 > 6.7 kPa) when this support was NHF. The data obtained from medical records were combined with birth certificate information to estimate incidence of RSV-hospitalization per area and month of birth.

Results:

A total of 265 children were included in the study (mean age 3.3 months ± 83 days). Most of the patients included were boys (55%), born during first part of RSV season (October to December for 50.2%), with siblings (mean 2.3 children ± 1.2 at home) and were from families living below the nation median standard of living) (54%). The incidence of RSV-hospitalization in the first year of life during RSV season was 42.5/1000 births and did significantly vary according month of birth and suburb living area. Among them

25 patients (9.4%) had severe RSV LRTI and 240 (90.6%) non severe RSV LRTI. Young age < 3 months ($p < 0.01$) at the admission was significantly associated with severity.

Conclusions:

These results highlight both the frequency and the severity of RSV LRTI, especially for children less than 3 months of age. Pharmaceutical and non pharmaceutical interventions should target this high risk group.

Systematic Review Registration:

N/A

ESPID19-0803
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Acute lower respiratory infections (alri) in pediatrics: influenza season in argentina. Multicenter study

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Background and Aims:

Respiratory disease is 3rd cause of death in Argentina. Influenza vaccine is mandatory for children between 6-24 months. The objectives of this study were to describe the clinical and epidemiologic patterns of ALRI and influenza (IF) infection and to describe factors associated with IF infection.

Methods:

A prospective, multicenter cross-sectional study of patients admitted for ALRI in four Argentina different regions (Buenos Aires province, Buenos Aires city, Rosario and Mendoza) between June and November 2018. Virological diagnosis: RSV, adenovirus(AV), influenza(IF) and parainfluenza(PI) was made by fluorescent antibody assay of nasopharyngeal aspirates or real time-PCR. A multivariate analysis was performed to found independent predictors (IP) of influenza infections factors comparing with others viruses.

Results:

A total of 1,220 ALRI were included; 97,8% tested and 43,8%(523) had positive samples. Viral distribution: VSR:84.1%, IF:7.5%(56% type A, 44% type B), PI:5.5%, AV:2.9%. Median age:8 months (RI=3-17mo). ALRI lethality: 0.1%(2/1220). Influenza vaccination coverage (6-24 months):37% (over 475 vaccination cards evaluated). Influenza(n=39) showed a seasonal epidemic pattern (late winter). Median age:17 months(IR:10-38 months). Age distribution:<6 months(7.7%), 6-23 months(53.8%), 2-5 yo(23.1%), >5 yo(15.4%). Most frequent clinical feature was consolidated pneumonia(66.7%); 49% recorded previous ALRI hospitalization, 21% were born preterm, 69% had comorbidities; 20% required intensive care. No influenza death recorded. From 6-24 months influenza cases (n=21), 16 had vaccination card and 4 had complete influenza vaccine schedule. The following were independent factors of IF infection: age ≥6 months OR:7.1(CI95%=2.1-23.9)p<0.001 and pneumonia as clinical presentation OR:3.49(CI95%=1.6-6.9)p<0.001.

Conclusions:

Half of IF cases had <17 months of age but 23% had 2-5 yrs (group of age involved in transmission). IF was distributed equally between types and it was more associated with children ≥6 months of age and pneumonia.

Systematic Review Registration:

N/A

ESPID19-0786
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Seroprevalence of mumps antibodies in the czech population and impact on immunization schedule

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Background and Aims:

Mumps outbreaks, especially in adolescents and young adults, have been reported in the Czech Republic. The aim of the presented study was to determine the seroprevalence of specific IgG antibodies against mumps in the adult population of the Czech Republic.

Methods:

The study was designed as a multicenter serological survey of adults aged 18 years and over. Specific IgG antibodies against mumps were detected in blood samples using an enzyme-linked immunosorbent assay (ELISA).

Results:

A total of 1,911 serum samples were examined. The overall seropositivity reached 55.3%. In individual age groups, the highest seropositivity 63% (63.5–65.2%) was recorded in adults aged 40 years and over; the lowest seropositivity was found in adults aged 18–29 years (27.4%). The difference in seropositivity rate between the 18–29 years age group and the 40 years and over age groups was statistically significant ($p < 0.001$). Only the 18–29 years age group included both vaccinated and unvaccinated (born in the pre-vaccine era) individuals. In vaccinated individuals, seropositivity was reported in only 19.1% of persons; in unvaccinated individuals, seropositivity reached 48.2%.

Conclusions:

Our results demonstrate the long-term persistence of antibodies following natural infection and the decrease in seropositivity that occurs after vaccination over time. This immunity waning may account for the higher susceptibility of adolescents and young adults to mumps. Based on seroprevalence studies and mumps surveillance data, the NIP was modified since 2018 in the Czech Republic.

Systematic Review Registration:

NA

ESPID19-0730
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Educative intervention on infectious disease and hiv in adolescent with hiv infection. Identifying and training "peer supporters". Smac study

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Background and Aims:

Antiretroviral treatment may interrupt HIV transmission, although new HIV cases are still occurring in Europe. Emotional frailty in HIV patients is constantly sustained by fear of discrimination and isolation. This may bring patients especially adolescents and young adults to refuse to correctly take ART. It appears imperative to analyze emotional status in HIV adolescent and young adults as well as invest on reducing discrimination in society by specific educational strategies. Like in other chronical diseases the investment in peer supporter strategies it's essential.

Methods:

49 perinatally HIV adolescents were investigated for cognitive, emotive and adaptive behavior. 22 patients was selected in two age groups: **10** from 14 to 18 and **12** from 18 to 30 y received an educational intervention on hygiene, health care, disease transmission and HIV. A questionnaire was administered pre and post course also to the other 27 HIV patients. Social platform and slide kit material was composed . Selection criteria to identify Peer Supporter was tested.

Results:

Preliminary data analysis of the 22 patients showed that 65% had mild anxiety distress, a greater empowerment resources and the awareness of health and diseases . The idea of "being taken care of" outside routine visits is already resulting in a willingness of patients to face medical and psychological related issues .

Conclusions:

Pediatric HIV infection still represents a life-long sentence. It appears crucial to draw and define therapeutic programs which goals are not only rapid virological suppression but also a serene self-awareness and acceptance of the disease that can one day bring to interruption of stigma and disclosure of diagnosis. Peer supporter could be integrated in the system that may bring an interruption of viral spread.

Systematic Review Registration:

SMAC study Thanks to Gilead

ESPID19-0729
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Viral health associated infections in a south london tertiary hospital neonatal unit

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Background and Aims:

Hospitalised neonates represent a population particularly at risk of Healthcare Associated Infection (HAI). Respiratory viral HAI (RV-HAI) in neonatal units are likely underdiagnosed, since testing for viral pathogens is not systematic. This study aimed to describe the epidemiology of RV-HAI in a Neonatal Unit at a tertiary level Hospital, between January 2013 and May 2018.

Methods:

Retrospective descriptive single centre cohort study of patients with a microbiologically confirmed RV-HAI, during their admission at the Neonatal Unit, from January 2013 to May 2018. Data was collected from the clinical and microbiology records, using a secure web-based instrument (REDCap). Variables included demographic and clinical data, diagnostics, virology results and outcomes.

Results:

77 cases were identified. 81.4% of cases occurred in the Neonatal Intensive Care Unit vs in the non-high dependency unit. The mean annual incidence was 2.3% (viral HAI/total admissions a year), with a peak in 2016 (20 cases, annual incidence 2.9%). Most cases occurred during the winter season (38.9%). The mean gestational age was 32 weeks (min 24, max 41; SD 6.4). The median days of admission prior to the positive viral PCR was 48 days (Min 1, Max 211; IQR 6-146). Respiratory symptoms and signs were documented in 71.4% of cases. Rhinovirus was the most common pathogen (54.6%), followed by RSV (7.8%). At diagnosis, 13% of the cases required mechanical ventilation whereas 32% were on CPAP. Most patients (68.1%) were still admitted 30 days after diagnosis.

Conclusions:

The incidence of RV-HAI was relatively low. A higher burden of infections was found among high risk neonates with Rhinovirus being the most common isolated. The detection of RV-HAI can support infection prevention and control measures, as well as antibiotic stewardship programs.

Systematic Review Registration:

N/A

ESPID19-0723
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Luxembourg 2018 vaccination coverage survey performed in children aged 25 to 30 months

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Background and Aims:

In Luxembourg, all vaccines recommended according to the universal immunisation schedule are provided free of charge at the point of care. This fifth survey aims at evaluating the national vaccination program among infants and toddlers, and to identify potential variations between groups of different national origins, in a population counting 48% foreign nationals.

Methods:

This survey was conducted from February to August 2018 on toddlers aged 25 to 30 months living in Luxembourg, on a random sample stratified by nationalities taken from the National Registry. A self-administered questionnaire was sent to parents and a copy of their child's vaccination card was requested to assess their immunisation status. Descriptive analyses identified the overall coverage as well as differences in vaccination coverage between groups of different nationalities.

Results:

Among the sample of 732 children, 472 participated in the survey (64.5%). 74.4% (95% CI: 70.4 – 78.3%) of the children received all vaccines recommended according to the 2018 scheme. This represents a slight improvement compared to the results of the previous survey (71.6%; 95% CI: 67.8 – 75.1%). Vaccination coverage greater than 95% was found for HBV, PCV13 and MenC. For the other vaccines, including MMRV, vaccine coverage approached 90%. Significant differences in overall immunisation coverage as well as for specific vaccines such as DTaP, IPV, Hib, HBV, PCV13, MenC and RV2 vaccines were observed between selected national origins, with higher coverage in Luxembourgish and Portuguese groups (P-value < 0.05).

Conclusions:

Full immunisation coverage of infant and toddlers according to the Luxembourg vaccination scheme reaches 74.4% in 2018, despite the multicultural background of the children in the sample. Continuing immunization coverage assessment is warranted to guide a rational approach to vaccination policy in Luxembourg.

Systematic Review Registration:

N/A.

ESPID19-0707
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Antibiotic resistance prevalence in bloodstream isolates from high-complexity paediatric units in madrid (spain): 2013-2017

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Background and Aims:

Increase in antibiotic resistance is becoming a threat. Although data about isolates from adults are broad, there are scarce for children. We aimed to describe antibiotic resistance prevalence in bloodstream isolates from high-complexity paediatric units in Madrid over a 5 year-period.

Methods:

From January 2013 to December 2017, all Enterobacterales, *Staphylococcus aureus*, *Enterococcus* spp., and *Pseudomonas aeruginosa* isolated from bloodstream in <18-year-old patients admitted to Paediatric Intensive Care, Neonatal or Oncology-Haematology wards at three tertiary referral hospitals in Madrid (Spain) were evaluated. The same isolate within 14 days of a previous one was excluded. Isolates with resistance or intermediate susceptibility were classified as non-susceptible according to EUCAST breakpoints.

Results:

A total of 770 isolates were included (436 Enterobacterales, 198 *Enterococcus* spp., 78 *S. aureus*, and 58 *P. aeruginosa*). The prevalence of multidrug-resistant (MDR) Enterobacterales was 6.9%; non-susceptible to aminoglycosides 30.7%, extended-spectrum cephalosporins (ESCs) 13.6%, fluoroquinolones 10.4%, and 3.7% to carbapenems. The prevalence of MDR *P. aeruginosa* was 22.4%; non-susceptible to carbapenems 31%, to fluoroquinolones 31%, to aminoglycosides 28%, and to antipseudomonal ESCs 22%. The prevalence of *Enterococcus* spp. non-susceptible to ampicillin and vancomycin was 15% and 3%, respectively. The prevalence of methicillin-resistant *S. aureus* (MRSA) was 5%. Overall, the prevalence of non-susceptible isolates over the study period was stable (figure), with a non-significant increase in Enterobacterales non-susceptible to fluoroquinolones (6.8% to 12.6%,p=0.063), and a non-significant decrease in MRSA (14.3% to 0%,p=0.134).

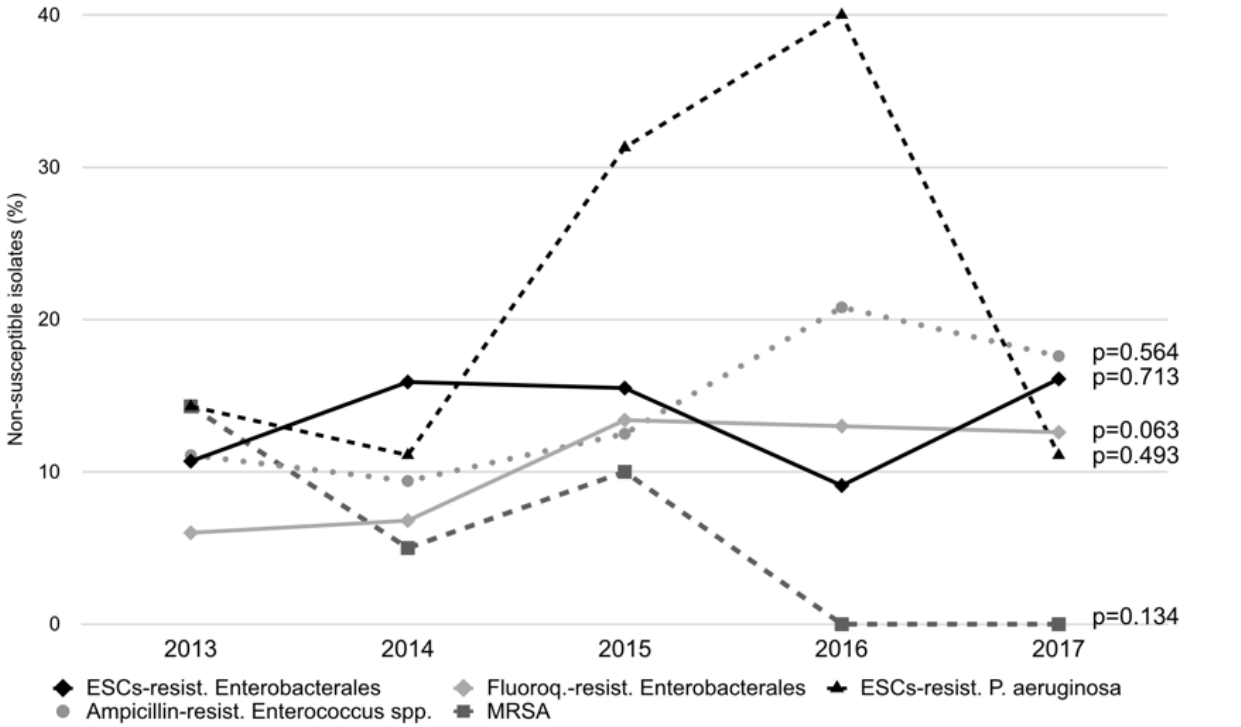

Fig. 1. Prevalece of antimicrobial non-susceptible isolates. P-value calculated using χ^2 test for linear trend. ESCs, extended-spectrum cephalosporins (antipseudomonal in the case of *P. aeruginosa)*; MRSA, methicillin-resistant *S. aureus*

Conclusions:

The prevalence of bloodstream isolates non-susceptible to antibiotics from high-complexity paediatric units was very high. Overall, resistance to antimicrobials has remained stable over time, but the increased prevalence of fluoroquinolone resistance among Enterobacterales is worrisome. It seems important to create a surveillance network to improve the antibiotic therapy in these units.

Systematic Review Registration:

ESPID19-0682
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Rotavirus genotypes after implementation of national immunization program against rotavirus in estonia

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Background

Estonia implemented national immunization program (NIP) against rotavirus in July 2014 with pentavalent vaccine, replaced by monovalent vaccine in October 2015. We aimed to compare the distribution of rotavirus genotypes after implementation of NIP (post-vaccine era) and prior to NIP (pre-vaccine era).

Methods

Stool samples from children (<5 years) with laboratory confirmed rotavirus gastroenteritis hospitalized between 01.01.2007-31.12.2008 to three Estonian paediatric hospitals (pre-vaccine era) and children (0-18 years) with laboratory confirmed rotavirus gastroenteritis hospitalized between 01.02.2015-31.08.2017 to seven Estonian hospitals (post-vaccine era) were genotyped by multiplex-PCR. In post-vaccine era, updated consensus primers and G3-, G9-, P[11]-specific primers and additional primers for G10, G12 were used compared with pre-vaccine era.

Results

Rotaviruses from total of 124 (72 in 2007, 52 in 2008) and 493 (374 in 2015, 119 in 2016) stool samples from pre-vaccine and post-vaccine era, respectively, were genotyped. Less rotaviruses were typeable in pre-vaccine than post-vaccine era (66.1% vs 96.1%). Five commonest genotypes G1P[8], G2P[4], G3P[8], G4P[8], G9P[8] caused most infections in pre-vaccine and post-vaccine era (57.3% vs 73.4%). The commonest genotypes were G2P[4] in 2007 (52.8%), G4P[8] in 2008 (26.9%) and 2015 (39.3%), G9P[8] in 2016 (37.8%) (Figure). Genotypes other than the five commonest caused largest proportion of infections in 2016 (39.5%; mostly G2P[8] (6.7%), G4P[4] (10.9%), G9P[4] (9.2%)). Diversity of G-genotypes (95.8% vs 97.8% of rotaviruses in pre- and post-vaccine era were G-genotypeable, respectively) in terms of Simpson's index of diversity (95% confidence interval) was similar in pre-vaccine (0.72; 0.67-0.76) and post-vaccine era (0.78; 0.75-

0.79).

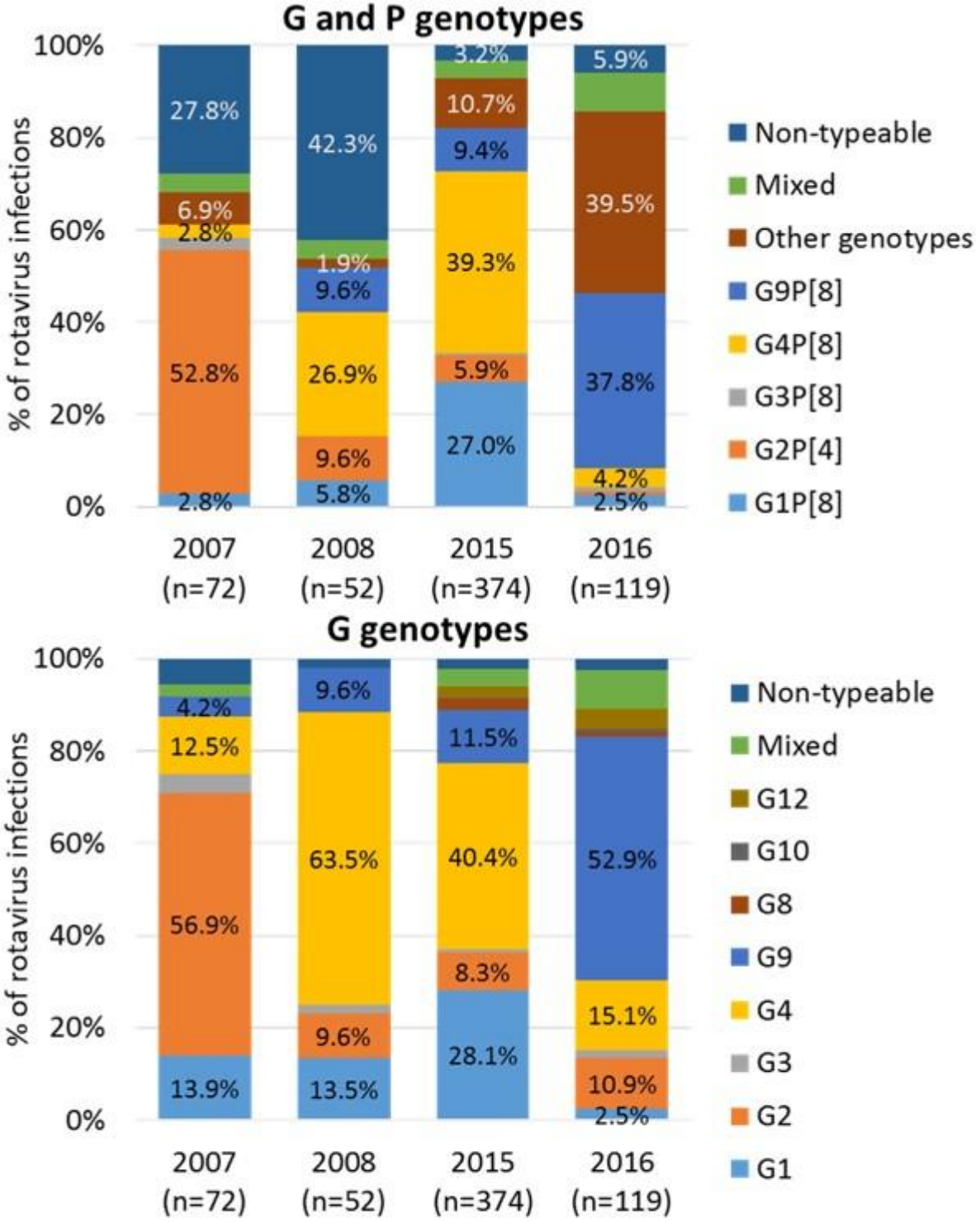

Figure. Distribution of G and P genotypes (upper panel) and G genotypes (lower panel) in 2007-2008 (pre-vaccine era) and 2015-2016 (post-vaccine era).

Conclusions

After implementation of NIP against rotavirus large proportion of rotavirus infections is still caused by five most common genotypes and genotypic diversity is similar to pre-vaccine era, suggesting no outselection of non-vaccine genotypes.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0678
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Detection and sequencing of zika virus in normocephalic newborns with congenital zika infection

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Background

In 2015, Brazil has experienced an unprecedented Zika virus (ZIKV) outbreak and later that year, an unexpected outbreak of newborns with microcephaly occurred in major cities in northeastern Brazil, associated with Congenital Zika Infection (CZI). Most descriptions and publications regarding CZI focus on the clinical presentation of newborns and infants with microcephaly. Scarce information is available concerning CZI without microcephaly.

Case Presentation Summary

During hospital surveillance for CZI in a reference maternity hospital, we identified 14 normocephalic newborns with confirmed CZI. The majority of mothers (60%) reported ZIKV symptoms during the first trimester of pregnancy. Eight (57%) of the newborns were female and the mean gestational age at birth was 38.46 ± 1.90 weeks. The mean of head circumference was 38.57 ± 1.40cm. The transfontanel ultrasonography was performed in 13 (92.9%), and no alterations were observed in any of the cases. All newborns had a positive RT-PCR confirming the diagnosis of CZI, mostly in urine samples (57%). In two of the cases, ZIKV were detected in 2 distinct samples. ZIKV-specific RT-PCR amplification products have been obtained and NS5 gene fragments (426-bp) were obtained using Sanger sequencing. The phylogenetic analysis showed that the isolate belongs to the Asian genotype and clusters closely with strong bootstrap support (>90%) with sequences isolated in Northeast and Northern regions of Brazil.

Learning Points/Discussion

With this, we infer that CZI could present in a broad spectrum of clinical manifestation, including the asymptomatic presentation at birth. It is necessary careful surveillance to identify cases with few or no symptoms at birth and a close follow-up for early detection of clinical manifestations of CZI and timely intervention.

ESPID19-0667
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Meningococcal hypervirulent strains and clinical manifestations in chilean children

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[2]Hospital de niños Dr Exequiel Gonzalez Cortes, Pediatric Infectious Diseases, Santiago, Chile
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Background and Aims:

Meningococcal hypervirulent serogroup W ST11 clonal complex (CC) strain has been associated with an increase in overall incidence and case fatality rate (CFR) in Chile since 2012. Comparative information regarding clinical manifestations among meningococcal strains is lacking. The aimof this study was to determine the relationship between hypervirulent strains of *Neisseria meningitidis* and clinical manifestations in pediatric patients

Methods:

Retrospective study in patients younger than 15 years, admited by meningococcal disease (MD) at three children's hospitals, between 2008 and 2015, whose strains were available at Public Health Institute. Genetic analysis based on multiple gene polymorphisms (MLST) and determination of CC were performed. Demographic and clinical information were collected from the patient files

Results:

85 patients were enrrolled. Infants:50, 1-5 yoa:22, and >5 yoa:14; males:64%; and 21% had comorbidities. MD was suspected in 10.5% of cases at first consultation. 70% required admission to PICU. CFR reached 10.6%. CC determination: ST11:49, ST41/44:15, ST32:5 and others: 2. ST32 was associated with petechiae ($p < 0.001$), symptoms onset <24 hrs ($p = 0.017$) and suspicion of MD at first consultation ($p < 0.001$). ST11 showed a notorius trend for diarrhea (20%) and lower presence of petechiae. FHbp allele gene identification was achieved in 51 patients, 70.6% corresponding to allele 22, which was associated with a lower presence of petechiae (13.9%). No other differences were found

Conclusions:

Presence of diarrhea and absence of petechiae could contribute to a low clinical suspicion at first consultation for MD. Although CFR is lower in children than adults, it is still high and frequently requires management at PICU. CC and MLST determination profiles could help us in understanding the clinical presentation, severity and evolution of patients with MD

Systematic Review Registration:

aa

ESPID19-0633
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Impact of 7- and 13-valent pneumococcal conjugated vaccine on pneumococcal serotype variability and susceptibilities to antibacterials in crete, greece

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Background and Aims:

Introduction of PCV7 and, more recently, of PCV13 was related to decreased *S. pneumoniae* morbidity and serotype replacement. We investigated the effect of PCV7 and PCV13 (introduced in our area in 2004 and 2010, respectively) on the serotype distribution and susceptibilities to antibiotics.

Methods:

This study covered the 20-year period 1999-2018, divided in three periods: pre-PCV7 (1999-2004), PCV7 (2005-2010) and PCV13 (2011-2018). It included all *S. pneumoniae* clinical isolates from children in the major healthcare facility of Crete.

Results:

A total of 382 *S. pneumoniae* isolates were included. PCV7-included serotypes decreased as compared to non-PCV7-included from the pre- to the post- PCV7 period (1999-2004, 2005-2018): 110/49 versus 68/155 ($p<0.0001$; OR 0.19, 95% CI 0.1-0.3); and mainly 6B (OR 0.40, 95% CI 0.19-0.84;$p=0.015$), 9V (OR 0.26,95% CI 0.07-0.7;$p=0.008$), 19F (OR 0.36, 95%CI 0.2-0.6;$p=0.0002$) and 14 (OR 0.23, 95%CI 0.2-0.9;$p=0.023$). In the post-PCV13 period significant decrease was observed for serotype 7F ($p=0.015$; OR 0), however increase of serotype 3 was noted ($p=0.04$; OR 1.93, 95% CI 1.03-3.60). Non-PCV included strains increased after the introduction of both vaccines, especially for strains 11A, 12F, 15A and 17F. Pan-susceptibility rates have increased from the first to the last period from 32.9% to 62.8% (OR 4.48, 95% CI 2.68-7.5) with reduction of multi-resistant strains (from 33.5% to 13.4%; OR 0.31, 95% CI 0.16-0.58). High resistance levels were noted against all macrolides (27.2-36.6%) and tetracycline (22.4%). All strains were susceptible to cefotaxime/ceftriaxone.

Conclusions:

Decrease in the PCV7-included serotypes was observed after the PCV7 introduction, whilst further surveillance is required for PCV13 serotypes. Vaccination was associated with increase of non-PCV strains, especially in the post PCV13 period. Both PCV7 and PCV13 were associated with decreased antibiotic resistance rates.

Systematic Review Registration:

NA

ESPID19-0568
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Peritoneal dialysis for children with malaria-related acute kidney injury in blantyre, malawi: a case series

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Background

Acute kidney injury (AKI) is a severe complication of malaria and a predictor of poor outcome. The burden of paediatric malaria-related AKI in low income settings is considerable and access to dialysis is often limited. Peritoneal dialysis (PD) treatment can bridge the time to recovery from AKI in order to prevent death from AKI-related electrolyte imbalances, fluid overload and uraemia.

Case Presentation Summary

We describe 9 patients who presented to Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi with Plasmodium falciparum malaria and dialysis-requiring AKI in the period from January 2016 to May 2017.

All 9 children, aged between 5 and 13 years, received peritoneal dialysis. The duration of PD treatment ranged from 3 to 28 days. Three (33%) patients had significant complications of PD: one patient had severe bleeding after the PD catheter insertion, two patients needed a PD catheter change because of infection or leakage. Six patients (67%) recovered kidney function and were discharged in good condition. One patient died after 3 days of PD, the death was unrelated to dialysis. In two patients, PD treatment was withdrawn after 23 and 28 days, respectively, because there was a strong suspicion of chronic kidney disease without signs of recovery. Chronic dialysis for children was not available at QECH at this time.

Learning Points/Discussion

AKI is a treatable complication of malaria and needs to be detected. We want to emphasize the importance of measuring urine output and serum creatinine in sick children with severe infection in resource-poor settings. Acute peritoneal dialysis is a life-saving treatment and can be delivered at low costs.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

A global plan to defeat meningitis: defining meningitis baseline estimates to monitor progress to 2030

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Background and Objective

Despite major advances in meningitis prevention over the past 20 years, much remains to be done. To accelerate progress, WHO have launched the Defeating Meningitis by 2030 initiative. As part of the meningitis taskforce we aimed to define the current burden of meningitis so that progress can be accurately monitored.

Methods

Meningitis estimates from the following models were compared: 1) Institute for Health Metrics and Evaluation GBD2017, 2) WHO Global Health Estimates 2016 (published 2018), 3) Maternal Child Epidemiology Estimation (MCEE)/ Johns Hopkins University (JHU) Child Mortality estimates (published 2018), 4) MCEE/JHU *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* (Spn) meningitis estimates in children (published 2018).

Learning Points Discussion

Our comparison demonstrated that:

- GBD2017 estimated there to be over 144,000 deaths in 2015 from meningitis in 1-59 month old children compared to WHO GHE's estimate of only around 95,000
- There was agreement that deaths due to meningitis are declining but at a slower rate than many other vaccine preventable diseases
- Mortality, incidence and proportions of meningitis deaths attributable to Spn and Hib in children aged 1-59 months differed substantially between GBD2017 and MCEE/JHU estimates
- Trends from modelled estimates in the countries within the meningitis belt differed from WHO enhanced surveillance estimates from those countries
- A high proportion of global child deaths (over 90% in one model) are based on verbal autopsy data leading to considerable uncertainty in these estimates

Differences in meningitis estimates across different initiatives make it difficult to define the current burden of disease. Further work to improve models is necessary to robustly define the current burden of disease and measure progress towards defeating meningitis by 2030.

ESPID19-0532
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Molecular characterization of streptococcus pyogenes strains isolated from vietnamese children during the scarlet fever outbreaks in asian countries

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Background

After the long period of decreasing scarlet fever incidence, a dramatic increase of scarlet fever outbreaks was noted in Asia during the past 10 years, including South Korea, Hong Kong, mainland China, among others. Goal of the study was to characterize *Streptococcus pyogenes* strains isolated from children in different Vietnam provinces in 2011-2015.

Methods

Bacterial DNA was isolated by phenol/chloroform extraction. *emm*-typing was done as recommended by the Centers for Disease Control and Prevention. PFGE, RAPD and PCR analyses were done as previously published. All strains were tested for susceptibility to erythromycin and tetracycline. Whole genome sequencing was done using MiSeq technology.

Results

S. pyogenes strains were isolated from 49 of 1359 (3,6%) examined children. *emm*-typing revealed different *emm* types, although *emm*12 was found to be predominant and specific for 14 of 49 (28,6%) *S. pyogenes* strains. All *emm*12 strains were resistant to tetracycline and MLS-antibiotics. Phylogenetic analysis of *emm*12 strains demonstrated that most of them belonged to the same clonal lineage, although strains were isolated in different regions of Vietnam. This clonal lineage was identical to genetic lineage of streptococci isolated during *emm*12 streptococcal scarlet fever outbreak in Hong Kong. Whole genome sequencing of *emm*12 Vietnamese strain revealed the presence of 61028 bp fragment homologous to integrative and conjugative element ICE-*emm*12 containing resistance genes to MLS-antibiotics and tetracycline. In all the strains ICE-*emm*12 was present in two forms: integrated linearized form and excised circular form with potential to be horizontally transferred.

Conclusions

The wide spreading of *emm*12 *S. pyogenes* strains containing ICE-*emm*12 genetic element and associated with streptococcal outbreaks in South East Asia, indicates the need of molecular epidemiological surveillance for circulation of these strains in other parts of the world.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0505
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Limitations of passive surveillance systems in the context of pneumococcal conjugate vaccines

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Background and Objective

Recent data suggest that the overall impact of currently available paediatric pneumococcal conjugate vaccines (PCVs) on invasive pneumococcal disease and pneumonia are comparable. Therefore, more countries consider opening competition between PCVs to generate savings. National passive surveillance systems monitor the effect of PCV introduction but are susceptible to biases.

Methods

We discuss potential limitations of passive surveillance systems for evaluation of PCV impact based on global literature and surveillance reports publicly available by end 2018.

Learning Points Discussion

- While passive surveillance systems are very valuable for monitoring disease patterns, we need to consider potential biases which may affect data interpretation, especially in case of vaccine changes (vaccine switch, implementation of a new program):
  - Underreporting of disease cases, consequently limiting the precision and representativeness of disease trends
  - A vaccine change can raise awareness, leading to increased reporting rates
  - Several confounders (e.g. flu season, changes in flu vaccine effectiveness, pneumococcal vaccination in the elderly) could influence the susceptibility of the population to pneumococcal disease
  - Changes in healthcare seeking behaviors and diagnostic´s sensitivity can influence reporting rates and proportion of cases, while changes in vaccine uptake can complicate assessment of vaccine impact
  - Vaccine transition periods are difficult to interpret due to mixed schedules and indirect effects from the previous vaccine
  - Short observational periods may prevent discrimination of vaccine impact from vaccine-independent trends
- When surveillance data are used to make decisions or to estimate epidemiological parameters, it is very important to understand when, where and how to extrapolate these data, and whether they accurately reflect changes in disease.
- Therefore, to understand the impact of a vaccine change, an existing stable surveillance system should be in place, avoiding any modifications which would make results difficult to interpret.

Funding: GlaxoSmithKline Biologicals SA

ESPID19-0496
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Etiology of gastroenteritis among children admitted to hospital.

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Background and Aims:

Acute diarrheal diseases are a great public health problem that leads to morbidity and morality of children particularly in developing countries and even in developed countries. It can be associated with vomiting-gastroenteritis form, and with fever.The aim of this study was to determine the etiology of acute diarrhea in young children admitted in pediatric infection diseases department of our hospital.

Methods:

This is a retrospective study. A total of 345 cases of acute diarrhea mainly in children below 5 years of age admitted at tertiary care pediatric hospital in university center: "Mother Theresa" over the period 2011-2013, were included in the study. Medical history, diarrhea symptoms, treatment prior to hospitalization and demographics were obtained from medical records. Stool sample were analysed for parasites, rotavirus and enteric bacteria.

Results:

The mean age with diarrhea was 20 months.191 cases(55.4%) were male.16 cases(4.6%) live in no good conditions,129(37.4%) in moderate and 200(58%) in good one. A single enteric pathogen was detected in 53.3% of children. Eight out of 11 bacterial(72.7%) pathogens were Salmonella enteritidis isolated in children above one year and 3 pathogens were Pseudomonas aeruginosa isolated in children less than one year. The prevalence of intestinal parasites Giardia Lamblia (4.6%), Entamoeba hystiolitica 8.4%,Criptosporidium spp1.7%, was significantly higher among children 1-4 years.87(25.2%) cases had one episode of diarrhea, 238(69%) repeated one.

Conclusions:

Etiologic data on diarrheal diseases are important tools for clinical management , control strategy and prevention. In Albanian children as a developing country acute diarrhea is very frequent and the most common symptoms that often lead to severe dehydration. Therefore is essential the introduction of rotavirus vaccine in the routine vaccination scheme, improvement of family hygiene, control of drinkable water system .

Systematic Review Registration:

N/A

ESPID19-0492
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Reasons for the low hpv vaccination coverage and intention to menacwy vaccination among adolescents and their parents in the netherlands

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Background and Aims:

Since 2015, the HPV vaccination coverage among female adolescents has decreased from 61% to 45.5% in 2017. In autumn 2018, a new MenACWY-vaccination was introduced for adolescents to stop the increase in the number of patients with meningococcal W disease. Reasons not to vaccinate against HPV and the intention to receive MenACWY-vaccination were studied.

Methods:

In March/April 2018 a survey was performed among parents of girls (born in 2003) who were invited for HPV vaccination in 2015 (N = 554 (7%)). In November 2017 a survey about MenACWY-vaccination was sent to adolescents of 14 years of age (N = 115) and parents (N = 106) of which 57 adolescent-parent pairs.

Results:

Parents reported they worried about side effects of HPV-vaccine (40%), had doubts about HPV-vaccine effectiveness (12%), had too few information about HPV-vaccination (10%) and heard negative stories about HPV-vaccination (10%).

Among adolescents, 61% had a positive intention to get MenACWY-vaccination, and 83% reported meningococcal disease is a serious disease, which was 70% and 91% among parents, respectively.**Conclusions:**

The intention in our survey was lower than the percentage of adolescents who received MenACWY-vaccination according to preliminary figures (83.6%). Both adolescents and parents perceived meningococcal disease as a serious disease despite a low chance of getting it. The MenACWY-vaccination campaign and positive media attention (especially about the seriousness of meningococcal disease) might have had a positive impact on HPV vaccination coverage. During the MenACWY-vaccination campaign, there were also girls who asked for the HPV vaccination. Whether the MenACWY campaign played a role in changes in worries about side effects of HPV-vaccination or other reasons needs to be further investigated.

Systematic Review Registration:

N/A

ESPID19-0482
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Enterovirus d68 seroepidemiology in taiwan in 2017

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Background

Enterovirus D68 (EV-D68) was discovered in 1962 and had unique characteristics as compared with other enteroviruses. There were only 699 documented cases before the epidemic in the United States in 2014, when more than 2000 cases were reported around the world and an increase of acute flaccid myelitis. Taiwan Centers for Diseases Control also confirmed EV-D68 has been endemic in Taiwan. To understand current EV-D68 serostatus, we performed EV-D68 seroepidemiology study in Taiwan in 2017.

Methods

After informed consent was obtained, we enrolled preschool children, 6–15-year-old students as well as women of childbearing age and adult males. They received questionnaire investigation and blood sampling for measuring EV-D68 neutralization antibody against a local circulating strain.

Results

Totally, 920 subjects were enrolled from the northern, central, southern and eastern part of Taiwan with a male-to-female ratio of 1.03. EV-D68 seropositive rate was 32% (26/82) (range: 14%–41%) in infants (which was presumably to derive from maternally transferred antibodies), 18% (27/153) in 1-year-old children (range: 11%–26%), 43% (36/83) (range: 11%–61%) in 2-year-old children, 60% (94/156) (range: 48%–71%) in 3–5-year-old children, 89% (108/122) (range: 81%–96%) in 6–11-year-old primary school students, 98% (118/121) (range: 94%–100%) in 12–15-year-old high school students, 100% (122/122) in 16–49-year-old women of childbearing age and 100% (81/81) in adult male in 2017. The seropositive rate varied among different geographic regions. Female tended to have higher seropositive rate than male (71% vs 63%, $p<0.01$).

Conclusions

EV-D68 infection was prevalent in Taiwan and its seropositive rates increased with age.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0453
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

No relationship between changes in organisational aspects regarding vaccination within youth healthcare and development in number of vaccinated children 2013-2017

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Background and Aims:

In recent years, slightly fewer children in the Netherlands have been vaccinated within the National Immunisation Programme (NIP); the decrease was stronger for the HPV vaccination (girls only). No definite explanation has yet been found. There were signs that parents visit child health clinics less often and see this as less self-evident. Therefore, the RIVM has investigated whether organisational changes in youth health care (JGZ) were related to the declining trend in vaccination coverage.

Methods:

By means of a questionnaire study (digital survey plus Excel-file) among JGZ organisations, supplemented by information from JGZ websites and data provided by the NIP department of RIVM, various organisational aspects with a possible link to vaccination uptake have been studied. A total of 33 questionnaires (77%) and 21 Excel sheets were received (64%).

Results:

JGZ organisations had a stable and high reach for infants (≥95% in 2013-2016). The number of child health clinics has fallen sharply (~40% in 2000-2017). However, the average distance to a clinic has remained the same (~2 km), and opening hours have expanded in the same period. The number of contact moments is becoming more flexible or reduced (i.e., only offered if there are concerns about the child or at parent request, and in different form such as digitally). The distance to a HPV vaccination location is about 5.5 km, and this has remained the same before and after the decrease in HPV vaccination coverage.

Conclusions:

Based on the available data, changes in the studied organisational aspects of JGZ do not appear to be related to the decrease in vaccination coverage. For the future, it is useful to collect these data at a regular base and with higher response.

Systematic Review Registration:

N/A

ESPID19-0434
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Hepatitis a in serbia - is universal childhood vaccination needed?

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Background and Aims:

Current recommendations call for universal childhood immunization against hepatitis A virus (HAV) in countries with intermediate endemicity. Endemicity assessment is based on estimated seroprevalence of anti-HAV antibodies, a biomarker particularly important in children given the commonly asymptomatic course of HAV infection in childhood. We determined the age-specific anti-HAV seroprevalence in Vojvodina Province, Serbia so as to identify susceptible age groups and guide vaccination policy decisions.

Methods:

We tested a representative serum bank of 3466 residual samples (1732 males/1734 females, age range: 1-83 years) collected in 2015-16 according to the specifications of the European Sero-Epidemiology Network 2 (ESEN2) project, for anti-HAV with an enzyme immunoassay (ADVIA Centaur HAV Total Assay). Relationships between anti-HAV positivity and demographic features of study subjects were examined by univariable and multivariable analyses.

Results:

Seropositivity (17% overall) increased with age, the only demographic variable independently associated with an HAV-seropositive status. Anti-HAV seroprevalence in one-year-old infants (15%) declined in the second year (5%) of life. By the time of school entry (6/7 years), only 1%-3% of children were immune. Seropositivity fluctuated around 10% until the age of 30. Natural infection provided immunity for a 31% and 57% of people in their 40s and 50s, respectively. Hence, the majority of children and adults < 40 years are susceptible to HAV and prone to a more severe disease course.

Conclusions:

The new national legislation recommends vaccination against HAV for high-risk groups in ≥ 16-year-old children and adults starting from 2019. The obtained HAV seroprofile in conjunction with the low incidence of hepatitis A (<5/100,000 population) in the past five years (2013-2017), place Serbia among the very low endemicity countries, supporting the current policy that does not recommend universal childhood vaccination

Systematic Review Registration:

N/A

ESPID19-0420
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Impact of acute watery diarrhea on the clinical presentation of severe malnutrition in under five bangladeshi children

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Background

Malnutrition in children is a major problem in South-East Asia. Malnourished children have increased risk of infection; and diarrhea is the commonest among them. Diarrhea is the second leading cause of death and accounts for nearly 9% of 5.9 million global deaths in children estimated in 2015. However, recent data on association of diarrhea and severe malnutrition are limited. We attempted to evaluate the impact of diarrhea on malnourished children and tried to identify the independent risk factors.

Methods

This was a prospective cohort study that recruited severely malnourished children of either sex, younger than 5 years, who were admitted to inpatient wards of the Dhaka Hospital of icddr,b from April 2011 through June 2012 with or without acute watery diarrhea (AWD). The study was approved by the Institutional Review Board of icddr,b.

Results

Among the 407 eligible children, 306 children had AWD. Death was proportionally higher in severely malnourished diarrheal children compared to those without diarrhea. In a univariate analysis, children with diarrhea more often presented with vomiting (OR: 9.90, 95% CI: 2.36-41.44, p<0.001), fast breathing (OR: 0.53, 95% CI: 0.34-0.859, p=0.01), hypernatremia (OR: 11.27, 95% CI: 1.51-83.66, p=0.001), hypokalemia (OR: 2.57, 95% CI: 1.50-4.42, p<0.001), hypocalcemia (OR: 2.68, 95% CI: 1.42-5.06, p=0.002) and metabolic acidosis (OR: 5.97, 95% CI: 3.34-10.66, p<0.001) than those without diarrhea. In multivariate analysis, after adjusting for potential confounders, vomiting (OR: 7.38, 95% CI: 1.70-32.08, p<0.001) and metabolic acidosis (OR: 4.19, 95% CI: 2.28-7.71, p<0.001) are independently associated with AWD.

Conclusions

Findings revealed that diarrheal children who had severe malnutrition were more likely to present with vomiting or metabolic acidosis at admission.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0416
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Characteristics of diarrheoal infants having acute kidney injury: report from the world's largest diarrhea hospital

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Background

Identification of AKI by laboratory investigation may be time-consuming and expensive in low resource settings, which may delay the treatment and thereby increase the risk of death. On the other hand, identification of simple clinical features might help in the earlier prediction of AKI in infants. Thus, the objective of our study was to describe the characteristics and associated clinical features of AKI in infants with diarrhea.

Methods

This was an unmatched case-control study. Diarrheal children aged 0-12 months, admitted to Dhaka Hospital of the International Centre for Diarrheal Disease Research, Bangladesh (icddr,b) from January 2015 to December 2015 and who had serum creatinine measured were enrolled in this study. The infants with raised serum creatinine (>50 µmol/L) constituted the cases (n=146) and randomly selected 150 infants from the remaining children with normal creatinine (≤35 µmol/L) constituted the control group.

Results

Among the 296 patients, 146 (93%) recovered during hospitalization and were discharged. A logistic regression analysis adjusting for potential confounders such as ORS intake at home, convulsions, abnormal mentation and hypoxemia, infants with AKI were independently associated with hypernatremia (OR=8.66, 95% CI=3.90-19.22; p<0.001), sepsis (OR=4.71, 95% CI=2.07-10.73; p<0.001) and dehydration (OR=3.76, 95% CI=1.78-7.95; p=0.001). Persistently raised creatinine was associated with radiological pneumonia (OR=2.16, 95% CI=1.09-4.31; p=0.025) and continued fever (OR=2.24, 95% CI=1.14-4.40 p=0.017).

Conclusions

Infants hospitalized for diarrhea having features of dehydration, sepsis, and hypernatremia should be screened for acute kidney injury so that treatment can be started earlier and AKI related consequences minimized.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0414
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Role of procalcitonin to determine severe bacterial infection in under five malnourished children with severe pneumonia: a prospective study of largest diarrheal disease hospital, bangladesh

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Background

Role of bacterial bio-markers in severely malnourished children with severe pneumonia has not been previously reported in resource-poor settings. The aim of this study was to determine the role of procalcitonin (PCT) to determine severe bacterial infection in severe pneumonia in severely malnourished under five children in Bangladesh.

Methods

This prospective study was conducted in inpatient ward of Dhaka hospital of icddr,b. Clinical characteristics and the isolation obtained from blood and nasopharyngeal aspirates of the patients who has raised PCT were compared to those having normal PCT. Bi-variate analysis was performed to determine associations between potential risk factors and raised PCT. Multivariable logistic regression was used to identify factors independently associated with suspected bacterial infection.

Results

Of 191admitted patients with severe pneumonia, 08 bacterial isolation and 135 viral isolation were yielded. Due to scanty bacterial isolation rate, we identify severe bacterial infection based on high PCT (>0.2 ng/ml) (n=150) with no bacterial infection based on low PCT (<0.2 ng/ml) (n=41). Male gender predominate (61%) and the mean age of the children were 9.82 months (IQR, ±6.97). On multivariable analysis, independent predictors of suspected bacterial infections were parental smoking (aOR=3.37, 95% CI= 1.43-7.95), diarrhea (aOR=3.01, 95% CI= 1.04-8.72), sepsis (aOR=2.72, 95% CI= 1.12-6.60) and CRP (aOR=1.44, 95% CI= 1.11-1.88).

Conclusions

This study showed that in the state of scanty bacterial yield, raised PCT can be used as a good marker to diagnose severely malnourished under five children having severe pneumonia. Alternatively CRP can be used as rapid bio-marker for identifying bacterial infection in severely malnourished children with severe pneumonia and thus initiate antibiotic treatment early.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0390
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

A descriptive longitudinal hospital-based epidemiology study to assess aom incidence density and nasopharyngeal carriage in korean children from birth to 24 months

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Background

This study was conducted to assess the status of nasopharyngeal (NP) carriage and AOM occurrence in Korean children less than 2 years of age, who received pneumococcal conjugate vaccines (PCVs).

Methods

We conducted longitudinal studies through four consecutive visits. At each visit, NP aspirates were obtained and subjects were asked to visit if AOM occurred.

Results

A total of 305 subjects were enrolled and received PCV13 (n=182) or PCV10 (n=123). In the PCV13 group, the NP carriage of *S. aureus* for each visit was 40.6%, 9.8%, 3.8%, and 0.5%, respectively. That of *S. pneumoniae* was 2.7%, 14.8%, 18.7%, and 15.9%. That of *H. influenzae* was 3.3%, 2.7%, 2.7%, and 5.5%, and that of *M. catarrhalis* was 1.1%, 9.3%, 4.9%, and 0.5%. In the PCV10 group, the NP carriage of S.*aureus* was 15.4%, 0.8%, 1.6%, and 0.8%, respectively, That of *S.pneumoniae* was 3.3%, 9.4%, 6.5%, and 4.1%. That of *H. influenzae* was 2.4%, 4.1%, 1.6%, and 0.8%, and that of *M. catarrhalis* was 4.1%, 1.6%, 0.8%, and 0.0%. AOM occurrence in the PCV13 group observed after primary dose and before booster dose was 20.8%, occurrence after booster dose was 11.0%, and the incidence of two or more AOM was 11%. In the PCV10 group, AOM occurrence was 9.7%, 7.3%, respectively, and the incidence of two or more AOM was 2.4%. The predominant *S. pneumonia isolated* were non-vaccine type (10A, 15A, and 15B).

Conclusions

AOM occurrence in Korean children has decreased after the implementation of PCVs, and it was lower in children received PCV10. This seems to be related to changes in ecology that brings a difference in NP carriage after vaccination, especially the difference in *S. pneumoniae* and *H. influenzae.*

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0382
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Vaccine failures after conjugated meningococcal c vaccine. Seasons 2000/2001 to 2017/2018, castilla y leon (spain)

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Background and Aims:

Notification of meningococcal disease (MD) to the Epidemiological Surveillance Net in Castilla y León (CyL) is mandatory and urgent. The CyL Immunization Programm with conjugated vaccine against meningococcal C (MCC) was implemented in 2000 with high coverage (infant schedule plus catch-up of teenagers), associated to a significant decrease in serogroup C (MenC) incidence. Since then and until 2017/18 season, 443 MD cases were notified. Case fatality rate (CFR) for the whole period was 13.1%. 333 cases (75.2%) were laboratory-confirmed, 236 (70.9%) corresponded to serogroup B and 63 (18.3%) to serogroupC.

Methods:

We characterized MCC vaccine failures (VFs) occurred in CyL between 2000/01 and 2017/18 seasons. Data were obtained retrospectively from epidemiological surveys of cases included in the CyL Epidemiological Surveillance Information System.

Time of presentation, demographic data, vaccination history, clinical presentation and outcome were analysed for each season. Confirmed VF was defined as every MenC patient who had received the complete vaccination regimen according to age at least 15 days before symptoms onset.

Results:

We identified 15 VFs (23.8%) out of the 63 MenC cases reported during the study period (12 in the first 7 seasons). 66.7% were men and 80% children under 10 years old. In 8 cases more than 3 years passed from last dose and symptoms onset. 53.3% received 3 doses, 20.0% 2 and 26.7%, 1 dose. Most frequent clinical presentation was meningitis (60%). Two cases died (CFR 13.3%).

Conclusions:

All VFs identified during the 18 seasons completed MCC vaccination regimen according to age and ongoing schedule. Public Health Information Systems have demonstrated utility for the MD surveillance and VFs monitoring, being critical to evaluate the impact of population immunization programmes and real vaccine effectiveness.

Systematic Review Registration:

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ESPID19-0355
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Frequency and clinical characteristics of cytomegalovirus infection in intrauterine growth restricted infants in a tertiary care hospital – a prospective study

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Background and Aims:

Congenital cytomegalovirus (CMV) infection is currently the leading cause of congenital infections. It has a common association with IUGR. This study was intended to observe the frequency and clinical characteristics of congenital cytomegalovirus infection in IUGR infants.

Methods:

This prospective study was conducted from February 2016 to July 2017. Institutional Review Board approval was taken prior initiation of the study. All admitted IUGR neonates were enrolled in the study after getting informed written consent from parents/guardians. Weight, length, and OFC were taken along with other clinical examination. Serum samples of infant with IUGR were sent for Anti CMV IgG, Anti CMV IgM and CBC. If Anti CMV IgG was raised more than fourfold of laboratory cut off value or Anti CMV IgM was positive then CMV infection was confirmed by urine for CMV DNA within 3 weeks of age. Follow up was done to observe clinical manifestation. Ophthalmologic and hearing evaluation was also done in all enrolled neonates.

Results:

Congenital CMV infection was confirmed in 11(13.9%) cases among 79 infants. Microcephaly (11/08, 72.7%) was the most common clinical characteristics followed by hepatomegaly (11/03, 27.3%), hepatosplenomegaly (11/02, 18.2%) and direct hyperbilirubinemia (11/02, 18.2%). No abnormality was found in hearing and ophthalmological evaluation. Congenital CMV infection was significantly higher in Symmetrical IUGR infants (72.7% vs 27.3%, p= 0.02).

Conclusions:

Frequency of CMV infection in IUGR infants was 13.9%. Microcephaly was the most common clinical manifestation. Ophthalmologic or hearing involvement was not observed. Thus, policy makers may use this observation to formulate national guideline on CMV infections in such population.

Systematic Review Registration:

N/A

ESPID19-0334
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiology situation of febrile seizures in pediatric albanian population during the year 2016

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Background and Aims:

Febrile seizures are frequent in children and a common presentation in our hospital. Febrile seizure activity is associated with fever (more than 38 degree) and has no other identifiable cause, like central nervous system or metabolic abnormalities. Objectives: the aim of this study is to show epidemiologic data, risk factor, clinical characteristic, its complications of this disease in our population

Methods:

In the study are included all children from age 2m-14years old presented in Pediatric emergency room, with typical febrile seizures during the period January-June 2016.The clinic criteria were age 6m-6year, generalized seizures which occur once in 24 hr and last less than 15 min. The epidemiologic characteristic where age, gender, months, the etiology of fever, the number of attacks, and the management of seizures.

Results:

186 children were presented with febrile seizures.111 cases (59.6 %) were male, 75 (40.4 %) female. The pick of incidence was on March, 49 cases (26.3%).The most common etiology was upper respiratory infection with 39% (73 cases) followed by lower one 16% (30 cases), meningitis 1 case, otitis media 10 cases(5%).126 cases (68%) were in the first episode,42 cases (23 %) with the second one, 18 cases (9%) the third one.137 cases (74%) have been self-limited. 34 cases (18.2%) stopped after rectal Diazepam, 15 cases needed intravenous therapy with phenobarbital.

Conclusions:

Febrile seizures are a dramatic situation for parents. Therefore the presentation number of febrile children in emergency room of our hospital is high independent of there clinic condition. Since there isn't any medication used to prevent the occurrence of febrile seizures, general prevention to avoid febrile illness are important to prevent febrile seizure episodes as well. Maybe in the future this will be possible.

Systematic Review Registration:

N/A

ESPID19-0318
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

The serotype distribution and antibiotic susceptibility patterns of children with invasive pneumococcal infection after the addition of pcv13 vaccine to the turkish national vaccine schedule

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Background and Aims:

The 7-valent pneumococcal conjugate vaccine (PCV7) was included in Turkish national immunization programme in a 3+1 schedule in November 2008 and it was replaced with 13-valent pneumococcal conjugate vaccine (PCV13) in June 2011. The aim of this prospective single-center study was to determine the serotype distribution and the antimicrobial resistance patterns of *S. pneumoniae* in children with invasive pneumococcal disease (IPD) after the period of vaccination with PCV13.

Methods:

The study was conducted on 48 Turkish children with IPD between ages 1 month and 18 years in Ankara, Turkey between June 2011 and December 2018. The serotype analysis of the isolates and the antimicrobial susceptibility were performed by Quellung reaction and E-test, respectively.

Results:

The median age of the patients was 32 months and the male/female ratio was 1.82. The most common diagnosis was sepsis/bacteremia (52.1%) followed by meningitis (14.6%), empyema (14.6%), and pneumonia (10.4%). During the overall study period, the PCV7-serotypes and PCV13-serotypes represented 17.5% and 42.5% of isolates, respectively. PCV13-serotypes made up 81.8% of cases of IPD in the pre-PCV13 era and decreased to 42.5% in the period of 7.5 years after PCV13. Similarly the percentage of PCV7-serotypes in the cases of IPD decreased from 45.5% to 17.5% in the same period. According to the MIC values of the isolates penicillin and ceftriaxone (for meningitis) resistance rates were 40.5% and 10.8%, respectively.

Conclusions:

In conclusion, a prominent increase in non-vaccine serotypes of Turkish children with IPD has seen after the implementation of PCV13.

Systematic Review Registration:

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ESPID19-0311
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Outcome of hiv- and dolutegravir-exposed newborns in two collaborative cohorts in spain (coris and nenexp)

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Background and Aims:

The preliminary results of the Tsepamo study in Botswana showed an increased risk of neural tube defects (0.9%) in children born to HIV-infected mothers treated with dolutegravir (DTG) at conception. To date, these data has not been demonstrated in European cohorts. However, the European Medicines Agency recommended, in May 2018, avoiding DTG in the case of women who are planning a pregnancy or become pregnant. The aim of this study was to assess the outcomes of children intrauterine-DTG-exposed in Spain.

Methods:

Observational, retrospective study of all HIV-infected women who received treatment with DTG at conception or during pregnancy in the Spanish CoRIS and NenExp networks, between 2014 and 2018. Mother's characteristics, pregnancy outcomes and newborn data were assessed. Birth defects were classified according to European Surveillance Congenital Anomalies (EUROCAT) recommendations.

Results:

There were 47 pregnancies in 45 women, median age 31.5y (IQR 27.0-36.75). Thirty-three (70%) infants were exposed to DTG during the first trimester. DTG was discontinued in 4 cases, due to EMA's recommendations. There were 2 voluntary abortions, unrelated to EMA's notification, and a miscarriage. At the time of analysis, 41 infants (22 female) were alive and three pregnancies were in progress. Eight (17%) newborns were preterm and no cases of small-for-gestational-age or HIV transmission occurred. Two newborn had congenital heart defects and one hydronephrosis. No neural tube defects occurred.

Conclusions:

As shown in other European cohorts, no cases of neural tube defects in infants exposed to DTG al conception or during the first trimester of pregnancy were detected in Spain. Data from collaborative cohorts is needed to further assess the safety of DTG in pregnancy. Other factors as folinate supplementation during pregnancy may be considered.

Systematic Review Registration:

NA

ESPID19-0299
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Infectious diseases and acute inflammations. Main cause of child morbidity and transfers from secondary to тertiary hospitals or to special departments of other health centers.

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Background and Aims:

It is well known and bibliographically documented that infections, infectious diseases, acute skin and soft tissues inflammations (as a total cumulative percentage), are the main cause of morbidity and transfers among children, especially among boys. The Aims of this study is to record all transferred children during 2017, both from our Paediatric Department (PD) and Neonatal Primary Care Unit (NPCU) to Tertiary Hospitals, and make comments on the results.

Methods:

Data were used from all the trasfers, 6% of a total number of all the hospitalised children (0-15 years old), that were recorded in our electronic archive of our Hospital. A total number of 59 children were transferred during this year, 26 from the PD (65% of them were boys) and 33 from the NPCU (76% of them were boys).

Results:

The main cause of transfers, were: respiratory distress, as manifestation of a primary infection or other identified infections and inflammatory conditions (62%). Transfer destination: the nearest Tertiary Hospital (94%). Greek nationality(72%), Roma(15%), other nationalities(13% Albania, Bulgaria). From PD, 26 children were transferred. Main causes of transfer, in decreasing sequence: Neurological(spasms-tumors-infections):10, Respiratory(lower respiratory tract infections):5, Pediatric Surgery:5 and of other Specialties:6 (including inflammations and abscesses).

Conclusions:

Notably, main cause of transfer is infections(including soft tissue inflammations) and respiratory conditions, mostly due to primary infectious causes.Transferred children are mainly boys(M / F=7/3) mostly neonates with primary respiratory problems. 3 out of 4 children are transferred during the first 24 hours and the rest of them until the 5th day of hospitalization. The ncreased incidence of transfers during the second semester from PD, due to epidemics, mainly to respiratory conditions, when at the same time, statistically, no significant difference was observed in the NPCU.

Systematic Review Registration:

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ESPID19-0298
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiological study of measles cases in our paediatric clinic, general-secondary hospital in central greece and their management (2017-2018)

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Background

In the past due to the effectiveness of vaccines as well as the high vaccination rates, many childrens' infectious diseases have been decreased, or eradicated (smallpox).Currently though due to the effect of the anti-vaccination movement and the incoherence with the complete vaccination schedule have led in the reappearance of respective diseases. The aim of this study highlights the cases of Measles infection in our hospital.

Case Presentation Summary

A prospective study carried out of all infected children with lab confirmation, from Octomber, 2017-June, 2018 thanks to used data from the submitted forms for the obligatory reported infectious diseases and from our electronic archive. In this period, 9 children (Roma community), were documented with measles infection, all of them being unvaccinated, Female/Male ratio (5/4), 75% infants <1 year old (mean age:7months). Out of them 7 were hospitalized, 2 families rejected hospitalization, 8 of them had lab confirmation (IgM abs positive), except for one neonate, that its mother had recent confirmed measles infection, who was treated empirically with γ-globulin, responding well to treatment. The mean duration of hospitalization was 8 days (after complete recession of exanthema/ respiratory symptoms). All children were kept in isolation, hydrated and therapeutic measures were taken when any complications were observed. All their siblings were vaccinated as well as the staff members, born after 1970, with low abs titration count, receiving a booster MMR dose.

Learning Points/Discussion

Our Paediatrics' clinic staff following the latest guidelines protocols dealt with this small Measles epidemic in Roma community controlling its furtherspread, vaccinating protectively when needed other family members. Although this have been a small measles outbreak it is yet to be found what will be the results for public health if the vaccination rates keep falling.

ESPID19-0277
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Prolonged intravenous antibiotic treatment in bone and joint infections in children from brasov area

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Background and Aims:

Introduction: Pediatric osteoarticular infections are rare but important diseases. They need to be identified early and treated appropriately in order to avoid long-term morbidity.

Aim of the study: To review the current epidemiology and etiology of pediatric osteoarticular infections in Brasov area, Romania.

Methods:

Patients and methods: A resprospective study was conducted over a ten year period (2007-2016) that included a number of 41 children aged from 19 days to 18 years with osteoarticular infections who were admitted to the Children's Clinic Hospital Brasov, Romania.

Results:

Prevalence of osteoarticular infection was 0.1%. Septic arthritis (SA) was found at 68% of the patients and osteomyelits (OM) at 31% of patients.70.7% of the patients were males and the mean age of our study group was 8.7 years.
Mean length of hospitalization (MLHS) was 20.31 days: 15.5 days for SA and 30.6 days for OM (p <0,05).
The majority (78%) did not receive antibiotic treatment prior to diagnosis. MLHS was longer in these children (13.66 days vs. 22.18 days in children who did not receive antibiotic treatment before admission).
Mean CRP was 10.24 mg/dl for OM, and 11.7 mg/dl for SA (NV: 0-1), mean ESR was 45mm/h for OM and 58mm/h for SA (NV:<10mm/h)
54.54 % of blood cultures were negative. *S.aureus* grow in 36% of cases followed by *Haemophilus influenzae* in 9%.
All the enrolled patients received iv antibiotic treatment, with an average of 34 days for OA and 15 days for SA. The most used antibiotics were Gentamicin, Cefuroxime, and Oxacillin. Empirical antibiotherapy was subsequently changed according to the microbiological results.

Conclusions:

Prevalence of bone and joint infections was 0.1%. Negative cultures were frequent, *S.aureus* was the most involved pathogen.

Systematic Review Registration:

N/A

ESPID19-0262
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiology and risk factors for serious bacterial infections in children aged 0 to 36 months presenting with fever without source

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Background and Aims:

Children younger than 36 months with fever without source (FWS) are at risk of serious bacterial infections (SBI). The risk of occult bacteremia has been greatly reduced in vaccinated children. In our hospital, we screen for occult bacterial infections on the basis of anamnestic and clinical risk factors. The aim of this study is to describe the epidemiology of SBI in children with FWS in our setting and to evaluate the performance of our management algorithm.

Methods:

We designed a prospective single-center cohort study. We included children aged 0 to 36 months presenting with FWS in our emergency unit. Demographic and clinical characteristics, investigations and management procedures were recorded at the time of inclusion. Information on clinical evolution, final diagnosis, and immunization history were obtained 10 days after the inclusion. Potential predictors of SBI were compared between patients with and without SBI.

Results:

Between October 2015 and September 2017, 173 children were recruited, with a median age of 4.4 months (2.1-11). 166 children (96%) were uptodate with their vaccinations. There were 47 children (27%) with a final diagnosis of SBI which were all urinary tract infections (UTI). Presence of chills (OR5.6, 95%CI 1.3-24.3), fever for more than 2 days (OR29.1, 95%CI 3.5-243.5) and being less than 9 months old (OR45.3, 95%CI 4.9-415.7) were statistically significant predictors of UTI on a multivariate logistic regression. Our management algorithm identified all cases of SBI.

Conclusions:

In a setting of high vaccination coverage, we couldn't identify a single case of occult bacteremia. The main limitation of this finding is a small study population. Patients with FWS needing a screening for UTI can be identified on the basis of anamnestic and clinical criteria.

Systematic Review Registration:

none

ESPID19-0231
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Salmonella spp. Bacteremia in children<14 years old in greece; a 7-year retrospective epidemiological study- national reference centre for salmonella (nrcss) data

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Background and Aims:

Salmonella spp. is responsible for two clinical syndromes, enteric fever and non-typhoidal paratyphoidal salmonellosis. Greek National Reference Centre for Salmonella and Shigella (NRCSS) collects isolates as well as the corresponding epidemiological data from public and private hospitals of the country. Following, NRCSS is responsible for their serotype-specific identification, biochemical analysis and antimicrobial resistance test to 16 selected antibiotics. The aim of this study was to determine serotype distribution of Salmonella spp. causing bacteremia among children <14years old in Greece, their antimicrobial resistance profiles and analyze the corresponding demographic data.

Methods:

A 7-year retrospective study (2011 - 2017) was carried out, based on the NRCSS data, among patients aged <14 years old.

Results:

Blood culture confirmed Salmonella spp. in 70 cases (overall 2347 strains were isolated). There was a higher rate among boys(64%). Infants (0-11 months) were found to be more susceptible(18.6%). The three commonest serotypes were Salmonella Enteritidis (n=10, 14.3%), Salmonella Oranienburg (n=8, 11.5%) and Salmonella Typhi (n=6, 8.6%). Regarding antimicrobial resistance rates, 66% of the identified strains were highly sensitive to the selected antimicrobials, while 17% were multi drug resistant (MDR). The highest rates of resistance were recorded against sulfamethoxazole (55,5%). Resistance rates against 3rd generation cephalosporins and ciprofloxacin were 2,5%.

Conclusions:

In our country, local data imply that antimicrobial resistance rates to clinically important 3rd generations cephalosporins and ciprofloxacin for Salmonella spp. strains causing bacteremia remain low.

Systematic Review Registration:

N/A

ESPID19-0229
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Salmonella spp. In children<14 years old in greece. A 7-year retrospective epidemiological study- national reference centre for salmonella (nrcss) data

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Background and Aims:

Salmonella spp. is responsible for two clinical syndromes, enteric fever (typhoid and paratyphoid fever) and non-typhoidal paratyphoidal salmonellosis. Greek National Reference Centre for Salmonella and Shigella (NRCSS) collects isolates as well as the corresponding epidemiological data from public and private hospitals of the country. Following, NRCSS is responsible for their serotype-specific identification, biochemical analysis, antimicrobial resistance test to 16 selected antibiotics. The aim of this study was to determine serotype distribution of Salmonella spp. among children <14years old in Greece, their antimicrobial resistance profiles and analyze the corresponding demographic data.

Methods:

A 7-year retrospective study (2011 - 2017) was carried out, based on the NRCSS data, among patients aged <14 years old.

Results:

Overall, 2347 Salmonella spp. strains were isolated (27 typhoid-parathyroid). The highest incidence was reported in August(18,9%). Infants (0-11 months) were found to be more susceptible(17,9%). Salmonella Enteritidis was the most prevalent serotype (n=669, 28.5%), followed by Salmonella Typhimurium (n=287, 12.2%) and Salmonella monophasic Typhimurium (n=245, 10.4%). Non-typhoid-parathyroidal strains displayed high rates of resistance to sulfamethoxazole (51.4%) but low resistance rates to cefotaxime (1%) and ciprofloxacin (0.3%). Among typhoid-parathyroid strains 55% were susceptible to all antimicrobials and 10% displayed antimicrobial multi-resistance. Resistance rates to cefotaxime and ciprofloxacin were 5%.

Conclusions:

Frequency of Salmonella serotypes isolated form children <14 years old, do not differ from those isolated from older people. In our country, local data imply that antimicrobial resistance rates to 3rd generation cephalosporins and ciprofloxacin for both non-typhoid and typhoid-parathyroid remain low. Notably there is an increasing prevalence of Salmonella monophasic Typhimurium strains that are associated with multiple antimicrobial resistance.

Systematic Review Registration:

N/A

ESPID19-0223
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Congenital syphilis in malta

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Background and Aims:

Congenital syphilis is a potentially disabling infection caused by vertical transmission of the spirochaete *T. pallidum*. All pregnant mothers are routinely screened for syphilis and are treated if found to be seropositive and without any evidence of past treatment. The aim of this study was to assess whether routine screening and treatment of seropositive pregnancies is effective in reducing vertical transmission of syphilis, thereby preventing congenital syphilis.

Methods:

This was a retrospective study which involved all seropositive mothers who were referred to the Paediatric Infectious Diseases Clinic at Mater Dei Hospital over a ten-year period, from 2008 to 2017. The standard used for this audit was the UK National Guidelines, published by the British Association for Sexual Health and HIV (BASSH). The data were then analysed to assess whether the management was according to guidelines

Results:

Over the ten-year study period, maternal syphilis was identified in a total of 41 pregnancies. The majority of pregnancies (68.3%) were in foreign mothers. Eighteen mothers (43.9%) received treatment for syphilis during pregnancy, mostly being given in the second or third trimester. None of the neonates showed signs of congenital syphilis at birth, however fifteen neonates (36.8%) were treated with benzylpenicillin, either because the mother was not or was inadequately treated during pregnancy, or because of serological evidence of possible congenital syphilis.

Conclusions:

There were no clinical or serologically confirmed cases of congenital syphilis in Malta in this ten-year. The study involved the entire population of serologically positive mothers and their management was according to the BASSH guidelines. The current antenatal screening programme and treatment of syphilis during pregnancy is an effective measure for preventing congenital syphilis in Malta.

Systematic Review Registration:

ESPID19-0221
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Trends in vaccination coverage of children and adolescents in germany

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Background and Aims:

Data from two subsequent studies of the "German Health Interview and Examination Survey for Children and Adolescents (KiGGS)" aimed for comparing the vaccination status and its determinants in 3- to 17-year-old children and adolescents at different time points and to assess trends of vaccination coverage in the 1985-2013 birth cohorts.

Methods:

Participants were representatively selected for the German population of the same age. Vaccination status was evaluated according to the German childhood vaccination schedule by available records in 13.731 (KiGGS-baseline, 2003-2006) and in 3,238 participants (KiGGS-Wave-2, 2014-2017).

Results:

In KiGGS-Wave-2 vaccination coverage was high for the majority of vaccinations for both girls and boys. Coverage has increased in all ages in the last 10 years. This applies particularly for vaccinations with strong deficiencies in the KiGGS-baseline study, such as: the hepatitis B- and the second measles vaccination in all age groups, the booster dose against pertussis (11-17-year olds) as well as the booster dose against tetanus in the 7-10-year-olds. Socio-demographic factors are still determinants of the vaccination status. Less than one child in two is vaccinated against hepatitis B (45.9%) when parents state fear of side effects or indicate vaccine-skepticism as reasons against vaccinations. Despite significant increases, vaccination coverage at the end of the second year of life is still far below 95 percent for all vaccinations (measles: 1. dose: 88.6%; 2. dose: 64.4%) even in the most recent birth cohorts.

Conclusions:

The results show where further efforts are needed to increase the vaccination coverage by the remaining last percentage points and to achieve the timely delivery of all vaccinations listed in the immunization schedule as well as to meet the defined elimination goals.

Systematic Review Registration:

no systematic review

ESPID19-0194
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Features of the hospitalized pediatric cases of clostridium difficile infections from bucharest municipality, romania

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Background

The incidence of Clostridium difficile infection (CDI) associated with medical care is high, even in populations previously thought to be at low risk, including children. The aim of this study was to describe the main features of the hospitalized pediatric CDI (ICD-10-CM, A04.7) cases from Bucharest Municipality in order to assist and support control.

Case Presentation Summary

Each case of CDI is reported by hospitals to the Infectious diseases surveilance Unit of the Public Health Authority of Bucharest Municipality (PHAMB). Reports includes patient's personal data (age, gender, media), lab data (type of diagnosis test) and clinical informations (onset date, recent exposures to hospitalization and antimicrobials, comorbidities and outcome). At PHAMB the content of the report is filled in an EpiInfo7 database which is interrogated as needed. This analysis include all consecutive pediatric CDI (age 0-15 years) cases with onset dates between January 1st 2016 and 1st December 2018 (n = 109 cases); a case of PCDI was defined as ≥ 3 loose stools per day with a positive test for C. difficile toxin determined by immunochromatogarphy and no other diarrhea causes.

Learning Points/Discussion

PCID represents 1.69% of all ages cases.

The median age in PCID was 1 (IQR = 2-6) and the prevalence of male gender was 49.54%. Based on the onset data cases were classified as follows: (a) health care associated: 63.3%, (b) community associated: 23.85% and (c) other: 12.85%.

Other frequent features were: (a) Prior exposure to hospitalization (in the last 3 months): 65.14% and (b) Prior exposure to systemic antimicrobial: 79.82%.

High prevalence of hospitalized cases and high prevalence of cases with recent exposure to antibioticrobial represents objective arguments for improving contact precautions and effective antibiotic stewardship.

ESPID19-0184
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Genotyping and genomic characteristics of human adenovirus infection among children with severe acute respiratory infection in shanghai

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Background

Limited data was reported on genotyping distribution and genome characteristic of the human adenovirus in children with severe acute respiratory tract infection in Shanghai area.

Methods

A total of 648 nasopharyngeal aspirate (NPAs) were collected from Children with Severe Acute Respiratory Infection (SARI) in Shanghai from February 2014 to August 2015. These NPAs were used for HAdV genotyping and 15 common respiratory viral tests. Viral isolation and identification of HAdV predominant strains were performed. Then genome-wide amplification and sequencing and phylogenetic analysis of the HAdV-B isolates were performed.

Results

A total of 104 samples were detected as HAdV positive among 648 NPAs from children in Shanghai area (2014.2-2015.8), with a positive rate of 16.05% (104/648). Of the 104 HAdV positive samples, 47 were HAdV detected alone (47/104, 45.19%).A variety of HAdV subtypes can be detected in Shanghai, including HAdV-B7 (54.81%, 57/104), HAdV-B3 (29.80%, 31/104), HAdV-C5 (3.85%, 4/104), HAdV-C6 (2.88%, 3/104), HAdV-C2 (2.88%, 3/104), HAdV-C1 (0.96%, 1/104), and HAdV-D53 (only 1 case).

HAdV-B7 was the most dominant subtype detected in this study. High homology (>99%) of genomic sequence was found among isolated HAdV-B and same subtypes of published HAdV-B3 and HAdV-B7 reference strains. Interesting, we found a 27bp deletion at DNA polymerase/terminal protein (pTP) of SH181 isolate (HAdV-B7). And a 24bp sequence deletion was found at the DNA polymerase/terminal protein (pTP) of SH3127 isolate (HAdV-B7).**Conclusions**

Human adenovirus (HAdV) is an important pathogen for childhood with SARI in Shanghai, and the most prevalence type is HAdV-B （mainly B3 and B7).We found a gene deletion at DNA polymerase/terminal protein (pTP) of 2 HAdV-B7 isolates from SARI children.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0144
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Herpes zoster infection after one dose of varicella vaccine to a 4 year old child in greece.

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Background

Varicella-zoster virus infection causes two clinical outcomes. Primary varicella infection results in chickenpox. Varicella-zoster virus can be reactivated years after the initial infection to cause herpes zoster (HZ). Varicella vaccines are highly effective at preventing disease, but herpes zoster may occur among vaccinated people. However children vaccinated against varicella appear to have a lower risk of HZ than people who were infected with wild type VZV.

Case Presentation SummaryA four year old girl presented with a painful vesicular rash on her right arm. The rash spread over C4, 5 and T1 dermatomes. She was fully immunized and she had received one dose of varicella vaccine (Oka strain) at the age of 15 months. There was no known contact with varicella. She was afebrile and otherwise well. She was initially treated with a combination of fusidic acid and betamethasone as topical cream. Two days later she returned because she developed further lesions on her arm and she was complaining of severe pain and headache. Herpes Zoster was clinically diagnosed and treatment with acyclovir and analgesics was given for ten days. Eosin as lotion also applied to the skin. The lesions started to crust very quickly and the child recovered completely without any further complications.**Learning Points/Discussion**

Varicella vaccination was introduced in Greece in 2004 for all children age 15 months and above. A second dose was added to the National vaccination programme in 2008 for children age 4-6years. There are no data available on the incidence of HZ in children especially those who have been immunized. Further studies needs to be done to monitor vaccination rates and its effectiveness.

ESPID19-0138
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Etiologic agents of acute gastroenteritis in children hospitalized at a secondary hospital during 2015-2018

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Background

Acute gastroenteritis (AGE) is the most important cause of hospitalization in children, but the majority of cases remain undiagnosed. Recently developed multiplex RT-PCR test could provide more insights into the epidemiology of enteric pathogens. The purpose of this study was to investigate the epidemiology of etiologic agents of AGE in hospitalized children.

Methods

We used multiplex RT-PCR kits for detection of enteric pathogens in stools collected from the children hospitalized with AGE at a hospital in Seoul, Korea between September 2015 and December 2018.

Results

Out of 1,523 stool samples tested for viral pathogens, 488 (32.0%) were positive for viral etiologic agents; norovirus (NoV)-II in 17.4%, rotavirus (RV) in 6.9%, adenovirus in 3.4%, astrovirus in 2.7%, and NoV-I in 0.8%. In 2018, RV positivity was increased to 13.8% (48/348) compared to 6.6% (35/527) in 2017. Otherwise NoV-II positivity was decreased to 13.5% (47/348) in 2018, although it was in the range of 21-22% during 2016-2017. NoV-II showed the highest peak positivity in January and RV in March. Enteric bacterial pathogens were positive in 95 cases (30.7%) of 309 stool samples and mixed infection was in 5 cases. Campylobacter species was the most frequently detected bacterial pathogen (32 cases, 10.3%), and highly found in May and June. Clostridium difficile toxin B was detected in 7.1%, Salmonella in 4.8%, Yersinia in 1.3%, and Shigella in 0.6%.

Conclusions

Although NoV was the leading etiologic agent in children with AGE after introduction of RV vaccine, this study showed the resurgence of RV in 2018 suggesting the emergence of novel recombination of RV strains. Otherwise Campylobacter spp. was the predominant cause of bacterial AGE in children.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0120
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

High frequency and diversity of parechovirus a in a cohort of malawian children

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Background

Parechovirus-A's (PeV-As) are highly prevalent viruses worldwide. While PeV-A infection is often asymptomatic or causes mild gastro-intestinal or respiratory symptoms, cases of severe neurological infections such as meningitis and encephalitis have been described. Currently, 19 types of PeV-A's have been identified, with PeV-A1 and –A3 being the most prevalent. Although the PeV-A types 7 through 19 seem to be rare, data on PeV-A prevalence is scarce, mainly in the continent of Africa. The aim of this study was to describe PeV-A circulation in a cohort of children in Malawi, Africa.

Methods

749 stool samples obtained from Malawian children aged 6 to 60 months were tested on PeV presence by real time PCR. Participants included children presenting at a hospital for various reasons, as well as healthy community controls. PeVs were typed by phylogenetic analyses. Associations between PeV prevalence and gender, and between PeV positivity and specific symptoms were tested by Mann-Whitney U test and Chi-squared test respectively.

Results

57% of the stool samples was positive for PeV-A. 15 different types were identified, with PeV-A1, -A2 and -A3 being the most prevalent types. Infected children were significantly younger than non-infected children. No association was found between PeV positivity and specific symptoms.

Conclusions

The prevalence and genetic diversity found in our study are remarkably high, as most other studies find PeV-A prevalences around 4% and no more than 6 different genotypes. However, studies conducted in Africa do show higher prevalences, up to 24%, and a higher number of genotypes. The results of this study further confirm these differences in PeV circulation between Africa and the other continents.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0107
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

High socioeconomic vulnerability among children exposed in utero to zika virus in brazil

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Background

In Brazil, a set of congenital abnormalities was linked to *in utero* Zika virus infection. This set of abnormalities was termed Congenital Zika Syndrome(CZS). Instituto de Puericultura e Pediatria Martagao Gesteira is a reference center for pediatric infectious diseases from all Rio de Janeiro, where children have free access to care. The aim of this report is to describe the cohort of children exposed *in utero* to Zika virus followed in this center, focusing on socioeconomic characteristics.

Case Presentation Summary

Methods: Descriptive study of a cohort of children exposed to Zika virus *in utero*, focusing on socioeconomic characteristics .

Results: We followed 41 children, 22 with CZS and 19 asymptomatic. A total of 20 with central nervous system abnormalities, 7(17%) with abnormalities on ophthalmoscopy, 4(10%) with BERA abnormalities, and 10(25%) with other malformations.

The median maternal age at delivery was 25 years(IQR=19-33), eight women aged 18 years or less. The median monthly family income was 0.4 Brazilian minimum wage(IQR = 0.3-0.7). One Brazilian minimum wage is 245 US$. The median number of study years was 10 (IQR=8-12). Fifteen (36%) women had a job, 2 (5%) were students, and 24 (59%) were unemployed. A total of 10 (25%) mothers used alcohol during pregnancy, 6 (15%) tobacco, and 2 (5%) illicit drugs. Six (15%) women did not want to get pregnant, among them, three (50%) tried to abort. Three (7%) women reported a history of sexual abuse during their lives.**Learning Points/Discussion**

Mothers of children exposed to Zika virus *in utero*,live in situation of very high social vulnerability in Brazil, with very low income, and high rate of unemployment. Considering the sequelae that this infection cause in the children, high social support need to be offered to them.

ESPID19-0056
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Consumption of systemic antimicrobials in pediatric patients of an infectious diseases clinic from bucharest, romania

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Background

Antibiotic stewardship interventions include counting the quantities of antimicrobials (AB) consumption. Comparing the own consumption data with AB consumption at EU/EEA level as reported by ESAC_net (*) is an attractive way to discover meaningful deviations. We used ESAC_net as a benchmark in order to compare with consumption of systemic AB used in pediatric department of our 500 beds infectious diseases clinic.

Case Presentation Summary

Methods

Two series of data were constructed as follows: (a) S1 (our data) the number of days of AB therapy found by collating of two separate PPS conducted in 2018 in pediatric patients (0-15 years old) were expressed as percents of each Anatomic Therapeutic Chemical (ATC) classification subclass of systemic AB (JO1) from total; (b) S2 (ESAC_net 2017 – hospital sector data) – the rates reported for each ATC subclass of systemic AB (JO1) were also expressed as percents from total consumption. The similarity of the two series was searched by correlation.

Results

A weak correlation was found between the two series (Pearson correlation: 0.524; p (2-taied): 0.182). The main discordances found between the two series were consumption of significantly les (- 23%) in J01C class and significantly more (+20 %) in J01C subclass AB in S1 (our data) set then in S2 (ESAC_net) data.

Learning Points/Discussion

Differences found between levels of AB consumption of our and EU data represents objectively documented targets for antibiotic stewardship interventions, as for instance finding ways for decreasing consumption of J01D subclass (cephalosporins 3+ generation and carbapenems) without significantly altering the clinical outcome.

ESPID19-0055
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Factors that augment the burden of hospitalized rotavirus enteritis in infants - results of a case control study

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Background

Analisys of a dataset of pediatric cases of rotavirus enteritis recently (ICD 10 – Code A0.0) hospitalized in our 500 beds clinic revealed that in patients aged under one the means of either duration of hospitalization and also the hospitalization cost were significantly higher that in the older (1-5 yrs af age) preschool aged patients (Kruskal Wallis: 28.6; $p < 0.05$ and Kruskal Wallis: 25.7; $p < 0.05$ respectively). The objective of this work was to clarify the reason(s) of the above discrepancy.

Case Presentation Summary

Methods

Cases of rotavirus enteritis consecutively hospitalized for at least two days between January 2017 and October 2018 were extracted from the hospital data base, listed in an separate MS Excel® tabel, sorted ascendently by age and alphabeticaly. Each patient aged under one (n=57) was assigned as "Case" and matched with an "Control" selected at random from the list of cases aged 1-5 years. For each member of a couple of Case-Control the following variables were noted: gender, HAI status and complications as thrombocytopenia (TCP), hepatocytolisis (HCL) or an acute respiratory infection (ARI). Epi Info 7 software was used for an odd analysis – a p value under .05 was selected to define stat signification.

Results

Univariate anlysis found that HCL and ARI complications were associated ($p < 0.05$) with cases; however logistic regression of these risc factors found that only ARI complication was statistically significant associated to cases (match OR: 2.80; 95% CI (1.28 – 6.12); Z-statistic : 2.58; p value: 0.0094) .

Learning Points/Discussion

Rotavirus enteritis is a vaccine preventable diseases. This paper is a modest contribution added to to efforts needs to drive political decisions and resurces for rotavirus vaccination

ESPID19-0026
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Prevalence of enterovirus serotypes in children with encephalitis/meningitis in shanghai, china, 2016~2017

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Background

Eneterovirus (EV) is a major cause of viral encephalitis/meningitis. This study aimed to investigate the prevalence of enterovirus-associated encephalitis/meningitis and the distribution of enterovirus serotypes in children with encephalitis/meningitis in Shanghai during 2016~2017.

Methods

We collected cerebrospinal fluid (CSF) specimens from pediatric patients with encephalitis/meningitis and stool specimens from children with viral encephalitis/meningitis followed with HFMD during 2016 ~2017. The nested RT-PCR and sequencing were performed to identify EV and serotypes.

Results

During 2016 ~2017, we obtained 295 non-duplicated CSF specimens from children with clinically diagnosis viral encephalitis/meningitis, and EV was positive in 163 (55.25%) specimens. Of which, 139 and 156 specimens were taken from inpatients and outpatients, respectively. EV was positive in 66 (47.48%) and 97 (62.18%) CSF specimens from inpatients and outpatients, respectively. Among inpatients with viral encephalitis/meningitis, 11 serotypes were identified including E30 (42.42%), CV-A6(12.12%), CV-A5 (10.61%), E6 (9.09%), E11 (7.58%), CV-A2 ,E9 , CV-B5 ,CV-A10 , CV-B3 , E14 . Among outpatients with viral encephalitis/meningitis, 13 serotypes were identifieds, including CV-A6 (31.96%), E30 (23.71%), CV-A10 (14.43%), E6 (7.22%), E9 (5.15%), CV-A2 , CV-A9 , CV-A5 , CV-B5 , EV-A71 , E14 , CV-B4 . Of the 5 cases with critically severe encephalitis who all survived, E9, CV-A2 and E6 was identified in 2 cases, 2 cases and 1 case, respectively. Besides, we obtained 61 stool specimens from children with viral encephalitis/meningitis followed with HFMD. And EV was positive in 56 (91.80%) specimens. 5 serotypes were identified including EV-A71 (85.71%), CV-A2 (5.36%), CV-A16 (23.57%), CV-A6,CV-A5 . All encephalitis/meningitis followed with HFMD were mild cases.

Conclusions

Multiple enterovirus serotypes co-circulated among children in Shanghai.Non-EV-A71 enteroviruses were responsible for viral encephalitis/meningitis, and E30 and CV-A6 were frequent serotype responsible for encephalitis/meningitis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1111
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Congenital measles prevelance during last year measles outbreak in western greece

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Background

The aim of our study was to identify the measles affected pregnant women as well as their offsprings. Because maternal measles as well as congenital measles are unknown medical conditions data on pregnant women and newborns are scarce.

Case Presentation Summary

We retrospectively studied the medical records in the Obstetrics ward of the General University hospital of Patras in Greece between November 2017 and November 2018.

We identified six pregnant women who were affected by the measles virus, one during the first trimester, one in the second trimester, three had the onset of disease few days prior to delivery and one was living in measles environment.

Seven neonates were delivered (one twin pregnancy) at mean gestational age 36^{7}weeks and their mean weight was 2764gr (1230-3720gr).One baby was IUGR whose mother acquired measles at 26 weeks of pregnancy. One baby, whose mother had measles during the first trimester, had amniotic fluid measles PCR which was negative.

Five neonates received immunoglobulin immediately after delivery and were isolated from their mothers (the two who weren't treated with immunoglobulin, were those whose mothers' acquired measles during the first and second trimester).All these five babies were also tested for measles virus with PCR (pharyngeal swab) and two were positive. None of these babies experienced any measles symptoms during the neonatal period and all had measles IgM negative at birth and measles IgG >300(immune).

The two babies with the positive PCR were contacted at nine months of age.

Learning Points/Discussion

There are limited data regarding the side effects of measles infection in neonates, so these babies who had positive measles PCR should have a close neurodevelopmental follow up.

ESPID19-0737
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

Epidemiological data and new approach to pneumococcal immunization programme in children in slovenia

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Background

Slovenia was one of the countries with the highest incidence of invasive pneumococcal diseases before the introduction of vaccination. From 2015 an optional and free of charge vaccination against pneumococcal infections with a conjugated 10 valent vaccine was introduced in NIP in Slovenia.

We want to confirm, that with the introduction of the optional pneumococcal vaccination, a decrease of incidence and reduction of the level of antibiotic resistance is detected.

Methods

1765 (305 from children and 1457 from adults) invasive *Streptococcus pneumoniae* strains, isolated in Slovenia, in the period from 2013 to 2018, were identified, tested for antibiotic susceptibility, typed and frozen at –70 °C.

Results

In Slovenia the pneumococcal vaccination coverage was 48,8% in 2015, 49,4% in 2016 and 55,2 % in 2017. The incidence in children under 14 years of age in 2015 was 15,6/100.000, in 2016 was 15,1 while 12,6 in 2017 and 15,7 in 2018. We do not notice any significant decrease in incidence yet. Furthermore the incidence in children under 2 years od age was in 2015 69,4/100.000 and in 2018 was even 74,6.

Serotypes 3, 1, 14, 4, 9V, 7F, 19A, 6A are predominant in adults while in children serotypes 14, 1, 19A, 6A, 9V, 6B, 23F, 19F. We can not talk about significant decrease of certain vaccine serotypes but we can see an increase of percentage of serotype 19A in adults from 2,7% in 2015 to 7,3% in 2018.

Conclusions

According to the data Slovenia decided to start the vaccination of children in NIP with 13 valent vaccine (due to higher serotype coverage of the vaccine and to avoid 19A serotype replacement).

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0273
E-Poster Viewing - May 7-10 - E-Poster Hours

Population studies and surveillance

The importance of hospital discharge for acutely unwell children in low and middle-income settings – findings from the childhood acute illness and nutrition network (chain)

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Background

Undernutrition underlies almost half of childhood deaths worldwide and increases mortality in all infectious syndromes. Current guidelines rely on limited evidence, and mortality remains high even when these are applied. The Childhood Acute Illness and Nutrition Network (chainnetwork.org) is a multicentre project funded by the Bill and Melinda Gates Foundation, aiming to optimize the care of hospitalized children 7-days to 23-months old in resource-limited settings to improve survival and growth using detailed cohort data to attempt to fully understand the factors contributing to poor outcomes, in the context of nutrition status.

Methods

A comprehensive assessment of vulnerability, including clinical, anthropometric, social, economic, environmental, and caregiver health are collected in a harmonised and standardised way. Data and samples are collected during admission, and at discharge, 6-weeks, 3 and 6-months post-discharge. Community participants representative of the hospital population are also enrolled at a single time-point.

Results

To date 3000 hospitalised 855 community participants have been enrolled. These have been stratified according to mid upper arm circumference (MUAC). Initial analysis shows that MUAC <11.5cm remains a major risk factor for poor outcome. Across clinical syndromes seen there are common risk factors seen. Current guidelines address the syndromes but not these risk factors.

Importantly it has emerged that there are significant differences between children who are discharged according to usual hospital procedures and those who abscond, leave against advice or are discharged early. This includes carriage of antibiotic-resistant organisms. Work on biomarkers of infection at the time of discharge to identify children at risk of post-discharge death is ongoing.

Conclusions

The discharge time-point could provide an opportunity for intervention. There are currently no guidelines regarding when or how a child should be discharged and followed-up.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESPID19-1052
E-Poster Viewing - May 7-10 - E-Poster Hours

Refugees and migrants

Imported malaria in a tertiary hospital in spain

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Background and Aims:

International travelers have grown significantly over last years, as well as imported diseases from tropical areas. Most of febrile syndromes in children coming from the tropics consist in mild cosmopolite infections. However, potentially severe diseases such as malaria may occur. Our objective is to describe imported malaria cases in a tertiary hospital in Spain.

Methods:

Retrospective review of patients ≤18 year-old presenting at a tertiary hospital and surrounding primary health care centers with stay in a tropical region during the last year between July 2002 and July 2018 with fever and a positive thick smear, immunocromatographic assay or polymerase chain reaction (PCR) for malaria.

Results:

Malaria accounted as the first individual cause of fever in children coming from the tropics in our hospital. There were 39 cases of malaria, mainly VFRs (56,3%; visiting friends and relatives) and recent arrival immigrants (32,4%), most of them coming from Equatorial Guinea. *Plasmodium falciparum*was isolated in 37 cases (95%); P. malariae in 2, and there was one case of *P. vivax*and *P. ovale* each. There were 3 mixed infections. PCR was performed in 25 cases with no discrepancies with thick smear reading results. Median parasitemia was 2,7% (IQR 0,7-6,4%). 12 patients were admitted to Intensive Care Unit due to severity criteria. No deaths were reported.

Conclusions:

Malaria may present as an unspecific febrile syndrome which may cause a severe disease. In our study, the most isolated species was *P. falciparum*. All patients came from Sub-Saharian Africa. No discrepancies were found between PCR and thick smears. One third of the patients was admitted to Intensive Care Unit.

Systematic Review Registration:

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ESPID19-1158
E-Poster Viewing - May 7-10 - E-Poster Hours

Severe - systemic fungal infections

Azole-resistant aspergillosis: an emerging problem

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Background

Increased azole resistance in Aspergillus fumigatus has become a significant challenge in effective management of aspergillosis. Here we present a complex case of an immunocompromised child with treatment failure despite the use of three different antifungal agents and salvage therapy with intrathecal non-liposomal Amphotericin B.

Case Presentation Summary

A 2 years old girl with mucopolysacharidosis type 1 who had a hematopoietic stem cell transplant on long term immunosuppresion with prednisolone and cyclosporin presented with respiratory distress and neuro-developmental regression. MRI brain showed hydrocephalus and a ventriculoperitoneal shunt was inserted. Three weeks after the VP shunt insertion she became febrile and lethargic. CSF examination showed infection with Enterobacter cloacae. The shunt was removed and replaced with an external ventricular drainage device. She was treated with intravenous Meropenem, Amikacin, Linezolid and intrathecal Amikacin. Ten days into treatment she developed left hemiparesis. A brain MRI showed multiple cerebral abscesses. PCR from CSF and brain biopsy was positive for Aspergillus fumigatus. She was treated with IV Voriconazole, liposomal Amphotericin B and Micafungin. A CT chest showed multiple fungal nodules. Intrathecal non-liposomal Amphotericin B was added as a salvage therapy. The resistance mechanism TR34/L98H was detected in the PCR suggestive of pan-azole resistance. Voriconazole was substituted with Flucytosine. The patient died despite 30 days of intense antifungal treatment.

Learning Points/Discussion

Azole-resistant A. fumigatus is an emerging concern. To guide optimal management, to understand the epidemiology and to assess the global burden, ideally a causative diagnosis including susceptibility testing should be made in every patient with a clinical suspicion of aspergillosis. Our clinical experience of treating cases with aspergillosis due to azole-resistant Aspergillus is still limited. Practical recommendations were recently published based on the best available evidence supplemented with expert opinion.

ESPID19-1110
E-Poster Viewing - May 7-10 - E-Poster Hours

Severe - systemic fungal infections

Presentation of pneumocystis jirovecii pneumonia among hiv-negative danish children

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Background and Aims:

Pneumocystis Jiirovecii (PJ) fungus can cause severe interstitial pneumonia (PJP) in patients with primary and secondary immune deficiency, including HIV, malignancies and immune modulating therapies. PJP may be difficult to diagnose, since symptoms are non-specific, co-infections frequent, and colonisation is well known, especially among young children.

In the present study we describe the clinical presentation in HIV-negative Danish children.

Methods:

All children < 16 years of age admitted to the tertiary hospital in Copenhagen in the period January 2002 to December 2013 were included, if PJ was demonstrated in the respiratory tract material (immunofluorescence microscopy, Grocott-Gomori methenamine silver stain microscopy or PCR) or PJP assigned as discharge diagnosis.

Demographic, clinical and para clinical data was obtained retrospectively from patient files in a structured questionnaire. For each patient, likelihood of PJP was evaluated.

Results:

Among the 48 children included, PJP diagnosis was evaluated as confirmed in 24 (50%), likely in 16 (33%), unlikely in 4 (8%) and unknown in 4 (8%). Underlying disease among the children with confirmed or likely PJP diagnosis, was hematologic malignancy in 20, primary immunodeficiency in 12, solid organ transplant in 3, chronic lung disease in 4 and in 1 no underlying disease was known. The majority presented with dyspnea, tachypnea, low grade fever, hypoxemia and interstitial pneumonia on chest x-ray.

Conclusions:

In this retrospective study of 48 Danish HIV negative children with PJ demonstrated in the respiratory tract material or assigned PJP discharge diagnosis, PJP diagnosis was evaluated confirmed in half of the children and likely in another third of the children. All but one had a known underlying disease. The majority presented with dyspnea, tachypnea, low grade fever and hypoxemia. PJP remains a challenge to diagnose in children.

Systematic Review Registration:

not-relevant

ESPID19-0971
E-Poster Viewing - May 7-10 - E-Poster Hours

Severe - systemic fungal infections

Immunocompetent 13-year-old patient with cryptococcus neoformans myocarditis

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Background

Cryptococcus neoformans is an opportunistic pathogen which most often affects immunocompromised patients. Myocarditis caused by *Cryptococcus ssp*. is extremely rare in all age groups. Only a few adult cases have been reported. Pediatric patients with *Cryptococcus neoformans* infection involving heart is close to non-existent in literature.

Case Presentation Summary

A previously healthy 13-year-old boy was admitted to Children's Clinical University Hospital in Riga, Latvia with complaints of fever, vomiting, chest and epigastric pain. On admission the heart rate was 90x/min, blood pressure was 102/63 mmHg, respiratory rate was 18x/min with clear lung auscultation bilaterally, no rash or peripheral edema was present. Abdomen soft and non-tender. Meningeal signs were negative.

ECG on admission showed negative T wave in leads I and aVL, ST elevations in lead II, aVF and V3, signs of right ventricle overload. Echocardiography showed anatomically normal hear with preserved systolic function. Serum troponine I was 39 393 ng/L and CK-MB mass – 82,79 ng/mL. CRP was 121 mg/dl, liver and kidney functional markers within normal range. WBC was 15,64x10^3/mL. CXR showed congestion in pulmonary vasculature. Cardiac MR with contrast showed preserved systolic function in both ventricles, however myocardial edema and late gadolinium enhancement was observed in basal and mid-ventricular region of left ventricle wall and in septum and apex. Some pericardial effusion was observed as well. In two blood samples *Cryptococcus neoformans* antigen came back positive in 1:40 titer. As cryptococcal infections are typical for immunocompromised patients, the patient was consulted by immunologist, however no immunodeficiency could be identified. The patient received fluconazole and recovered well.**Learning Points/Discussion**

Cryptococcus neoformans can cause myocarditis in immunocompetent pediatric patients. CMR is a noninvasive diagnostic test that can help to confirm the diagnosis of myocarditis.

ESPID19-0103
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Where have all the parasites gone? A malariometric survey to determine the species of plasmodium causing clinical malaria in nigeria

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Background

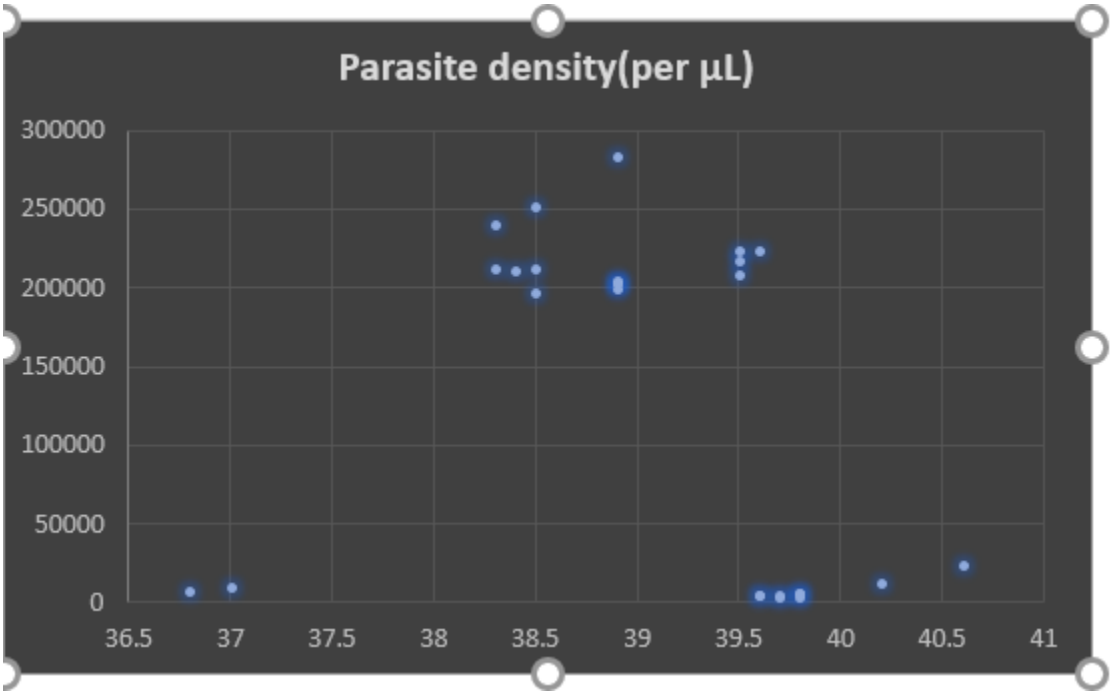
The global incidence of malaria in 2017 was 59 cases per 1,000 population, a vast majority of these occurring in Africa. Malaria is caused by 5 known species of the Plasmodium parasite: in 2017, *P. falciparum* was reportedly responsible for 99.7% of all cases in Africa, as reported by the World Malaria Report 2018. In Nigeria, there have been ongoing reports of falciparum monoparasitaemia. However these studies were not designed specifically to detect other parasite forms. We aimed to determine the relative proportions of parasite species causing clinical malaria in Sokoto, Nigeria.

Methods

The study was conducted in Wamakko Local Government Area of Sokoto, Nigeria, with coordinates 13°2′16″N 5°5′37″E. It included prospectively, 1017 children aged 2 to 10 years. The children had a physical examination and samples taken for malaria testing. A trained investigator stained the slides with giemsa and identified species. All children found to have clinical malaria were treated and those with severe malaria were referred, after resuscitation. The data was analysed using SPSS version 22.

Results

A total of 1136 subjects were screened for inclusion in the study, of which 1017 were eventually included. 354 subjects had positive malaria parasitaemia, of which 305 were adjudged to have clinical malaria. of that number, 26 were found to have severe malaria, with only 279 were assessed as having uncomplicated malaria parasitaemia. All the parasites found were *P. falciparum*, including for all the cases of severe malaria.



Conclusions

The study affirms the findings of the World Malaria Reports from 2015 to 2018, which suggest monoparasitaemia with *P. falciparum*. These findings can be confirmed with molecular tests and form the basis for interventions for malaria control.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0099
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Is there a change in malaria transmission intensity? An appraisal of malaria control efforts in northwestern nigeria

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Background

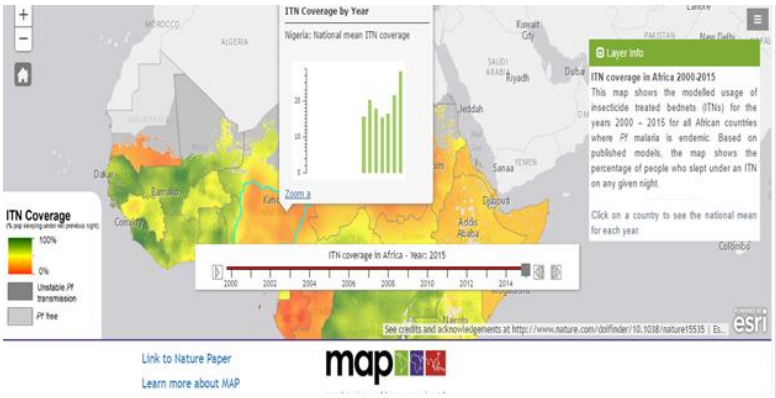
Malaria is a preventable disease with a widespread distribution. In 2017, an estimated 219 million cases of malaria occurred worldwide, marginally reduced from 239 million in 2010. The global data suggested no significant progress has been made towards reducing the burden of malaria. The burden of malaria is substantially higher in Sub Saharan Africa and particularly in Nigeria and The Democratic Republic of Congo, which together account for about 40% of the global morbidity and mortality due to malaria. This study aimed to measure the prevalence of malaria in Sokoto, Northwestern Nigeria and appraise malaria control efforts in Nigeria.

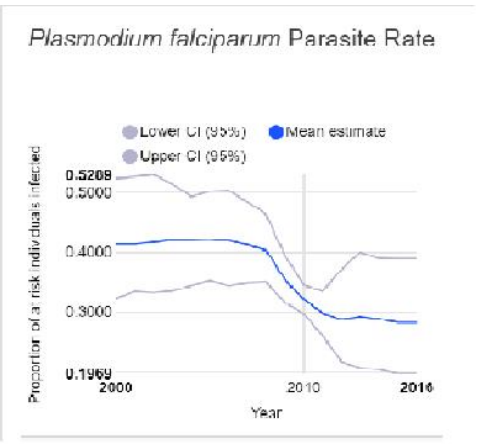
Methods

We conducted a two-point survey to measure the intensity of transmission of malaria in Wamakko Local Government Area of Sokoto, Northwestern Nigeria. Children aged 2 to 10 years were included in the study. Each participant had a physical examination and a blood sample for a thick and thin film for malaria parasites and a Rapid Diagnostic Test for malaria. The presence of any malaria parasitaemia was documented along with species and parasite count was documented. The data were analysed using SPSS version 22.

Results

The overall prevalence of malaria for the study was 34.8% using microscopy and 33.8% using Rapid Diagnostic Tests. Higher among males (35.6% vs 33.9%). The prevalence is in keeping with other studies conducted during the same period. It confirms a gradual transition in malaria endemicity, coinciding with a period of rising coverage of Insecticide Treated Nets in Nigeria and globally.





Conclusions

There has been some reduction in the prevalence of malaria in Nigeria, likely due to increased malaria control activities although the prevalence remains high, with intermediate transmission intensity. The information provided can guide further malaria control efforts.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0384
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

A souvenir with different faces and a long-lasting taste

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Background

Melioidosis, caused by *Burkholderia pseudomallei*, is endemic in north Australia and Southeast Asia. Contamination occurs mainly via percutaneous inoculation, inhalation, aspiration, and occasionally by ingestion. Particularly in children it may present as skin abscess, pneumonia, parotitis or osteomyelitis.

Case Presentation Summary

A 2-year-old previously well Swiss boy, was seen for evaluation of fever for 10 days after family vacation (December) in Thailand visiting cities and staying at a beach resort. He had coryza, diarrhoea but was otherwise well in himself. On his arm he had a papule which according to his mother might had been from an insect bite. Search for Malaria, Dengue, Chikungunya, Q-fever, Tularemia were negative. Repeated blood cultures and bacterial and viral stool examination remained negative. 10 days later the papule progressed to an abscess, cough persisted. Aspirate was positive for *B. pseudomallei*. Whole-body MRI revealed a pulmonary abscess but no further organ involvement. Ceftazidime was started. After 2 days fever defervesced. After 3.5 weeks iv. Ceftazidime, the eradication phase with oral trimethoprim-sulfamethoxazole was started and continued for 6 months.

Learning Points/Discussion

This is a rare paediatric case of imported Melioidosis from Thailand manifesting as cutaneous and pulmonary abscesses. We postulate percutaneous inoculation facilitated by the skin breach from an insect bite. Melioidosis may have a wide range of clinical manifestations, and severity varies from an acute fulminant septic illness to a chronic infection. It should be part of a differential diagnosis in returning travellers from South-East Asia presenting with an acute or chronic febrile illness particularly with an abscess and/or pneumonia. Antimicrobial treatment consists of an intravenous intensive phase followed by a prolonged eradication phase.

ESPID19-1155
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Atypical manifestation of disseminated sporotrichosis in an infant from an indigenous community in costa rica : diagnostic challenges

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Background

Sporotrichosis is an unusual disease in children. This fungi is most typically found in warmer temperatures and tropical climates around the world. In spite of its typical signs, it is often confused with other skin diseases, what delays diagnosis. This study aims to present the clinical case of an infant with a complicated lymphatic-cutaneous sporotrichosis.

Case Presentation Summary

A 9-months old patient from a rural indigenous community in Costa Rica was referred to our hospital, with 3 days of respiratory symptoms and cellulitis with violaceous plaques on the lower limbs. Some signs of malnutrition with oedemas were present. She lived with other five children in precarious conditions, in a wooden house with a water well and some dogs. Blood test: 16280 leucocytes (43% N 50%L); CRP 285 mg /L. Cefotaxime and clindamycin were started (A methicillin-resistant *Staphylococcus aureus* cellulitis was initially suspected). Peripheral and central cultures resulted negative. Mantoux negative. HIV negative. Metapneumovirus positivity was determined in his aspirate. After 10 days of treatment she presented an unfavourable evolution. Bone marrow aspiration: negative for Leishmania, bacteria, fungi and micobacteria. A Biopsy of the lesions showed reactive paniculitis; bacterial and fungal cultures were negative. New lesions arose, and in a smear fromt one of them some fungal structures suggestive of *Sporothrix* were isolated. Itraconazole was started. Six days after, a spontaneous drainage was observed (*drain cultures* were all *negative*) and reconstructive surgery was required. A biopsy of the lesions was informed as suppurative panniculitis.

Learning Points/Discussion

It is often difficult and challenging to diagnose sporotrichosis in children because the lesions do not always follow the typical sporotrichoid pattern. Cutaneous sporotrichosis should be considered in the differential diagnosis of cutaneous ulcers, particularly if unresponsive to first-line therapies.

ESPID19-1141
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Severe eosinophilia in a european no travelling child: a challenging diagnosis

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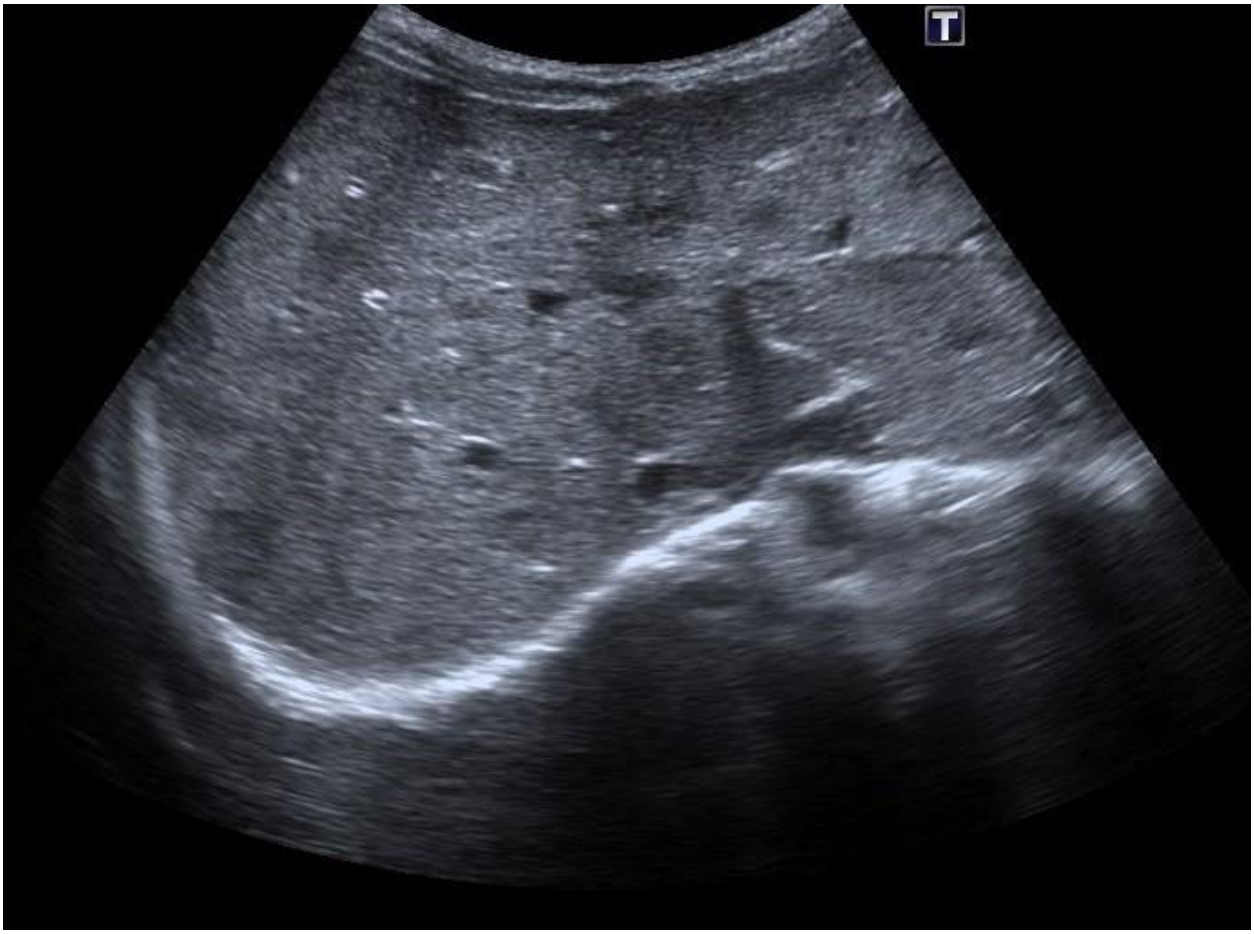
[4]Hospital Universitario La Paz, Paediatric Infectology Department, Madrid, Spain

Background

Severe eosinophilia (>5000 eosinophils/µL) represents a diagnostic challenge, to establish the aetiology in developed areas as well as to investigate secondary organ damage.

Case Presentation Summary

Spanish 21-month-old male presenting severe eosinophilia and fever for six days. Background: rural and animals environment, no travel history, recent treatment with amoxicillin/clavulanic-acid and ibuprofen, normal previous eosinophils count. Physical exam: active and pale, generalized lymphadenopathies, tachypnea with lung crackles. Initial studies: leukocytosis ($34x10^3$/µL), eosinophilia ($21x10^3$/µL), IgE 476 kU/L, hypergammaglobulinemia, high erythrocyte sedimentation rate; negative extensive microbiological studies; chest X-ray: peribronchial oedema; abdominal ultrasound: nonspecific adenopathies. Stable during hospitalization, with persistent low-graded fever, evanescent urticaria and tachypnea. Remarkable tests: polymerase chain reaction and direct visualization of parasites on several feces samples were negative; second abdominal ultrasound: multiple liver focal lesions; bone marrow aspiration: intense reactive eosinophilia, negative microbiological studies; chest tomography: diffuse lung pattern. No parasites were detected on liver and gastric biopsies, duodenal aspiration and bronchoalveolar lavage. Hematologic or solid neoplasia, inflammatory disease, immune dysregulation or allergic disorder were ruled out. *Toxocara canis* immunoserological test became positive on day +13 and level significantly increased on day +21. Diagnosis: visceral larva migrans. There was no ocular or neurological involvement. Steroid treatment and two cycles of albendazole resulted in a decrease of blood eosinophils count and improvement of hepatic lesions.



Learning Points/Discussion

Toxocara should be checked out when studying an eosinophilia. Severe *Toxocara* infections are rare in developed areas but occur, more likely, in young children with pets living close; they can lead to a life threating disease. Diagnosis is based on clinical disease, exposure history and positive specific serological testing. Active infection is confirmed by demonstrating a significant rise in antibody level over time, leading to a delayed diagnosis.

ESPID19-1135
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Intravenous artesunate for imported severe malaria in children treated in four tertiary care centers in germany

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Background and Aims:

Intravenous artesunate (ivA) is the standard treatment for severe malaria. Data systematically evaluating the use of ivA in paediatric patients outside malaria endemic regions are limited. The aim of this case series was to summarize efficacy and safety of ivA for imported severe malaria in children in Germany.

Methods:

Our retrospective case series included pediatric patients with imported severe malaria treated with at least one dose of ivA (Artesun®, Guilin Pharmaceutical; Shanghai, China) at four German tertiary care centers. Severe malaria was defined according to WHO criteria.

Results:

Between 2010 and 2018, 14 children with a median (IQR) age of six (1;9.5) years were included. All children were of African descent. All but two patients had *P. falciparum* malaria; one child had *P. vivax* malaria and one child had *P. falciparum* and *P. vivax* co-infection. Median (IQR) parasitemia at admission in patients with *P. falciparum* was 9.5% (3;16.5). Patients were treated with 1 to 10 (median (IQR) 3 (3;4)) doses of ivA. All but one patient consecutively received a full course of oral antimalarial treatment. Parasite clearance was achieved within 2-4 days, with the exception of one patient with prolonged clearance of peripheral parasitemia. Three patients experienced post-treatment hemolysis but none needed blood transfusion. Otherwise ivA was safe and well tolerated.

Conclusions:

Intravenous artesunate was highly efficacious and safe in this pediatric cohort. We observed episodes of post-treatment hemolysis in approximately a quarter of patients. The legal status and usage of potentially lifesaving ivA should be revalued in Europe.

Systematic Review Registration:

NA

ESPID19-0834
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Travelling with children - the experience of a terciary portuguese hospital

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Background and Aims:

Travelling with children around the world is becoming increasingly common. Receiving appropriate pre-travel medical advice is essential as some destinations may require specific preventive measures.
The aim of this study was to characterize children travel patterns and the medical advice offered by our centre.

Methods:

Review of the pre-travel consultation records of children under 18 years of age, at an international travel vaccination centre of a tertiary Portuguese hospital in the year of 2018.

Results:

A total of 241 children sought pre-travel consultation. The mean age was 7.68 years (1 month to 17 yo) and 56.4% were male. Ninety-five percent were portuguese. The mean time between the consultation and the departure date was 27.4 days (1 to 184 days).
Forty-five percent were travelling to Africa, 31.1% to South America, 13.7% to Asia, 8.3% to Central America and 1.7% to North America. Brazil was the most common destination (30.3%), followed by Angola (16.2%) and 10.4% visited more than one country. The main reasons for travel were tourism (76%), emigration (10.4%), volunteering projects (3.7%) and visiting friends and relatives (3.3%). The mean duration of the trip was 21 days (3 to 180 days) and 10.8% were staying for an undetermined time. Fifty percent of children stayed at a hotel and 37.3% with relatives.
The most frequently prescribed vaccines were against hepatitis A (59.3%), yellow fever (46.9%), typhoid fever (15.8%) and meningococcal ACWY (8.7%). Chemoprophylactic drugs against malaria were advised in 28.8% of travelers.

Conclusions:

A high number of northern Portuguese children travelled in 2018. Portuguese-speaking countries were the main destination and are localised in (sub)tropical regions, so health education and travel prevention measures are crucial to minimizing the risk of traveller's diseases.

Systematic Review Registration:

N/A

ESPID19-0811
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Sporotrichosis, neglected infectious disease: case series in a pediatric university hospital in rio de janeiro for a 10 years-period

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Background

Sporotrichosis is a neglected infectious disease caused by *Sporothrix schenckii* complex. In the last decades an epidemic has been observed in Rio de Janeiro, Brazil, related to contact with domestic cats, with many cases among the pediatric population. The aim of this report is to describe clinical and epidemiological characteristics of children and adolescents diagnosed with sporotrichosis treated at a reference center for pediatric infectious diseases in Rio de Janeiro.

Methods

Case series including individuals aged 0-17 years followed from Jan/2008 to Oct/2018, with clinical or microbiological criteria of *Sporothrix* sp. from lesions.

Results

We followed 54 subjects, 51% were male. The median age at diagnosis was 87 months(7-204 months). The time from onset of symptoms to diagnosis ranged from 7 to 240 days(median= 40). 25% had comorbidities as HIV-infection and allergies. Only 25% remembered previous cat scratch. Contact with cats was reported in 74%(64% intradomiciliar) and 19% with relatives with probable sporotrichosis. Inoculation lesions were reported in 50% of cases. The most frequent clinical forms were the cutaneouslymphatic (43%),fixed cutaneous(31%) and extracutaneous(22%). The cutaneous forms predominated on the upper limbs(43%) and face(40%). In 32%, mucosal areas were affected: 13 cases with conjunctivitis, 2 with dracryocystitis, and 2 with nasal mucosal lesions. 3 children presented erythema nodosum. Five children were lost during follow up, among the remaining, 92% had microbiological diagnosis. Itraconazole was the first-line treatment. Twenty-nine patients were cured, 8 were lost to follow-up during treatment, 8 were referenced to another hospital and 3 had spontaneous regression of lesions.

Conclusions

Childhood sporotrichosis is frequent in Rio de Janeiro with zoonotic transmission. The main clinical presentation is the cutaneouslymphatic form, and had a good therapeutic response with itraconazol.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0795
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Diarrhea is a presenting symptom of plasmodium falciparum malaria in african children and resolves with antimalarial treatment

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Background and Aims:

Malaria is among the leading causes of morbidity and mortality in children ≤5 years worldwide. Intestinal barrier damage in children with *Plasmodium* infection has been postulated. However, clinical data on the incidence of gastrointestinal (GI) symptoms are highly variable, and the role of *Plasmodium* in the etiology of acute diarrhea in developing countries remains controversial. We aimed to investigate the prevalence and risk factors for GI symptoms in malarial children in an endemic area.

Methods:

A retrospective case-control study in children aged 1 month to 5 years hospitalized for fever at St Mary's Hospital in Gulu, Uganda, from January 1st 2016 to December 31st 2016. Children receiving a final diagnosis of *P. falciparum* malaria were enrolled as *cases*, and feverish children in which malaria was excluded, were enrolled as c*ontrols*. A propensity score was estimated using a logistic regression model. The prevalence of GI symptoms was considered as primary outcome.

Results:

Among the 451 malarial children (209/46.3% females, median age 30 months), 46.1% had GI symptoms at admission: 24.8% had diarrhea, 35.5% had vomiting. In the propensity-matched population, the frequency of diarrhea (29.0% vs 11.5%, p<0.001) and vomiting (38.2% vs 15%, p<0.001) were significantly higher than that reported in controls. The presence of diarrhea at admission expressed a significantly higher risk of receiving a diagnosis of malaria (OR 3.14, 95%CI 1.99 – 5.07), with an age-related distribution being diarrhea more frequently reported in young children. Diarrhea resolved within the first 24 hours after artesunate in 78.8% cases.

Conclusions:

The study shows a 3-fold increased probability of having *P. falciparum* malaria in feverish children < 5 years living in an endemic area, who present with GI symptoms. Symptoms rapidly resolve with intravenous artesunate.

Systematic Review Registration:

N/A

ESPID19-0374
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Plasmodium malariae: an uncommon agent in a not so uncommon disease

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Background

Malaria is a major public health problem, with a high morbidity and mortality burden. Most cases are due to *Plasmodium falciparum*, responsible for a more severe course of illness. Other *Plasmodium* species are less studied and less documented. A Portuguese study reported other species to be responsible for 8.4% of all cases diagnosed in the country, with *P. malariae* being responsible for only 3.1%.

Case Presentation Summary

A 4-year-old girl is admitted to the Emergency Department with fever (one daily peak in the afternoon for one month, maximum of 39.8ºC), associated with epigastric/left hypochondrium pain. She recently returned from Guinea-Bissau, where she stayed for 45 days.
She presented a palpable spleen, with an otherwise normal physical examination.
Complete blood count showed bicytopenia (3710 erythrocytes/uL, 13000 platelets/uL), biochemistry revealed elevated aminotransferases, a slightly elevated urea with normal creatinine and CRP 40.9 mg/L.
Light microscopy was performed to screen for malarial parasites. Parasites were absent in the smear and antigen detection test was negative.
She was admitted for further evaluation and exclusion of other infectious diseases. On the second day, however, light microscopy was repeated and *Plasmodium* spp was visualized in the peripheral blood smear. PCR assay detected *P. malariae*.

Learning Points/Discussion

P. malariae infection has a relatively low prevalence and doesn't usually cause severe illness.
Nonetheless, it has been associated with hepatorenal dysfunction and there are cases of persistent infection.
Fever frequently occurs at 72h periodicity (*quartan* malaria), but not necessarily.
P. malariae exhibits a relatively low parasitic load, which can difficult the diagnosis. Even though our case was symptomatic, parasites were not observed in the first blood smear.
Repeated blood tests are crucial in the appropriate clinical and epidemiological context.

ESPID19-0265
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Visceral leishmaniasis: review of the last 19 years in a endemic area

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Background and Aims:

Visceral leishmaniasis is a life-threatening disease, especially in children, with complications such as secondary infections, *hemophagocytic lymphohistiocytosis(HLH) and renal injury. We present a cohort of children from the last 19 years.*

Methods:

Retrospective 19 years(2000-2018) observational study of all visceral leishmaniasis cases in a pediatric population of an endemic area. We collected age, sex, temperature(ºC), days of fever, hemoglobin(g/dl), platelets(/mm3), neutrophils(/mm3), lymphocytes(/mm3), monocytes(/mm3), CRP(mg/L), procalcitonin(PCT)(ng/ml), LDH(U/L), GOT(U/L), GPT(U/L), splenomegaly/hepatomegaly on admission, *HLH,* length of stay(days), Polymerase Chain Reaction(PCR) of Leishmania and histopathologic demonstration of parasite in bone marrow. Statistical analysis was made with the SPSSv.23 program.

Results:

We collected data from 27 patients. The average stay was 11,7 days (median 11 days, standard deviation 5). The median of age was 22 months (SD 25), days of fever 10(SD 9), hemoglobin 8(SD 1,3), and CRP 64(SD31). 1(55%) were male. All of them had splenomegaly and 14(53%) hepatomegaly. 2(7,7%) developed *HLH, and they show a longer average stay(p 0,006). PCR in bone marrow was performed in 11(40%) patients. In 3 of them (27%)* histopathologic demonstration of parasite was negative. A direct correlation was found between GOT and GPT on admission with the hospital length of stay(0,413 p 0,036; 0,431 p 0,028

respectively).

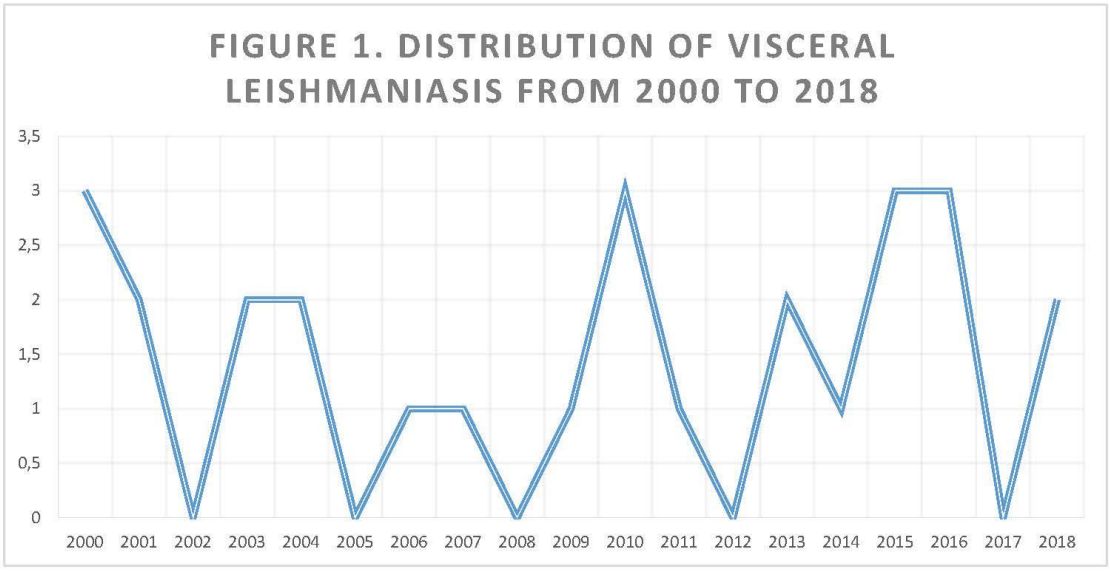
FIGURE 1. DISTRIBUTION OF VISCERAL LEISHMANIASIS FROM 2000 TO 2018
3,5
3
2,5
2
1,5
1
0,5
0
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018

Conclusions:

New cases of visceral leishmaniasis remains stable over the years in our area. Gender distribution is similar to the published data. All of them had splenomegaly(96% in other studies) and 53% hepatomegaly(similar to the published data). 2(7,7%) developed *HLH, with a longer average stay.* Histopathologic demonstration of parasite in bone marrow has 27% of false negatives in our sample. In a globalized world It's important to get a better knowledge of this disease, especially for travelers from non-endemic areas.

Systematic Review Registration:

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ESPID19-0230
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

The inter-rater reliability and prognostic value of coma scales in nepali children with acute encephalitis syndrome

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Background

Acute encephalitis syndrome (AES) is a common cause of coma in Nepali children. The Glasgow coma scale (GCS) is used to assess the level of coma in these patients and predict outcome. Alternative coma scales may have better inter-rater reliability and prognostic value in encephalitis in Nepali children, but this has not been studied. The Adelaide coma scale (ACS), Blantyre coma scale (BCS) and the Alert, Verbal, Pain, Unresponsive scale (AVPU) are alternatives to the GCS which can be used.

Methods

Children aged 1–14 years who presented to Kanti Children's Hospital, Kathmandu with AES between September 2010 and November 2011 were recruited. All four coma scales (GCS,ACS, BCS and AVPU) were applied on admission, 48 h later and on discharge. Inter-rater reliability (unweighted kappa) was measured for each. Correlation and agreement between total coma score and outcome (Liverpool outcome score) was measured by Spearman's rank and Bland–Altman plot (figure 1). The prognostic value of coma scales alone and in combination with physiological variables was investigated in a subgroup (n = 22). A multivariable logistic regression model was fitted by backward stepwise.

Results

Fifty children were recruited. Inter-rater reliability using the variables scales was fair to moderate. However, the scales poorly predicted clinical outcome. Combining the scales with physiological

parameters such as systolic blood pressure improved outcome prediction.

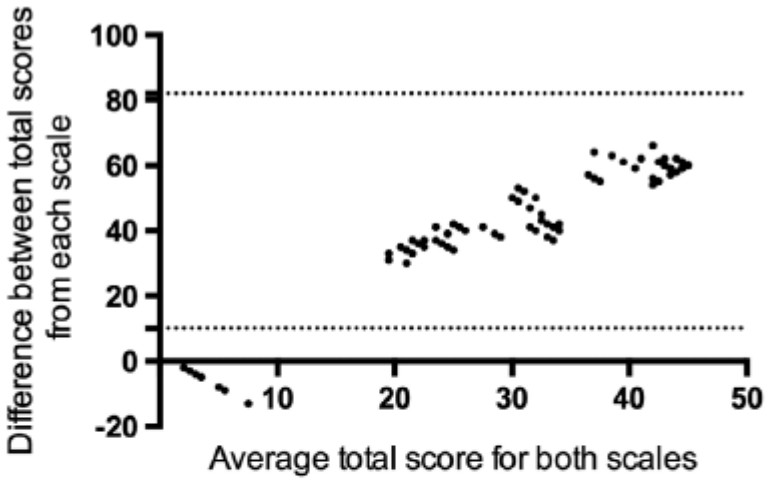

Figure 1. Bland–Altman plot measuring agreement between total Glasgow coma score and outcome (Liverpool outcome score). The plot displays mean (*X* axis) and difference (*Y* axis) in the total LOS (scored on discharge) and total GCS scores (scored on admission) in child AES patients ($n = 50$). Dotted lines demarcate the limits of agreement (±2 standard deviations from the mean difference). Forty-three children had scores for both the LOS and GCS within the limits of agreement. Seven children plotted below the lower limit of agreement.

Conclusions

This is the first study to compare four coma scales in Nepali children with AES. The scales exhibited fair to moderate inter-rater reliability. However, the study is inadequately powered to answer the question on the relationship between coma scales and outcome. Further larger studies are required.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0178
E-Poster Viewing - May 7-10 - E-Poster Hours

Tropical - parasite infections & travel medicine

Aetiology, neuroimaging and sequelae of febrile coma in malawian children

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[5]Michigan State University, Department of Osteopathic Medical Specialties, East Lansing, USA

Background

Fever and altered consciousness in children is a common presentation in sub-Saharan Africa. Historically, the majority of cases were cerebral malaria (CM), but with recent drastic reduction in malaria incidence, non-malarial coma becomes a larger proportion of cases; which are often diagnostically challenging.

Methods

This prospective case-cohort study, in Blantyre, Malawi, has being recruiting for 11 months (total 24 planned). It includes febrile children aged 3 months to 14 years in deep coma (Blantyre coma score ≤2). We are investigating aetiology (PCR and metagenomic NGS on blood/CSF), host response (RNA/proteomics) and performing MRI and EEG. Detailed neuro-developmental outcome (Liverpool Outcome Score/Malawi Developmental Assessment Tool) is assessed 1 and 6 months post-discharge.

Results

We have recruited 106 participants, with 62% (n=66) CM controls and 38% (n=40) non-malarial cases. Focusing on cases, PCR and MRI increased diagnosis from 8% (n=3) to 65% (n=26). These include acute bacterial meningitis (12%, n=13), encephalitis (7%, n=7), TBM (2%, n=2) and acute viral meningitis (1%, n=1). Causal pathogens have been identified in 55% (n=22) so far; most prevalent is *Streptococcus pneumoniae* (23%, n=9), followed by Herpes Simplex Virus (10%, n=4) *and Salmonella* Spp (8%, n=3). There were abnormal findings on MRI in 77% (27/35), including neurocysticercosis, acute disseminated encephalomyelitis secondary to *Salmonella typhimurium* and an Artery of Percheron infarction secondary to *Staphylococcus aureus* meningitis. Mortality is higher in the non-malarial group (30% vs 12%).

Morbidity is also higher ([median Liverpool Outcome Score] moderate vs mild neurodisability).

AETIOLOGIES	Number {%}
CEREBRAL MALARIA RETINOPATHY POSITIVE	**45 {42%}**
Co-infections (*S. pneumoniae* (n=3), HSV-1 (n=2), TB (n=1), *H.influenzae* n=1)	7
CEREBRAL MALARIA RETINOPATHY NEGATIVE	**21 {20%}**
1 Co-infection *(S. pneumoniae)*	1
ACUTE VIRAL MENINGITIS	**1 {1%}**
Cytomegalovirus	1
ACUTE BACTERIAL MENINGITIS	**13 {12%}**
Streptococcus pneumoniae	9
Salmonella spp	2
Staphylococcus aureus	1
Unknown	1
TUBERCULOUS MENINGITIS	**2 {2%}**
Mycobacterium tuberculosis	1
Presumed MTB	1
ENCEPHALITIS	**7 {7%}**
Herpes simplex virus type 1	4
Varicella zoster virus	1
Cytomegalovirus	1
Unknown	1
NEUROCYSTICERCOSIS	**1 {1%}**
TOXOPLASMOSIS & HIV ENCEPHALOPATHY	**1 {1%}**
ADEM	**1{1%}**
Salmonella Typhimurium	1
UNKNOWN ENCEPHALOPATHY	**14 {13%}**

Conclusions

Malaria remains the most common cause of coma in our setting, however non-malarial comas contributed more to the mortality. Systematic PCR and MRI identified diverse non-malarial aetiologies. The cause remains unknown in 13% (N=14); further antibody and metagenomic diagnostics are underway.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0988
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Osteoarticular tuberculosis in children, a diagnostic challenge

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Background

Estimating tuberculosis disease (TB) data in children is complex since there is no standard case definition and definitive diagnosis is difficult to be established. Osteoarticular TB accounts for 10 to 20 percent of cases of extrapulmonary TB, however it is associated with high morbidity. While the majority of case reports of osteoarticular TB have been reported in highly endemic areas, here we present 3 cases of our hospital.

Case Presentation Summary

Case 1. 27-month-old girl with progressive loss of right hip function. She visited the emergency department in several occasions, all of them with normal clinical exploration and imaging tests. After 2 months without improvement she was admitted to our Unit.

Case 2. 36-month-old girl with frequent visits for hip and lower back pain. 6 months later, a progressive swelling in the lower back region appeared. Following another 6 months, an MRI was performed which showed a L2-L3 fracture and a retroperitoneal mass, so she was admitted to the Oncology department.

Case 3. 34-month-old boy with knee pain and swelling for 4 months. It was attributed to a mild fall. In the first visit, they suspected cellulitis and started oral antibiotics. After three days without improvement, he was admitted to his local hospital for intravenous antibiotics. 3 weeks later, the pain and swelling persisted, so he was transferred to our Unit.

A summary of clinical and laboratory parameters is presented in Table 1.

OSTEOARTICULAR TB	CASE 1	CASE 2	CASE 3
YEAR	2009	2014	2018
AGE	27 months	36 months	34 months
COUNTRY OF ORIGIN	Romania	Spain/Poland	Morocco
PRESENTING COMPLAINT	Limp	Limp, lumbar mass, hip and lower back pain	Limp, knee pain and swelling
FIRST CLINICAL SUSPICION	Transient synovitis of the hip	Neuroblastoma	Cellulitis
DIAGNOSIS DELAY	2 months	12 months	4 months
TUBERCULIN SKIN TEST	22 mm	20 mm	15 mm
HIV SEROLOGY	Negative	Negative	Negative
IMAGING TESTS	Chest X-ray: LUL consolidation	Chest CT: Calcified mediastinal nodes	Chest X-ray: RML consolidation
	Hip X-ray: Decreased bone density Hip US: Joint effusion	Lumbar MRI: L2-L3 fracture and right retroperitoneal mass (13x5x4 cm)	Knee X-ray: Soft tissue swelling and bone lytic lesions
MICROBIOLOGY TESTS	Gastric lavage smear and culture: Negative	Gastric lavage: Smear, PCR and culture: Negative	Gastric lavage: Smear, PCR and culture: Positive
	Joint effusion smear and culture: Positive	Bone biopsy smear, PCR and culture: Positive	Joint biopsy smear, PCR and culture: Positive
BIOPSY	-	Granulomas with caseous necrosis	Granulomas with caseous necrosis
DEFINITIVE DIAGNOSIS	TB hip arthritis	TB spondylitis (Pott disease)	TB knee arthritis
DRUG SUSCEPTIBILITY TESTING	Susceptible	Susceptible	Susceptible
TYPE OF DRUG AND DURATION OF TREATMENT	H+R+P+E: 1 month H+R+P: 2 months H+R: 9 months Total: 12 months	H+R+P: 2months H+R: 10 months Total: 12 months	-
SEQUELAE	No	Lumbar kyphosis	-

LUL: Left upper lobe, RML: Right middle lobe, MRI: Magnetic resonance imaging, PCR: Polymerase chain reaction, H: Isoniazid, R: Rifampicin, P: Pyrazinamide, E: Ethambutol

Learning Points/Discussion

Osteoarticular TB is uncommon in children and easily unperceived by clinicians. Delays in diagnosis and subsequent treatment are frequent. The country of origin and possible TB contacts are key questions in the history. A high index of suspicion is required to reach the diagnosis.

ESPID19-0964
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

The challenging diagnosis of peritoneal tuberculosis in previously healthy children

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Background

Despite being considered a rare type of tuberculosis (TB), peritoneal TB is associated to severe disease and complications. Due to its nonspecific clinical, laboratory and radiological findings, the diagnosis is a huge challenge for clinicians. Here we report two cases of peritoneal TB in previously healthy children from Brazil, part of the “high burden country list for TB” by WHO.

Case Presentation Summary

CASE 1: A 14-year-old previously healthy boy was admitted with a history of abdominal pain, diarrhea, fever, and weight loss. On physical examination he had a distended abdomen, with ascites. Ascitic fluid revealed predominance of lymphocytes. Abdominal computed tomographic (CT) scan showed peritoneal thickening and diffuse lymphadenopathy. Exploratory laparotomy revealed miliary nodules and peritoneal and omental thickening. Biopsy specimens showed granulomas, positive for acid-fast bacilli (AFB). Quadruple combined therapy (Rifampicin, isoniazid, pyrazinamide and ethambutol) was initiated, but had to be replaced with an alternative IV therapy (amikacin, linezolid and levofloxacin) after an ileal perforation occurred in the early postoperative period. After 21 days, the patient died.

CASE 2: An 11-year-old previously healthy girl was admitted with progressive ascites for the past 5 months. Abdominal CT scan showed intestinal enlarged lymphadenopathy with omentum and peritoneal thickening. Peritoneal biopsy revealed granulomas and ascitic fluid showed serum-ascites albumin gradient lower than 1,1 mg/dl, both were negative for AFB and PCR. Quadruple combined therapy was introduced, with satisfactory response.

Learning Points/Discussion

Peritoneal TB should always be considered in the differential diagnosis of children with ascites, particularly in endemic countries, where it remains a serious public health problem.

Although a favorable prognosis is anticipated, when early diagnosis and prompt treatment is implemented, severe illness and complications leading to death may occur.

ESPID19-0728
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Central nervous system tuberculosis: consequences of a severe disease in a pediatric population

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Background

Tuberculosis is an important health problem worldwide, accounting for 1.7 million deaths in 2016. The central nervous system (CNS) disease is its most severe presentation, with high mortality. It is more common in infants and immunosuppressed patients. We collected data of all children admitted with tuberculosis of the CNS (CNS-TB) in a tertiary hospital in São Paulo from 1998 to 2018.

Case Presentation Summary

We found twelve patients with SNC-TB (median age=31.5 months; male n=9). Six patients had comorbidities or were immunosuppressed. Ten children received BCG-vaccine. Five patients had an identified index case.

Median time from first symptom to diagnosis was 22.5 days (3-500). Main symptoms were fever (n=8), lethargy (n=8), seizures (n=5), cough (n=4) and vomit (n=3). Seven patients had concomitant pulmonary tuberculosis.

Cerebrospinal fluid results showed moderate pleocitosis with predominant lymphocytic reaction, raised protein levels and consumed glucose. Adenosine deaminase was elevated in 75% of patients. Eleven patients had CNS imaging, all abnormal. Five patients had a Mantoux test, three were positive. Eight patients had microbiological confirmation.

All patients received treatment for tuberculosis, median time was 320 days. Main adverse effect was hepatotoxicity. Lincoln classification was I in five patients, II in five patients and III in two patients. Two patients died, seven had neurological sequelae, one fully recovered; two lost follow-up.**Learning Points/Discussion**

Our study shows a 16% lethality and 58% rate of sequelae in patients with CNS-TB. The main determinant of mortality in CNS-TB is the clinical stage at diagnosis. We found than even patients in stage I had an unfavorable outcomes, confirming the severity of the disease.

In countries with high incidence of tuberculosis, vaccination with BCG and early recognition and treatment are essential for prevention of morbidity and mortality.

ESPID19-0455
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Tuberculosis infection in our pediatric population

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Background and Aims:

Tuberculosis (TB) is one of the main causes of morbidity and mortality worldwide. In pediatric period, there are more diagnostic difficulties and a greater probability of progression to disease with severe and extrapulmonary presentations.

Objective of our study: to describe the clinical and epidemiological characteristics of TB in our pediatric population and to analyze diagnostic and therapeutic tools available.

Methods:

A descriptive, retrospective study was performed, reviewing pediatric patients diagnosed with TB (pulmonar and extrapulmonar forms) in two hospitals of Madrid, between June 1991-December 2017. There were 170 patients included (53.5% males)

Epidemiological, clinical, diagnostic and treatment variables were collected and analized. The statistical system SPSS 20 for Windows was used for the analysis.

Results:

Average age: 4.5 years, predominantly <2-year-old and adolescents. 21.8% were immigrants. 21.2% were born in Spain from immigrant parents (South-America(28.2%)).BCG in 14.3%.

Main symtomps: contact with TB(20.6%) and fever(15.3%). 61.8% reported an epidemic environment. At diagnosis: 30.6% were asymptomatic. Mantoux >10mm:64.1% and pathological X-ray: 90.0% (condensation(59.4%) and hiliar adenopathy(48.2%)). Extrapulmonary forms: 8.2%(skin and lymphadenopathies).

CRP and ESR were elevated in 28.2% and 30.6% of children. IGRA positive in 70.6% of cases when performed. When gastric juice(JG) or sputum(E) samples were collected BAAR staining, cultures and *M.Tuberculosis*-PCR were performed(See figure 1). Resistances to H:1.8%. Treatment with H+R+P:70.6% (co-formulations:15.9%).

Figure 1. Microbiology test.

	Gastric Juice	Sputum
Positive BAAR staining	12.4%	21.4%
Positive culture for *M.Tuberculosis complex*	36.9%	40.9%
***M.Tuberculosis*-PCR**	32.2%	20.7%

Conclusions:

Tuberculosis still affects young children and adolescents. Almost half of cases in our area are from foreign origin (South-America and Morocco) and referred epidemic enviroment. Diagnosis in children continues to be difficult, although tools such as *M.Tuberculosis*-PCR in gastric juice or sputum can improve it and allow us to know possible resistances. Low resistance to H permits us to treat our patients with H+R+P once sensitivity is demostrated.

Systematic Review Registration:

-

ESPID19-0443
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Miliary tuberculosis with pulmonary and central nervous system involvement

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Background

Transmission of tuberculosis (TB) in <3 months of age children, can be due to intrauterine infection (congenital TB) or airborne transmission from baciliferous adult. Due to high risk of hematogenous spread, it is important to carry out early TB-disease study and treatment.

Case Presentation Summary

3-month-old girl, daughter of Guinean parents, with catarrhal symptoms since 6 days and fever the last 12 hours. Initial examination: febrile, polypnea and respiratory distress; weight, height and cephalic-perimeter <p3. Lab test at 24 hours of admission: 21660 leukocytes / mm3 (8360N), PCR 76mg/L; Chest x-ray showed reticulonodular pattern with bilateral nodular opacities and left-upper-lobe infiltrate. Intravenous cefotaxime and clindamycin were started and study of possible TB was performed: Mantoux (48h): 8mm; IGRA positive. *M.tuberculosis complex* was isolated in sputum and gastric juice. Four antituberculosis drugs and corticosteroids were started, modifying to isoniazid+rifampicin+pyrazinamide after knowing *M.T.C* sensitivity (Genotype MTBDRplus and Xpert MTB / Rif techniques). Discharged after one month, continued follow-up: asymptomatic after complete treatment. Neurological evolution is normal and ponderal and linear growth is recovered.

In TB-contact investigation, two siblings (2 and 7 years old) were diagnosed with lung disease, and another (16 years old) and their parents, with a latent infection. To rule out possible congenital infection, an endometrial biopsy on the mother was performed, being normal. Some months later an index case was found, thanks to Preventive and Public Health Service (uncle that previously lived at home, now in another city).

Figure 1. TB-disease study

	Results
Cerebrospinal Fluid	8 cells, glucose 48mg/dL, ADA 0.8UI/L
Ultrasound and brain MRI	Multiple tuberculomas without ventricular dilation
Abdominal US	Non specific liver lesion
Eye fundus	Bilateral: normal.

Learning Points/Discussion

Early diagnosis and treatment is critical in miliary tuberculosis. In the absence of known postnatal contacts it is recommended to rule out maternal genital TB. Study of contacts and search for the index case is elementary but not always easy, especially in immigrant population.

ESPID19-0429
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Tuberculous meningitis – disabling form in a teenage girl

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Background

Tuberculosis remains a global health problem. The most lethal and disabling form is tuberculous meningitis (TBM); diagnosis is often delayed by the insensitive and lengthy culture technique.

Case Presentation Summary

A healthy 11-year-old Brazilian girl was diagnosed with pneumonia and pleural effusion, successfully treated with amoxicillin-clavulanate and clarithromycin for 10 days.
Two months later, she went to ER with a 5-day history of headache, vomit and fever. She was hospitalized, initially treated with ceftriaxone. The initial CSF (2nd day ceftriaxone) presented 152 leucocytes (6%neutrophils,92%lymphocytes), 20glucose, 604protein. After 5 days she evolved with altered consciousness, strabismus and anisocoria and maintained the same CSF. We reviewed previous medical records and checked the culture of pleural effusion, positive 40days after for *Mycobacterium tuberculosis*. We started rifampicin+isoniazid+pyrazinamide+ethambutol and corticosteroids. After 30days the initial liquor culture was positive for *Mycobacterium tuberculosis*.
She evolved with CNS venous thrombosis, with gradual recanalization without anticoagulant therapy. She presented optic neuropathy secondary to intracranial hypertension and paralysis of the left 3rd cranial nerve; these complications were treated with acetazolamide and repeated lumbar punctures. She was discharged after 2 months; now she is receiving rifampicin+isoniazid with clinical improvement.

Learning Points/Discussion

Tuberculosis infections are established with the inhalation of bacilli and hematogenous dissemination; our case first presented pneumonia and pleural effusion that resolved without anti-tuberculosis treatment, which progressed to TBM.
This diagnosis is challenging, clinical symptoms are nonspecific and definitive diagnosis is provided by CSF mycobacterial culture with a long incubation period.
Prompt initiation of treatment is vital. Complications must be tackled quickly; guidelines suggested ventriculoperitoneal shunt for persistent intracranial hypertension, but we managed without surgery. They are at risk for venous thrombosis, but guidelines failed to show a significant association between aspirin and stroke prevention.

ESPID19-0979
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Electrolyte disturbances as first symptoms of central nervous system tuberculosis

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Background

Tuberculosis of central nervous system is a severe demonstration of tuberculosis but occurs very rarely with a frequency of about 1% of all cases. Its symptoms are unspecific and the diagnosis is difficult due to the lack of sensitive methods to examine central nervous system.

Case Presentation Summary

The case includes a 16-month old girl, diagnosed at birth with Turner syndrome, vaccinated against tuberculosis during neonatal period. She presented with subfebrile temperature, nausea and vomiting that lasted for five days. Basic blood laboratory tests revealed low sodium levels. The girl was treated with both oral sodium chloride and intravenous fluids containing higher concentration of sodium. Blood and urine tests results did not meet the criteria of SIADH. After a week her condition started to deteriorate with quantitative disturbances of consciousness. An MRI scan of her head revealed basal meningeal enhancement while the analysis of cerebrospinal fluid showed pleocytosis with low chloride levels. T.SPOT-TB as well as her blood and cerebrospinal fluid were positive for *Mycobacterium tuberculosis* as tested with molecular methods. No signs of pulmonary tuberculosis were detected. We started treatment according to drug susceptibility pattern with rifampicin, isoniazid, pyrazinamide and aimed to minimalize electrolyte disturbances. During next days electrolyte imbalance resolved but paralysis of right arm and muscular weakness of right half of the body occurred. Basal meningeal enhancement and thalamus infarcts were found in control head MRI. The patient is still undergoing treatment but her general condition improved.

Learning Points/Discussion

Diagnosis and treatment of central nervous system tuberculosis are still challenging because of unspecific symptoms, insensitive diagnostic methods and *M.tuberculosis* drug resistance. Early recognition an prompt treatment are essential. The BCG vaccine does not guarantee full protection from this form of tuberculosis.

ESPID19-1136
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Diagnostic work-up of bone lesions with uncertain aetiology: the role of tests for mycobacterium species

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Background

The management of bone lesions in children may be a challenge because it may lead misdiagnosis between bone tumours and osteomyelitis.

Methods

We retrospectively enrolled all children with bone lesions referred to our centre from 1st May 2016 to 10th January 2019 to undergo a bone biopsy in the suspicion of a neoplastic lesion.

Results

Overall, 92 children presenting with osteolytic, cystic or hyperplastic bone lesions were included; about 53% were boys and the median age was 9 years (12.2-6.5 IQR).

One or more microbiologic tests were performed on bone samples in 73/92 (79.3%) children. Considering those children, culture was done in 63/73 (86.3%) cases, polymerase chain reaction (PCR) for the most common pathogens of osteomyelitis in 44/73 (60.3%) and mycobacteria microbiology in 36/73 (49.3%) children. The whole microbiologic work-up was performed in about one third of the children (26/73, 35.6%). Four mycobacterium cultures (4/36) and two common bacterial cultures (2/63) are still ongoing.

The histologic exam defined 12/92 (13%) malignant lesions and 72/92 (78.3%) benign lesions. Two histologic analysis were non-conclusive and 6 are still ongoing. About 12% of all lesions (11/92) had inflammatory features, suggesting osteomyelitis.

Overall, 3/92 (3.3%) children had a positive microbiological test. Considering only those with inflammatory features, *Mycobacterium* spp. was identified in about 20% (2/11) of cases. In particular, *Mycobacterium intracellulare* and *Mycobacterium tuberculosis* were found in two children with granulomatous lesions. A bone sample with non-conclusive histology had a slightly positive culture for *Staphylococcus hominis*. All other microbiologic tests were negative.**Conclusions**

The diagnostic work-up of bone lesions of uncertain aetiology should include a microbiological assessment. Tests for mycobacterium spp. might be part of this screening, especially if risk factors are identified.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1124
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Contribution of quantiferon-tb gold-in-tube to the diagnosis of mycobacterium tuberculosis infection in young children in a low tb prevalence country

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Background

WHO recommends for children (less than 5 years old), who had recent contact with a pulmonary tuberculosis patient, to screen and initiate preventive treatment even before infection can be demonstrated. Interferon Gamma Release Assays (IGRA) have proven to be useful tests in adults, for tuberculosis infection, as an alternative for tuberculin skin testing.
Less is known about IGRA performance in younger children, who are especially vulnerable to develop tuberculosis disease after exposure.

Methods

Referred children (5 years or less) were simultanously tested with tuberculin skin test (TST) and QuantiFERON-TB Gold-In-Tube (QFT-IT), a commercially available IGRA.
Children with a recent exposure to pulmonary tuberculosis underwent a second screening at least 8 weeks after the contact.

Results

Results of 61 children and 100 blood samples for QFT-IT were available for analysis.
87% of the children (53/61) were not infected, 6.5% (4/61) had latent tuberculosis infection and 6.5% (4/61) pulmonary tuberculosis.
Agreement was 91% between TST and QFT-IT (Kappa 0.62). Positive predictive value of QFT-IT was 0.72 and negative predictive value was 0.94.
For children who didn't receive BCG, agreement was 96.25 % (Kappa 0.80).
QFT-IT was negative in two out of four patients classified as latent tuberculosis infection based on positive tuberculin skin test.

Conclusions

In this prospective study of a cohort of young children at high risk of tuberculosis in a low tuberculosis prevalence country, QFT-IT, a commercially available IGRA test, proved to have substantial agreement with TST.
More studies in children are needed to determine if discordant TST+/IGRA- results are false negative IGRA results or false positive TST results, or a mixture of both.
For now, the more prudent approach would be to consider these as false negatives and treat accordingly.

Clinical Trial Registration (Please input N/A if not registered)

yes

ESPID19-1121
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Disseminated tuberculosis- a case of late diagnosis or severe immune dysfunction.

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Background

Joint or bone TB accounts to 4-5% of childhood-TB. A 14-year-old Afro-Caribbean boy born in the United Kingdom presented with non- specific back-pain; was diagnosed with extensive disseminated-TB.

Case Presentation Summary

A 14-year-old Afro-Caribbean boy presented to emergency-department with three-month history of back-pain. He had no symptoms of fever, cough or weight-loss. No neurological-signs or weakness. He attended mainstream-school and enjoyed street dancing. He was born in the UK, no reported TB-contacts. No reported travels out of the UK. 10-years ago, he presented with signs of intestinal-obstruction secondary to tricho-bezoar. He underwent small-bowel resection. Histopathology-granulomas in the intimal region of small intestine.

In his current admission, point tenderness over L4-5 noted, raised skin-lesions over nasal-bridge, right-forearm and a surgical abdominal-scar. Full-blood-count -normal. CRP-50 mg/l. Spinal-x-ray- evidence of discitis at L4–5 level. MRI-spine –osteomyelitis/discitis of L4-5 level; impingement on nerve -roots; large anterior-abscess in psoas-region (Fig-1). Chest-X- ray- left upper-lobe opacity, bronchial-wall thickening and left hilar-lymphadenopathy. Quantiferon-positive. Interventional radiology-guided drainage of psoas-abscess relieved back-pain. Pus drained- *M tuberculosis* PCR positive. Sputum microscopy- Acid-fast-bacilli negative but culture positive at 7-days. Whole-Genome-Sequencing confirmed *M tuberculosis,* sensitive to all first-line anti-TB medication. Standard 4-drug treatment was commenced for 12-months and steroids for potential nerve-root impingement. HIV-serology –negative. Respiratory-burst taken prior to steroids showed indeterminate result. Low CD4-count of 371 cells/microL with a reversed CD4:8 ratio was noted.

Learning Points/Discussion

- This young-man presented with minimal systemic symptoms and widely disseminated TB involving lungs, spine,psoas and skin.
- Interestingly, he had non-specifically low CD4-count and indeterminate respiratory burst. This may be a result of his being unwell and is planned for repeat.
- It is unclear if intestinal- granulomas noted 10-years ago represent TB-infection or underlying chronic-granulomatous-disease or just normal inflammatory response to tricho-bezoar.

ESPID19-0868
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Atypical mycobacterial infections are often a pointer towards an underlying immunodeficiency in children

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Background

Atypical mycobacterial infections are often a pointer towards an underlying immunodeficiency in children. We report 2 cases of MAC who turned out to have an underlying immunodeficiency.

Case Presentation Summary

Case1:12 year old boy was symptomatic for 1 year with abdominal pain.He was treated with ATT with no clinical improvement.He was noted to have hepatosplenomegaly.HIV serology was reactive.Ultrasonography revealed mesenteric lymphadenopathy,FNAC showed acid-fast bacilli;GeneXpert was negative,culture showed no growth.After 4 weeks,he was started on ART;abcavir, lamivudine, efavirenz.However, 5 months later,he presented with worsening abdominal pain.Ultrasonography of abdomen revealed mesenteric lymphadenopathy and FNAC showed numerous acid-fast bacilli;GeneXpert was negative and culture showed Mycobacterium avium intracellulare(MAC).He was started on a modified ATT with levofloxacin and azithromycin.**Case2:**A 4-year-old-boy presented with a history of chronic neck and back pain.He was diagnosed to have BCG lymphadenitis at 3 months for which he received a 6 months of ATT.He had restriction of movements in neck and a pretibial collection below the right knee.PCR of pus from pretibial collection revealed Mycobacterium tuberculosis,GeneXpert was negative.HIV serology was non-reactive.Lymphocyte subset were normal.Dihydrorhodamine assay showed normal oxidative burst.Interferon gamma receptor 1(IFNγR1) expression was not reduced.Despite 8 months of ATT there was a progression in lesions.CT scan revealed progression of lesions with prevertebral and retropharyngeal abscess.Pus showed acid-fast bacilli,GeneXpert was negative,culture at this time revealed MAC.Detailed investigations were carried out to rule out mendelian susceptibility to mycobacterial disease(MSMD).NGS showed partial dominant mutation in IFNγR1 (c.816_819delAATT) in exon 6.He was started on a modified ATT regimen with addition of azithromycin and levofloxacin.He showed prompt clinical improvement at 6 months of follow-up.

Learning Points/Discussion

Infection with MAC are unusual.Isolation of MAC should prompt a work-up for an underlying immunodeficiency.After ruling out HIV infection,a full workup for MSMD is warranted.

ESPID19-0807
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

A new threat for tuberculosis: biological agents

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Background

The use of tumor necrosis factor alpha (TNF-α) inhibitors in autoimmune diseases is increasing and provides satisfactory results. On the other hand, suppression of TNF-α rises tuberculosis (TB) risk. Herein, we present an adolescent girl with pulmonary TBwhich had occurred during the use of anti-TNF-α agent.

Case Presentation Summary

A 16-year-old who had been diagnosed with iridocyclitis admitted to our emergency department with respiratory distress. When the history was deepened, it was learned that she had been using anti-TNF-α for 36 months. Before the initiation of anti-TNF-α, her physical examination and postero-anterior chest radiography were normal and the tuberculin skin test (TST) was 0 mm. At the 21st month of follow-up, TDT was detected as 6 mm and isoniazid (H) was started for latent tuberculosis since her chest X-ray was normal. She was given H for 9 months. During the course; her malar rash was observed and detailed work-up revealed the diagnosis of systemic lupus erythematosus and was started on methylprednisolone (MP). After 3 months of systemic MP treatment, she admitted with sudden onset of respiratory distress and fever lasting for several days. Posteroanterior imaging showed widespread infiltration in the middle and lower zones. Thorax tomography imaging revealed lymphadenopathies forming conglomerate with central necrosis in the right para-tracheal chain, diffuse symmetric miliary nodules in bilateral lung parenchyma and ‘tree in bud’ appearance strongly suggesting TB(Fig-1). She was started on quadripuletanti-tuberculosis [H + rifampicin(R) + pyrazinamide(Z) + streptomycine(SM)] treatment. Fasting gastric lavage culture yielded four-drug sensitive(HRZSM) *Mycobacterium tuberculosis complex* growth. The patient is still being followed-up in our clinic without complication.

Learning Points/Discussion

This case shows thateven the patients who had received treatment for latent TB are under the risk of active TB during anti-TNFα treatment.

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E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Anti-tuberculosis medicine hypersensitivity in a patient

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Background

Drug reactions against anti-tuberculosis treatment can be seen in a wide range from rash to anaphylaxis. Here, we present an adolescent girl who developed an early type of drug reaction after the initiation of anti-tuberculosis treatment.

Case Presentation Summary

A healthy 14-year-old female patient was admitted to the external center because of fever and cervical lymphadenopathy lasting for two weeks. She was referred to our clinic after supraclavicular lymph node excision specimen yielded rifampicin-sensitive *M. tuberculosis complex* with EXPERT-MIB. Computerized chest tomography showed widespreadalveolitistogether with centrally necroticlymph nodes located in the right para-tracheal area(Fig-1). She was started on four-drug anti-tuberculosis therapy (HRZE) and methylprednisolonedue to bronchial lymph node compression. On the 11th day of the treatment, therapy had to be ceased she complained of vomiting and newly-onset abdominal pain. Laboratory study revealed increased liver transaminases.HRZE treatment was started one week later after liver transaminases became normal. She experienced dyspnea and hypotension 2 hours after the initiation of anti-TB therapy. She responded well to symptomatic treatment. A week later, she was givenamikacin and levofloxacin after consultation with allergy department. Then, ethambutol and pyrazinamide were started. Two months later, since no clinical, laboratory or radiologic improvement was observed, she was planned to be given H+R. She was hospitalized and H+R were started by the suggested desensitization protocol. Levofloxacin and amikacin were ceased after that.

Learning Points/Discussion

Although severe systemic reactions to anti-tuberculosis drugs are not frequent, desensitization should be attempted under appropriate conditions after stabilizing the patient to ensure effective treatment.

ESPID19-0785
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Endobronchial ultrasound (ebus) guided fine needle aspiration (fna) is an important tool for the diagnosis of mediastinal tuberculosis

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Background

The diagnosis of tuberculosis (TB) is often challenging, especially in children, who typically have paucibacillary disease. Isolation of the causative agent, *Mycobacterium tuberculosis* (*MTb*), is crucial to direct antibiotic treatment, as resistance to first-line drugs is increasing globally. Endobronchial ultrasound (EBUS) is a technique that facilitates the visualisation and sampling of mediastinal lymph nodes. Although used extensively in adult medicine, few healthcare centres have the capability to perform this procedure in children and adolescents.

Case Presentation Summary

A 15-year-old girl of Afghani origin presented with a 5-month history of intermittent cough, significant weight loss and night sweats. Initial blood tests showed an unremarkable white blood cell count and CRP, but elevated ESR (27 mm/hr) and a positive T-SPOT.TB result. A chest x-ray showed no pulmonary parenchymal changes, but prominence of the hilar regions and the right paratracheal region suggestive of lymphadenopathy. Induced sputum samples were negative on acid-fast bacilli staining and *MTb* PCR (Xpert MTB/RIF). A chest CT revealed paratracheal and subcarinal lymphadenopathy with heterogeneous density and enlarged hilar lymph nodes bilaterally. EBUS was performed and fine needle aspirates of the subcarinal lymph nodes were obtained, showing no acid-fast bacilli, but subsequently fully-sensitive *MTb* was grown in culture. Following the procedure she was empirically started on standard quadruple anti-TB treatment (HRZE), resulting in complete resolution of her symptoms within 4 weeks.

Learning Points/Discussion

In this patient EBUS was instrumental in securing a microbiological diagnosis and confirming that the causative *MTb* strain was susceptible to first-line anti-TB drugs. EBUS is minimally invasive and complications associated with this procedure are rare. The use of EBUS in children and adolescents with suspected TB should be expanded to other centres specialised in Paediatric TB.

ESPID19-0782
E-Poster Viewing - May 7-10 - E-Poster Hours

Tuberculosis and other Myocbacterial infections

Rapid diagnosis of miliary tb facilitated by xpert mtb/rif molecular assays

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Background

Timely diagnosis and treatment of miliary TB are crucial due to its high associated morbidity and mortality. We report a case of miliary TB in whom PCR-based testing facilitated same-day diagnosis.

Case Presentation Summary

This 12-week-old boy was born at term after an uneventful pregnancy to Romanian parents living in England. There was no known TB contact; he was not BCG-vaccinated. At 5 weeks-of-age he developed signs suggestive of bronchiolitis, requiring oxygen support at his local hospital. His respiratory situation failed to improve over the next weeks, and he developed pyrexia. PCR-based tests detected RSV in respiratory secretions. A moderate-sized arterial duct was noted on echocardiography. Serial chest x-rays (CXR) showed gradual worsening of interstitial opacifications. Given those findings and clinical deterioration, he was transferred to our PICU for further investigations as underlying cardiac failure was suspected. His CXR on arrival showed widespread, bilateral reticulonodular pulmonary opacifications highly suggestive of miliary TB. After obtaining respiratory samples via bronchoscopy and performing a chest CT, which showed marked mediastinal lymphadenopathy, consolidations in the left upper and right lower lobe and wide-spread nodules, empiric anti-TB treatment was started (HRZE). An Xpert MTB/RIF assay performed on those samples later that day detected rifampicin-susceptible *Mycobacterium tuberculosis*, confirming the presumptive diagnosis. A cranial MRI revealed multiple inflammatory lesions in the meninges and the cerebrospinal fluid showed pleocytosis, suggestive of meningitis; consequently prednisolone was added.

Learning Points/Discussion

This case highlights some important points. Firstly, molecular assays can greatly expedite microbiological confirmation of suspected miliary TB. Secondly, clinicians should have a high level of suspicion in children with disseminated reticulonodular pulmonary opacifications on imaging, and not be discouraged from starting empiric anti-TB treatment by the detection of other pathogens.

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Tuberculosis and other Myocbacterial infections

Tuberculous peritonitis mimicking intestinal lymphoma

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Background

In settings where tuberculosis (TB) is highly endemic or where there is high risk of exposure to TB, a single dose of BCG vaccine should be given to all infants. Revaccination with BCG does not provide additional protection in adolescents and adults and is therefore not recommended. Here we present a 13 years old female patient from a North African country who developed abdominal TB following BCG vaccination.

Case Presentation Summary

The patient presented with abdominal pain, fever, and malaise. She was evaluated at her country for 3 weeks but a definite diagnosis could not be reached. On physical examination a body temperature of 38.5 C˚, pallor, and a palpable mass on right abdominal quadrant were reported. Laboratory: WBC 19,000/mm^3, Hb 7.71 g/dL, albumin 3.8 g/dL, ALT 15 IU/L. A 110x43 mm mass with lobulated and cystic parts located at retroperitoneal region was detected on abdominal ultrasound. Echinococcus indirect hemagglutination negative. Abdominal computed tomography (CT) showed multiple conglomerated lymphadenopathy at right para-iliac fossa and free pelvic fluid. Thorax CT was normal. Bone marrow examination revealed normal cellularity. Core biopsy was taken from ovoid, hypoechoic solid lesion located at right iliac fossa. Samples were taken from 110x43 mm macro-lobulated, cystic necrotic lesion at mesenteric plain and purulent fluid from cystic lesion. Necrotizing granulomatous inflammation with abscess formation was reported on histopathological examination. Laparoscopic findings were thickened peritoneum with adhesions and omental thickening mimicking a mass. *Mycobacterium tuberculosis* complex growth was detected and identified as *M. bovis* BCG variant

Learning Points/Discussion

Peritoneal TB occurs most commonly by reactivation of latent foci from hematogenous spread from pulmonary TB. Infection from BCG vaccine is very rare. Identification is very important since vaccine strain is not sensitive to pyrazinamide.

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Tuberculosis and other Myocbacterial infections

Localized bcg adverse event interferes with tuberculin skin test and it is relevant for tuberculosis diagnosis

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Background and Aims:

Tuberculosis (TB) remains a public health problem in Brazil and vaccination with BCG vaccine is recommended at birth in order to protect children against severe forms of TB. We investigated tuberculin skin test (TST) and interferon-gamma release assay (IGRA) in children under 2 years exposed to different antigenic stimuli.

Methods:

This is a prospective study conducted at the Federal University of São Paulo, Brazil. Three groups were investigated: a BCG-vaccinated group not exposed to TB (TB-unexposed, n=51), a group with localized adverse event to BCG vaccine (BCG-AE, n=18) and a group with latent or active TB (LTBI-TBD, n=10). All parents signed an informed consent. TST was used in the evaluation of all children. An IGRA was performed in all children from LTBI-TBD and BCG-AE groups; in TB-unexposed group, in those who had any induration of TST other than zero mm.

Results:

Results are shown in Table. Comparing TB-unexposed with LTBI-TBDgroup, the best TST cut-off was 4.5 mm (AUC:0.917; 95% C.I. 0.794-1.000), 90.0% sensitivity and 88.2% specificity.

Demographic, clinical characteristics, TST and IGRA results

Parameters	*TB-unexposed(n=51)*	*BCG-AE(n=18)*	*LTBI-TBD(n=10)*	*p value*
Male (%)	*27 (52.9)*	*11 (61.1)*	*6 (60)*	*0.800*
Age in months, median (range)	*9.8 (5.0-16.7)*	*8.8 (2.3-22.9)*	*8.9 (3.2-19.4)*	*0.355*
Age at BCG in days, median (range)	*2.0 (0-88.0)*	*1.0 (0-56.0)*	*2.0 (0-22.0)*	*0.424*
TST in mm, median (range)	*0 (0-8)*	*5.5 (0-10)*	*10 (0-35)*	*0.003*
IGRA	*All negative*	*All negative*	*All positive*	*<0.05*

Conclusions:

Most children not exposed to TB and BCG-vaccinated presented a TST of zero mm and can be distinguished from those exposed to TB. By contrast, a large proportion of children with BCG-AE developed a greater TST induration, suggesting the need for a complementary laboratory analysis if they are exposed to TB.

Systematic Review Registration:

FAPESP 2017/01124-6

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Tuberculosis and other Myocbacterial infections

Pediatric tuberculous meningitis – a 5-year retrospective study in a portuguese tertiary center

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Background and Aims:

Tuberculous meningitis (TBM) is the most severe form of disseminated tuberculosis, with children aged <5 years at highest risk. The authors aim to review the demographic, clinical and imagiologic features of pediatric TBM admitted to a tertiary hospital over a 5-year period.

Methods:

All pediatric cases of confirmed TBM admitted in our hospital between January 2014 and December 2018 were retrospectively reviewed.

Results:

Three cases of confirmed TBM were included, two were females. The mean age was 12 months, ranging from seven to 20 months. All children were immunocompetent and previously healthy, none had *Bacillus Calmette-Guérin* vaccine. Mean time from symptom onset to diagnosis was 1.8 months. All patients had fever, altered mental status and seizures on admission and two presented poor feeding. Mean cerebrospinal fluid values on admission were white blood cells 163 cells/microL, glucose 30 mg/dL, and protein 114 mg/dL. Two had a miliary appearance on chest X-ray/CT. Mean length of hospital stay was 78.7 days; all were treated with tuberculostatic therapy and concurrent steroids (iatrogenic hepatotoxicity occured in two cases). An index case was identified in two patients. Initial CT scans revealed hydrocephalus and hypodense periventricular lesions. All required neurosurgical procedures, namely external ventricular drainage (3/3), ventriculoperitoneal shunt (2/3) and decompressive hemicraniectomy due to intracranial hypertension (1/3). No deaths were reported but one child had cerebral infarction/vasculitis and developed major neurological sequelae.

Conclusions:

Early suspicion and appropriate long-term antituberculosis therapy together with corticosteroids may reduce mortality and morbidity in TBM patients. Implementation of consensus definitions and high-quality clinical trials are needed to clarify optimum therapy.

Systematic Review Registration:

N/A

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Tuberculosis and other Myocbacterial infections

Impact of baseline tuberculin skin test and isoniazid chemoprophylaxis on subsequent quantiferon-tb gold-in-tube performance in young children assessed after tuberculosis contact in catalonia

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Background

To evaluate serial testing with QuantiFERON-TB Gold in-Tube (QFT-GIT) assays in previously healthy children <5 years assessed after contact with tuberculosis (TB), and to determine the potential impact of tuberculin skin tests (TST) and primary chemoprophylaxis (PCP) on QFT-GIT results.

Methods

Prospective observational study at two Paediatric TB Units in Catalonia, Spain. Patients <5 years-of-age that were assessed after TB contact at baseline with TST and QFT-GIT simultaneously. Those who had concordantly negative results were retested after the window period. Data on baseline, and serial TST and QFT-GIT results, as well as use of PCP (isoniazid) were collected.

Results

114 patients were included (56 females; median [IQR] age: 24 [13-39] months). Ninety-six (84.2%) children received PCP during the window period. At reassessment (11.7 [10.4-12.1] weeks), final diagnoses comprised: uninfected (n=104), latent TB infection (LTBI, n=8) and TB disease (n=2). Positive TST results were observed in all LTBI and TB cases (100%) but QFT-GIT conversions were only seen in 7 (70%) cases (both children with TB disease TST+/QFT-GIT+). Concordance between TST and QFT-GIT at reassessment was very good (97%; κ[SE]= 0.878[0.085]). Discordance was observed in 3/103 (2.9%) cases, all of whom had a TST+/QFT-GIT- result constellation and were diagnosed with LTBI. In uninfected children, neither TST at baseline nor PCP showed an impact on QFT-GIT results at reassessment (see Table).

	At baseline	At re-assessment	*p*
Uninfected patients			
TST (mm)	0 (0-0)	0 (0-0)	1.000
Mitogen -nil IFN-γ levels (IU/mL)	9.30 (4.00-11.08), n=41	8.67 (5.71-10.20), n=41	0.767
TBAg-nil IFN-γ levels (IU/mL)	0.00 (0.00-0.01), n=102	0.00 (0.00-0.01), n=102	0.125
	Isoniazid chemoprophylaxis	**No chemoprophylaxis**	***p***
Uninfected patients			
TST (mm)	0 (0-0)	0 (0-0)	1.000
Mitogen -nil IFN-γ levels (IU/mL)	8.67 (6.10-10.25), n=39	2.27, n=2	0.295
TBAg-nil IFN-γ levels (IU/mL)	0.00 (0.00-0.01), n=39	0.00, n=2	0.858
LTBI and TB patients			
TST (mm)	9 (7-11, n=4)	18 (15-22), n=6	0.010
TBAg-nil IFN-γ levels (IU/mL)	0.66 (0.13-0.99), n=4	8.27 (0.74-13.98), n=6	0.171

Conclusions

In a low-TB-burden region both performing TST at baseline and PCP have no impact on QFT-GIT results at the end of the window period. This adds further evidence that prior TSTs do not impact significantly on the performance of interferon-gamma release assays (IGRA), or induce IGRA result conversion. Serial QTF-GIT testing identified fewer LTBI cases than serial TST testing.

Clinical Trial Registration (Please input N/A if not registered)

N/A

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Tuberculosis and other Myocbacterial infections

Molecular epidemiology of methicillin-sensitive staphylococcus aureus in neonatal intensive care unit

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Background and Aims:

Infection control of methicillin-sensitive *Staphylococcus aureus* (MSSA) as well as methicillin-resistant *S. aureus* (MRSA) in neonatal intensive care unit (NICU) is considered to contribute to the improvement of the prognosis of neonates. In order to clarify the nasal MSSA carriage prevalence and the genetic origin and the transmission pathway to neonates in NICU, epidemiological analysis of isolated MSSA was performed.

Methods:

Samples were collected from neonates admitted to NICU at Juntendo University Hospital, their parents and all medical staff of NICU. We rubbed the bilateral nasal vestibule with a swab and applied it to mannitol saline medium to isolate *S.aureus*. DNA were extracted from isolated *S. aureus* and were detected *nuc* and *mecA* gene at PCR methods. Phage Open-reading Frames Typing (POT) were performed for isolated MSSA samples. Twenty samples of MSSA were subjected to whole genome analysis using the next generation sequencer, and Multilocus Sequence Typing（MLST）, spa typing, SNP analysis were performed.

Results:

MSSA was identified in 28 of 135 subjects, of which 4 were neonates, 4 were parents, 10 nurses and 10 doctors. As a result of molecular analysis, there were three groups considered to be carrying the same strain, one group consisting of one patient and three healthcare workers, and the other group was two healthcare workers.

Conclusions:

Although it was a limited subject of 20 cases, it was suggested that a medical staff may be involved as a transmission pathway to neonates. We will collect specimens periodically at monthly pace and obtain more results.

Systematic Review Registration:

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Tuberculosis and other Myocbacterial infections

The black sheep of flu season

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Background

Febrile syndrome is a very frequent reason for consultation in pediatrics. Likewise, influenza causes considerable morbidity and mortality, it is a cause of multiple medical consultations, bacterial infections, hospitalizations and deaths, every year in the world. On the other hand, tuberculosis is the most important infectious disease in the world worldwide and has been a hidden epidemic due to its low infective capacity and low incidence compared to the adult population. We present a 26-month-old patient whom during influenza season, was admitted due to 17 days of fever.

Case Presentation Summary

She was visited in multiple occasions in the primary care center, at the beginning she was diagnosed with herpetic gingivostomatitis. Due to persistent fever with cough and mucus, she was diagnosed with lower respiratory tract infection and was treated with amoxicillin(80mg/kg/day). Ten days after she was remitted to our center. She was clinically stable and her blood tests showed: normocytic normochromic anemia (Hb 9.2g/dl), 14590 leukocytes with neutrophilia, CRP 21.8mg/dl; normal urine sediment; rapid influenza test positive for influenza B. Chest X-ray with generalized nodular pattern and mediastinal widening. She was admitted to our pediatric ward for study and treatment. TST was positive (15mm), with a radiologic pattern compatible with miliary tuberculosis.

Learning Points/Discussion

It is interesting to discuss the extension study that has to be performed in this case: HIV, thoracic CT, abdominal ultrasound, lumbar puncture, fundus examination, echocardiography and brain MRI; as well as our findings, the treatment and it's schedule, the follow-up and the measures to be taken in case of side effects. The interest lies not only in the extensive management required but also in the differential diagnosis of a prolonged fever case in context of flu season.

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Tuberculosis and other Myocbacterial infections

The potential role of ifn-γ/mcp-1 and ifn-γ/tnf-α ratios for the diagnosis of tuberculosis infection in children

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Background

Diagnosing tuberculosis (TB) in children remains challenging. Determining cytokine concentrations in blood may contribute to the diagnosis of both latent and active TB since cytokines play an important role in TB pathogenesis. On that basis, we evaluated the diagnostic value of a range of plasma cytokines in children at different stages of TB infection.

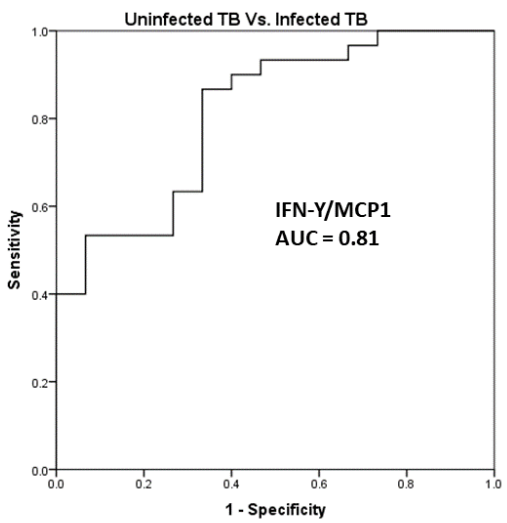
Methods

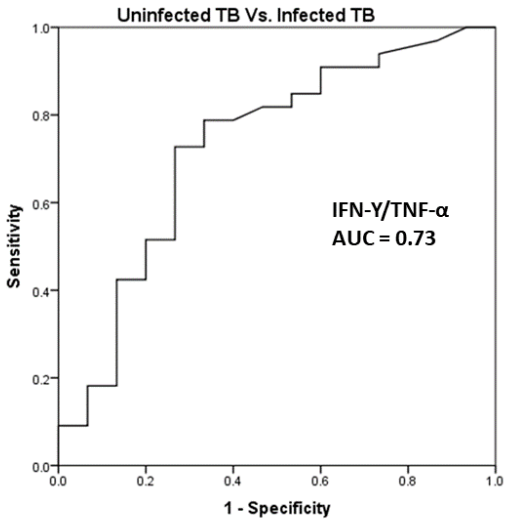
Plasma concentrations of 14 different cytokines were measured in unstimulated blood samples from 15 TB-uninfected children (controls) and 33 children with TB infection (8 latent TB, 19 probable active TB, 6 confirmed active TB) using Luminex-based multiplex sandwich immunoassays. Groups were compared by non-parametric Mann-Whitney U tests. The performance of each parameter was determined by area under the curve (AUC) receiver operator characteristics.

Results

Median IFN-γ, IL-2, IL-9 and MCP-1 plasma concentrations were higher in children with TB infection (latent and active TB groups combined) than in the uninfected control group. The IFN-γ/MCP-1 ratio was significantly higher in children with TB infection than in the uninfected controls (median value in TB-infected individuals 0.20 vs. controls 0.08; p=0.001). The same applied to the IFN-γ/TNF-α ratio (TB-infected individuals 0.45 vs. controls 0.35; p = 0.009). The IFN-γ/MCP-1 ratio achieved an AUC of 0.81, and high sensitivity (86.7%) and accuracy (80.0%) at the optimal cut-off (>0.1). The IFN-γ/TNF-α ratio achieved an AUC of 0.73. Neither of the two ratios differed significantly between individuals with latent TB and patients with active

TB.





Conclusions

Our data show that IFN-Y/MCP-1 and IFN-Y/TNF-α ratios in unstimulated plasma may be useful biomarkers for the diagnosis of TB infection in paediatric populations. However, in common with interferon-gamma release assays, they do not allow to discriminate between latent TB infection and active TB.

Clinical Trial Registration (Please input N/A if not registered)

N/A

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Tuberculosis and other Myocbacterial infections

Lymphadenitis and pulmonary tubercolosis infection secondary to bcg vaccine

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Background

According to WHO guidelines, BCG vaccination is recommended for children living in coutries where TB in endemic. The vaccine is given to about 100 milion children per year globally. To date, 17 different vaccines are available. Reactions to BCG vaccine are possible but rare. Most children may develop local reactions; less commonly BCG can cause either suppurative and nonsuppurative lymphadenitis (1/1000-10000 infants). BCG ostemyelitis, pulmonary involvements and disseminated BCG are rare and traditionally occur in immunocompromised patients.

Case Presentation Summary

CASE 1

Moroccan female, 8 months-old. BCG vaccine (Imovax) 4 months before.

Admitted for left axillary suppurative lymphadenitis. Intravenous antibiotic therapy was not beneficial. Intradermal Mantoux was positive (16 mm); negative Quantiferon TB-Gold Plus; negative CRP; neutrophil leukocytosis. A 5 mm spleen hypoechotic lesion was found on abdomen US. Chest X-Ray was unremarkable. Lung CT scan showed cavitations in RUL and LUL.

CASE 2

Tunisian male, 5 months-old. BCG vaccine (unknown the type) 3 months before.

Admitted for right lateral cervical suppurative lymphadenitis. Intravenous antibiotic therapy was not beneficial. Intradermal Mantoux was positive (15 mm); negative Quantiferon TB-Gold Plus; CRP mildly positive; neutrophil leukocytosis. Chest X-Ray and CT scan unremarkable.

Both case 1 and 2 underwent surgical drainage of the involved lymph node. Mycobacterium bovis was isolated on culture. Treatment: Rifampin, Isoniazid and Ethambutol for 2 months, then Rifampin and Isoniazid for other 4 months.

At 6-months follow-up, full recovery on imaging and physical examination.

Learning Points/Discussion

BCG vaccination is still the only effective tool to prevent disseminated TB, TB meningitis and pulmonary TB in countries where TB in endemic. Vaccine related infections are uncommon, even if reported. After vaccine administration, all children should be followed-up for the early detection of vaccine related infections.

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Tuberculosis and other Myocbacterial infections

Extra-regional complications of bcg vaccine in two immunocompetent children

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Background

All healthy newborns receive Bacille Calmette-Guérin (BCG) vaccine at birth in Singapore. Most reported complications are localised abscess, regional lymphadenitis, or rarely disseminated BCG-osis in children with primary immunodeficiency. We present 2 cases of distant localised BCG infection in healthy children.

Case Presentation Summary

An 8 month old boy had fever and painful erythematous right dorsal foot swelling for 1 day. Magnetic resonance imaging (MRI) indicated metatarsal osteomyelitis. Surgical debridement found a 1st metatarsal shaft and base cortical breach and collection, organised unhealthy granulation tissue and pus. Histology showed acute on chronic granulomatous inflammation and acid fast bacilli.

A 2 year 9 month old girl presented with a 3cm hard non-tender chest wall swelling for 3 days. MRI showed a focal enhancing anterior abdominal collection extending into rectus abdominis muscle with inflammatory changes. Tissue histology after incision and drainage showed acute necrotising granulomatous inflammation, Ziehl-Neelson stain negative.

In both cases, *Mycobacterium tuberculosis* complex (MTBC) MPT64 antigen detection assay was positive; culture grew *Mycobacterium bovis (M.bovis)*.

Both children were previously healthy and received BCG-Japan (Tokyo 172) vaccine at birth. They had no risk factors for *M.bovis* exposure or features suggestive of primary immunodeficiency. Inflammatory markers were mildly elevated. Extensive investigations for BCG dissemination and primary immunodeficiency were normal.

They initially received isoniazid, rifampicin, ethambutol and pyrazinamide; pyrazinamide was stopped when *M.bovis* was confirmed. The boy improved at 5 months follow up. The girl underwent another debridement, with persistent wound discharge after 3 months.

Learning Points/Discussion

Extra-regional BCG vaccine complications are rare and may have a long latency period before symptoms appear. BCG and *Mycobacterium tuberculosis* both belong to MTBC; presence of MPT64 antigen in certain BCG strains can lead to initial identification as *Mycobacterium tuberculosis.*

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Upper respiratory infections and carriage studies

Molecular epidemiology of human respiratory syncytial virus infections among children with acute respiratory tract symptoms in northern india

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Background and Aims:

Acute respiratory tract infections (ARTIs) are a relentless and pervasive public health issue worldwide, especially in developing countries. It is estimated that every seventh second a child less than 5 years of age dies due to ARI usually with pneumonia, accounting for 30% of all deaths in children.

Methods:

Cross-sectional hospital based prospective study from 2009 – 2014with an objective toassess the contribution of RSV in hospitalized children with acute respiratory tract disease in our setting by molecular techniques Detection of Respiratory Syncytial Virus (RSV) in clinical specimens by real time PCR, isolation by cell culture. A subset of positives were sequenced. All patients presenting to the OPD/IPD <15 years of age with symptoms, i.e. Fever >38ºC, cough, pharyngitis and Dyspnea, coryza, hoarseness with duration of illness at 2 to 5 days (less than 72 h)

Results:

In the present study, out of 1653 samples, 199 (12 %) samples were tested positive for RSV by real time RT-PCR. Out of those samples 27 samples (20 RSV A, 7RSV B) were subjected to sequencing. Overall 10% samples were positive for RSV-A and 3.5% for RSV-B. None of the patients had mixed infection. Both strains A and B, circulated at the same epidemic season, with Group A predominance. Phylogenetic analysis detected all RSV-A glycoprotein sequences obtained in this study were clustered in GA2 and ON1 group of NA1, NA2 subtypes.

Conclusions:

Estimating the burden of RSV in a large number of population and over a long period, will be helpful in understanding overall transmission patterns and community burden in Northern India, as well as developing effective control and prevention strategy

Systematic Review Registration:

NA

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Upper respiratory infections and carriage studies

Use of influenza rapid diagnostic testing in children hospitalised for acute respiratory infections in 2017/18

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Background

Globally, large observational studies show that most acute respiratory infections (ARI) in children are caused by viral infections. In Europe, the 2017/18 influenza season was longer and more severe than in previous years. Oseltamivir is available for treatment of influenza but is only effective when given early in the course of disease. Therefore, studies describing the prevalence, symptoms and time of presentation with ARI and specifically influenza are important.

Methods

The EU-funded Paediatric Multi-centre EuRopean study of MAjor Infectious Disease Syndromes (PED-MERMAIDS) enrols children under the age of 5 years hospitalised for ARI across 11 EU countries. Information on symptoms, course of disease and clinical management is collected prospectively. In an interim analysis we used descriptive statistics to assess the use of influenza rapid diagnostic testing (RDT) and to compare symptoms in children tested positive for influenza compared to those tested negative.

Results

198 children, median age 1.26 years (IQR 0.48, 2.77) were enroled with a median of 3 days of symptoms prior to hospital admission. Upon admission, 104 (52.8%) had recessions, 76 (38.6%) wheezed, 57 (29.9%) decreased feeding, 9.2% required oxygen and 3.5% needed ICU admission at presentation. An influenza RDT was done in 80 (40.4%) of which 17 (21.3%) yielded a positive result. Clinical characteristics did not differ between children tested positive or negative for influenza (see table).

Conclusions

The majority of hospitalised children presented in time to allow initiation of oseltamivir treatment within 3 days of symptom onset. However, use of influenza RDT was low. In the subgroup tested for influenza, infection was not associated with more severe disease at presentation. In the final analysis (summer 2019) we will also be able to assess outcomes.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESPID19-0620
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Immunoprophylaxis of influenza and acute viral respiratory infections in orphanage children

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Background and Aims:

Low influenza vaccination rates among closed organized children community are associated with higher influenza infection rates, influenza-related hospitalizations, and higher influenza mortality rates. The purpose was to study the clinical effectiveness of influenza vaccination in early age children in closed organized groups (orphanage).

Methods:

According to the methodology of vaccination were formed two groups, 25 children received a double inactivated split virus vaccine dose with interval of one month (in October and November), 26 children vaccinated by once dose (in October). The other 24 children had permanent or temporary contraindications for vaccination (control unvaccinated group).

Results:

It was found that frequency of acute respiratory infections after vaccination was significantly lower in children, who received a double (1,5±1,3 case per year) or once vaccine dose (1,9±1,2 cases per year) than in the unvaccinated group (3,0±1,5 cases per year, P<0,05). Average duration of acute respiratory viral infection was respectively 6,5±4,7 days in double dose vaccinated children, 11,0±6,2 days in once dose vaccinated children and 10,6±4,9 days in unvaccinated group (PI:III<0.05). Once dose vaccination was more effective to reduce the incidence of acute respiratory viral infections (not more two times a year) and frequency of hospitalization, but not sufficiently effective to prevent complications of acute respiratory viral infections. Double dose influenza vaccination compared to once dose vaccinations was characterized by the relative risk reduction of complications by 27,2% and the relative risk reduction of hospitalization by 48%.

Conclusions:

Influenza vaccination is a highly effective method of active immunization of early age children in a orphanage. Revaccination at intervals of one month can significantly reduce the risk episodes of acute respiratory viral infections, frequency of hospitalization and complications compared to unvaccinated and unrevaccinated children.

Systematic Review Registration:

Systematic Review Registration

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E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Seasonality of distinct respiratory viruses among children with acute respiratory infection in a tropical city

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Background and Aims:

Acute respiratory infection (ARI) imposes a considerable burden among children worldwide. Respiratory viruses are recognized to be the most frequent causative agents of ARI. However, the seasonality of distinct viruses in tropical regions is poorly known. We assessed the seasonality of distinct respiratory viruses among children with ARI in a tropical.

Methods:

This retrospective cross-sectional study was conducted in Salvador, Brazil, between July 2014 and June 2017(age ≤ 18 years). Respiratory viruses were searched by direct immunofluorescence and real-time polymerase chain reaction for the detection of common respiratory viruses, including respiratory syncytial viruses (RSV), influenza viruses (Flu) A and B, Adenovirus (ADV) and parainfluenza viruses (PIV) 1, 2 and 3. Data were registered in a standardized questionnaire, then entered and analyzed in the software SPSS and STATA. Seasonal distribution of infection by respiratory viruses was evaluated by Prais-Wisten regression.

Results:

Of 387 cases, the median age was 26.4 (10.5-50.1) months and 229 (59.2%) were male. Respiratory viruses were found in 106 (27.4%) cases. RSV was the most common one (19.6%), followed by Flu A (2.8%), Flu B (1.8%), ADV (1.3%), PIV 1 (1.3%), PIV 3 (0.8%), and PIV 2 (0.3%). Two samples had co-detections found: RSV and Flu A, Flu A and PIV 1. Overall, 92 (23.8%), 105 (27.1%), 75(19.4%) and 115 (29.7%) cases with ARI occurred and 24 (26.1%), 45 (42.9%), 14 (18.7%) and 23 (20.0%) respiratory viruses were detected in summer, fall, winter and spring, respectively ($p<0.001$). Frequency of RSV (b3=0.626; p=0.003), PIV 3 (b3= -0.148; p=0.002), Flu A (b2=-0.224; p= 0.030), Flu B (b3= -0.163; p=0.031), and ADV (b3= -0.175; p= 0.005) had different seasonal patterns.

Conclusions:

RSV, Flu A, Flu B, ADV and PIV 3 showed seasonal distribution.

Systematic Review Registration:

N/A

ESPID19-0379
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Upper respiratory infections and carriage studies

Burden of respiratory syncytial virus infection during the first year of life

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Background

Respiratory syncytial virus (RSV) is the leading cause of hospitalization for acute respiratory infection in infants worldwide. Although the burden of RSV-associated bronchiolitis and pneumonia is great among young infants, it is important to understand that only a small proportion of RSV-infected children are admitted. The full burden of RSV among young children treated as outpatients is currently poorly understood.

Methods

In a prospective study, we followed up a cohort of 431 children <1 year of age during the respiratory season of 2017-2018. The children were examined at the study clinic every time they had any signs or symptoms of respiratory tract infection. During each illness, nasopharyngeal flocked swabs were obtained and subjected to a multiplex-PCR assay for 16 different viruses. The parents filled out daily symptom diaries during the entire 10-month follow-up period.

Results

A symptomatic RSV infection was diagnosed in 134 (32.8%) of 408 actively participating children during their first year of life (incidence rate, 328/1000 children; 95% CI, 286-377). Excluding 6 children with double viral infection, acute otitis media developed as a complication of RSV illness in 99 (77.3%) of 128 children, and 91 (71.1%) children received antibiotic treatment. 11 (8.6%) children were referred to the paediatric emergency department, and 8 (6.3%) were hospitalized. The median duration of RSV illness was 11 days (25-75% range, 9-14).

Conclusions

During the first year of life, approximately one-third of children suffer from symptomatic RSV infection, but the overwhelming majority of them are treated in the outpatient setting. Acute otitis media is a strikingly frequent complication of RSV that in most countries usually results in antibiotic treatment. Effective preventive and treatment strategies against RSV infections in young children are urgently needed.

Clinical Trial Registration (Please input N/A if not registered)

N/A

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Upper respiratory infections and carriage studies

Respiratory microbial colonization in children with neurological disorders

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Background and Aims:

Children with severe neurological disorders are at increased risk for respiratory infections significantly deteriorating quality of life and prognosis. The aim of this study is to evaluate respiratory microbial colonization and factors associated with chronic lung disease in neurologic patients.

Methods:

Children with neurological disorders were prospectively studied. Cough swabs obtained post inhaled hypertonic saline were sent for bacterial culture. Factors contributing to the airway microbial colonization and morbidity were evaluated. The Eating and Drinking Ability Classification System (EDACS) was used to measure eating and drinking ability of these children.

Results:

A total of 21 children with documented neurological disease were enrolled. Thirty-three (42%) were boys and the median (IQR) age was 3,5 (1-16) years. Twelve patients (57.2%) had been diagnosed with epileptic encephalopathy, 6 (28.5%) with neurogenetic diseases and 3 (14.3%) with cerebral palsy. Most frequent commorbidities included constipation (28.5%) and gastroesophageal reflux disease (14.3%), while scoliosis was presented in 23.8%. Eating and drinking disorders were observed in 16 patients (76.2%) and 4 children (19%) had gastrostomy or jejunostomy. EDACS≥3 was noted in 15 children (71.4%) and was associated with ≥3 respiratory infections (61.9%) and hospitalization ≥2 times within past 24 months (42.8%). Previous administration of antimicrobials was documented in 10 patients (47.6%) and frequent use of inhaled salbutamol in 5 patients (23.8%). Airway microbial colonization with potential pathogens was identified in 14 (66.6%) patients. EDACS was positively associated with isolation of bacteria in sputum cultures (OR:3.39, CI:1.01-11.35, p=0.048).

Conclusions:

This study implies that for every unit increase in EDAC score there were > 3 times increase in the likelihood of a positive cough swab culture and emphasizes the importance of multidisciplinary support of these patients.

Systematic Review Registration:

N/A

ESPID19-1137
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Primary vaccination and pertussis... It happens!

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Background

Pertussis still remains highly prevalent in developed countries and is the least well controlled of all vaccine-preventable diseases. Protection afforded by vaccination or from past infection is not lifelong.Undiagnosed and untreated Pertussis is a source of infection transmission.
Clinical presentation may vary from asymptomatic to severe complications. High suspicion of a cough with a catarrhal stage progressing to a paroxysmal phase is key for the diagnosis.

Case Presentation Summary

A 13-month-old previously healthy male child, with completed primary pertussis immunization schedule (2, 4, 6 months), was admitted to the emergency department (ED) with a 4-day history of cough, apneas and episodic perioral cyanosis (without fever).
Lab tests, comprising complete blood count and biochemistry, and chest x-ray were unremarkable, so patient was discharged with azithromycin empirical therapy. Nasopharyngeal aspirate was collected for PCR and parents were instructed to maintain strict surveillance.
The child returned to ED after 5 days (last day of azithromycin) without clinical improvement and with 94% of peripheral oxygen saturation. He was hospitalized for further surveillance. The sputum PCR results collected on first admission detected Pertussis DNA.
Clinical outcome was good and the patient discharged 3 days later.
Pertussis was notified to the public health authorities, according to national policies, and azithromycin was prophylactic prescribed for cohabitants.

Learning Points/Discussion

Isolated cases of failure of primary immunization are not uncommon. The efficacy of primary 3 dose immunization for pertussis vaccine ranges from 85–90% in previous published literature.
Clinicians should keep a high level of suspicion for a differential diagnosis of Pertussis in cases presenting with respiratory symptoms consistent with the infection, even when it is a patient with immunization plan updated.

ESPID19-1010
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Respiratory infections as factors with negative impact on asthma control in children

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Background

Currently, asthma control is set as the goal of asthma management. Whilst control is a composite and an ambitious target, several of its determinants provide the practitioners with opportunities of effective interventions. We performed a study to evaluate impact of respiratory tract infections on asthma symptoms and management.

Methods

Children with asthma (n=148, 81 boys, age 10,3+/-5,2 yrs.) attending a Regional Asthma Surveillance Centre for Children were included in the study. Asthma control was measured using the Childhood Asthma Control Test. After adjustment for potential confounders, multivariable linear regression was used to evaluate the association between number of episodes and type of respiratory tract infections during the last 12 months and asthma control.

Results

There was a significant association between 4 or more episodes of respiratory tract infections during the last 12 months and partially controlled and uncontrolled asthmatic children (p=0,003). There was a threefold increase of better control in teenagers than in preschoolers adjusted by number of common cold episodes (95% CI -4.0 to -2.3). Acute otitis media episodes yielded no significant association with asthma control, regardless the age of the children.

Conclusions

Data collected during the study support the negative impact of respiratory tract infections (especially by number of episodes) on asthma control in children. The practitioner should address the issue of respiratory tract infections as an important tool in achieving control in children with asthma.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0993
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Efficacy of pertussis vaccination during pregnancy: the reality of a level ii hospital in portugal

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Background

Pertussis is an acute infectious disease responsible for significant morbility and mortality in young infants. Vaccination is part of portuguese national vaccination plan (NVP) since 1996. Since then, there has been progressive disease control but with a residual endemicity pattern. Maternal prenatal immunisation was introduced in several countries and is 90% effective at preventing infant hospitalization from pertussis. Since January 2017 this vaccine is part of the NVP. We aim to characterize the cases of pertussis hospitalized from 2015 to 2017 in a level II hospital.

Case Presentation Summary

In all analysed cases pertussis afected babies come from mothers that weren't vaccinated during pregnancy. Epidemiologic context of close contact with persons presenting respiratory symptoms were also verified. In all cases *Bordetella pertussis* was identified by PCR and antibiotics with azitromicin was performed. In 5 cases the child had already the first dose of primary vaccination.
Between 2015 and 2017, 10 cases of pertussis were diagnosed. The mean age was 2 months and 5 days. In 6 cases children needed oxygen suply. In 4 cases chest Xray was performed but no images were sugestive of pulmonar complications. In 1 of the 6 cases that went trought blood analysis, high leucocitosis and neutrophilia was observed but it was associated. Subsequent favorable clinical progression was registered.
Until December 2018, the last diagnosed case occured in September 2017.

Learning Points/Discussion

There is a high risk of severe disease and death from pertussis before 3 months of age. The suply of pertussis antibodies through vaccination during pregnancy will provide children passive protection until the start of vaccination. In our series this positive effect is demonstrated since no cases were identified for the 9 months since the inclusion of this vaccine in NVP.

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Upper respiratory infections and carriage studies

Multiple bacterial species are more often present in recurrent acute otitis media (raom)

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Background and Aims:

RAOM occurs in 5-30% young children, may involve several bacterial species and can lead to spontaneous otorrhea. Tympanocentesis is not routine in Portugal. To study aetiology, we recruited children with AOM and spontaneous otorrhea (AOMSO).

Methods:

Preschool children with AOMSO (<3-day history of signs and symptoms and otorrhea without otitis externa), presenting December 2013 - April 2016, were studied. Recurrence was defined as >3 episodes in last 6M or >4 in 12M. Clinical data were recorded, paired swabs taken from the nasopharynx(NP) and otorrhea(OT) without ear canal toilet or aspiration. Swabs (stored at -70°C in STGG broth until batched analysis) had DNA extracted and single gene qPCRs for *S. pneumoniae* (Sp-lytA), *H. influenzae* (Hi-hdp), *M. catarrhalis* (Mc-ompJ), *S. aureus* (Sa-nuc) and *S. pyogenes* (GAS-ntpC) were performed. Ct values <36 were considered positive.

Results:

151 children were included, 56% boys, mean age 31M(2-6Y). Sp was detected in OT in 71(47%), Hi in 82(54%), Mc in 45(30%), Sa in 32(21%) and GAS in 37(25%). Sp, Hi and Mc were more frequently detected in NP and Sa and GAS in OT. When present in OT, Sp was also present in NP in 83%, Hi in 85%, Mc in 89%, GAS in 73% and Sa in 28%. The 27/151 (18%) with RAOM had similar gender distribution, mean age and PCV vaccine coverage to the 124 without recurrence but had >1 bacterial species in 85% compared to 52% in the 124 (p= 0.001).

Conclusions:

Hi and Sp are the most frequently-found species in RAOM in the PCV era. Bacteria in OT are usually also in NP except Sa that frequently derives from skin. Multiple bacterial species are more often present in RAOM perhaps in complex biofilms.

Systematic Review Registration:

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ESPID19-0652
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Clinical features and outcomes of parapharyngeal and retropharyngeal inflammation in korean children

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Background and Aims:

Deep neck infection (DNI) can cause life-threatening complications, and therefore, prompt diagnosis and management are necessary. Kawasaki disease (KD) may manifest as only fever and cervical lymphadenopathy or accompany with deep neck inflammation; clinically confusing with DNI. This study was performed to evaluate clinical features and outcomes of children with parapharyngeal/retropharyngeal inflammation (abscess and cellulitis).

Methods:

Children, who were diagnosed with parapharyngeal/retropharyngeal inflammation using a cervical computed tomography (CT) between 2013 and 2017, were included in this study. Medical records of the enrolled children were retrospectively reviewed.

Results:

Among 47 children diagnosed with parapharyngeal/retropharyngeal inflammation, 11 (23.4%) were eventually diagnosed with Kawasaki disease (KD) and the remaining 36 (76.6%) children were diagnosed with DNI. No clinical and laboratory characteristics were significantly different on admission between children diagnosed with KD and DNI; however, significantly more children with KD were febrile for ≥3 days after admission compared to those with DNI (P=0.009). Deep neck abscesses on neck CT were observed in 16 (44.4%) children with DNI and no (0.0%) child with KD (P=0.009); the remaining 20 (55.6%) children with DNI and 11 (100.0%) children with KD showed deep neck cellulitis. In children diagnosed with DNI, no clinical and laboratory characteristics were significantly different on admission between children with cellulitis and abscess. Children with abscess were hospitalized longer than those with cellulitis (11 days vs. 8 days, P=0.026). Six (16.7%) children received surgical management, and the remaining 30 (83.3%) were cured with antibiotic therapy.

Conclusions:

Antibiotic therapy can be applicable to children with DNI as an initial treatment. However, children with fever lasting for ≥3 days after admission should be considered for alternative diagnoses including KD or surgical management for DNI.

Systematic Review Registration:

N/A

ESPID19-0552
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Pharyngitis – an unusual presentation of haemophilus influenzae infection?

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Background

Streptococcus pneumoniae (SP), *Haemophilus influenzae*(HI) or *Moraxella catarrhalis*(MC) are not commonly considered as causes of pharyngitis. The aim of this study was to evaluate their role as pathogens based on serological responses in children with febrile pharyngitis.

Methods

This was part of a prospective study done in an emergency department (ED) in febrile children 1-16 years of age with pharyngitis diagnosed by the ED physician. Throat swabs and blood samples were collected. Bacteria were detected by throat culture and identified by standard methods, including MALDI-TOF. Multiplex bead-based immunoassay method was used to detect immune responses against 8 SP, 3 HI and 5 MC protein antigens in paired serum samples.

Results

In total, 83 children (median age 5.5 years) were recruited in to the study. Paired serum samples were available for analysis from 48 patients (median age 6.7 years). Throat cultures were positive for SP, HI and MC in 1, 11 and 1 patients, respectively. A 2-fold or greater titer increases against any of the SP antigens were seen in 2 and against HI antigens in 5 patients. No titer fold increases against MC were recorded. SP was not detected by throat culture in either of the patients with positive SP serology. HI was detected by throat culture in 3 out of 5 patients with positive HI serology. Two of these patients produced 6-fold titer increases against HI. Clinical presentation in these patients included pharyngeal exudates and/or intensive redness.

Conclusions

Haemophilus influenzae is a common colonizer of the throat in young children. However, it might be considered as a potential cause of pharyngitis in some patients. SP and MC seem to be less important as pharyngitis pathogens.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0358
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Development of qpcr multiplex real-time influenza a/b and baloxavir resistance assays

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Background

Baloxavir is a new antiviral drug for treating influenza infection in adolescents and adults. However, baloxavir resistance has been observed through acquisition of a mutation at position 38 in the protective antigen (PA) gene. In this study, we analyzed a simplified, 'collection-to-detection' system for rapid qPCR detection of influenza A/B viruses and identification of baloxavir resistant strains.

Methods

A multiplex qPCR assay targeting conserved regions of influenza A and B matrix gene and an allelic discrimination assay targeting position 38 of PA gene was developed from strains obtained from GenBank and evaluated using targeted DNA controls on an ABI-7500 instrument. For qPCR limit of detection, a quantified influenza stock culture was serially diluted and tested. Prior to qPCR, replicate RNA extractions were performed using Qiagen Viral RNA and Longhorn PrimeXtract extraction kits. A panel of influenza A/B and other respiratory viruses collected in PrimeStore were evaluated to determine specificity.

Results

The optimized multiplex influenza A/B assay was sensitive across five 10-fold serial dilutions of quantified viral RNA and exhibited no cross reactivity to non-influenza viruses. Viral RNA extracted from samples was detected by qPCR in all samples (25 of 25) using Qiagen RNA Viral (Avg CT=31.5, SD=0.74) and Longhorn's PrimeXtract (Avg. 31.5, SD=0.42). Baloxavir resistance was detected in a blinded panel of influenza A control targets.

Conclusions

The rapid qPCR multiplex influenza A/B and baloxavir assays were shown to be highly sensitive and specific. Molecular influenza detection assays that include identification of strains resistant to baloxavir are urgently needed. Since children often amplify community acquired viral infections, these qPCR assays could facilitate a broader understanding of antiviral resistance and be useful in patient care and public health.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0292
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Otomastoiditis: thirteen years of active surveillance in a northern mexican hospital (mexico-usa-border): pneumococcus as leading cause, and effectiveness of pneumococcal 13-valent conjugate vaccine.

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Background and Aims:

We have published several studies related to Invasive Pneumococcal Disease, and effectiveness of Pneumococcal Conjugate Vaccines: 7-valent (PCV7) and 13-valent (PCV13). The Tijuana, Mexico – San Diego, California border is the highest transited in the planet.

Methods:

Since October/1st/2005 until September/30th/2017, prospective/active surveillance to identify all children < 16 years old with OM at the Tijuana General Hospital was performed. OM was diagnosed with otoscopy, and tomographic signs of OM. Bacterial identification was either by conventional cultures, or PCR. For *S. pneumoniae* isolates, serotyping was performed by the Quellung Reaction (Statens Serum Institute®) or PCR. Analysis of all information was merely descriptive.

Results:

Twenty cases of OM were identified. Median age at admission was 32 months (6 months – 15 years). Median hospitalization days of 10 (5 – 115). Mastoidectomy was performed in 13 (62%), one patient developed OM along with meningitis (by *S. pneumoniae* serotype 19A). Bacterial isolation (either from mastoids and/or supramastoids abscesses) was successful in 18 (85.7%). *S. pneumoniae* was isolated in 14 (82%), followed by *S. pyogenes, S. anginosus* and *P. mirabilis*. For Pneumococcal OM: before PCV7 introduction (19 months of surveillance) there were 0.158 cases per month (6A, 18C, 7F, one of each), post-PCV7 universal vaccination (61 months of surveillance) decreased to 0.114 cases per month (serotypes 19A(3), 3(2), 7F(1), 12F(1), PCV7 impact of 27.8%), and following PCV13 implementation (76 months of surveillance) dropped to 0.052 cases per month (serotypes 3(1), 33F(1), 35B(1), 24F(1), PCV13 impact of 67%).

Conclusions:

This is the first Active/Prospective study searching for OM children in Mexico. Although relatively uncommon, OM was associated with important morbidity (mastoidectomy) and long hospitalization. *S. pneumoniae* was the leading cause, with high effectiveness of PCV13.

Systematic Review Registration:

N/A

ESPID19-0289
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Comparative severity of influenza a and b infections in hospitalized children

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Background and Aims:

Although both influenza A and B virus infections predispose children to hospitalization and a wide range of complications, influenza A viruses are conventionally thought to cause more severe illnesses than B viruses. However, when comparing the severity of influenza A and B infections in children, all outcomes should be adjusted for age because children with influenza A are generally younger than those with influenza B.

Methods:

This retrospective study consisted of all children under 16 years of age hospitalized with laboratory-confirmed non-nosocomial influenza A or B infection at Turku University Hospital during a 14-year period of 1.7.2004-30.6.2018. Data on clinical presentation and outcomes, management, and duration of hospitalization were retrieved from the medical records of the children. For comparison of influenza A and B infections, the children were divided into three age groups: <3, 3-9, and 10-15 years of age.

Results:

A total of 391 children were hospitalized with influenza during the study period (influenza A, n=279; influenza B, n=112). Children hospitalized with influenza A infection were significantly younger than those with influenza B infection (4.2 vs 6.4 years, p <0.0001). When analyzed within different age groups, no statistically significant differences were observed in any variables between children with influenza A and

B infections (Table).

Table.

Comparison of selected outcomes between influenza A and B infections in hospitalized children in different age groups.

Variable	A <3 yrs (n=152)	B <3 yrs (n=39)	A 3-9 yrs (n=86)	B 3-9 yrs (n=44)	A 10-15 yrs (n=41)	B 10-15 yrs (n=29)
Highest fever (°C)	38.9	39.1	39.4	39.4	39.2	39.2
Pneumonia	21 (14%)	5 (13%)	14 (16%)	6 (14%)	9 (22%)	8 (28%)
Otitis media	47 (31%)	9 (23%)	12 (14%)	6 (14%)	2 (5%)	2 (7%)
Blood culture	52 (34%)	14 (36%)	30 (35%)	13 (30%)	19 (46%)	12 (41%)
CSF culture	7 (5%)	4 (10%)	7 (8%)	4 (9%)	2 (5%)	3 (10%)
Intensive care	19 (13%)	8 (21%)	13 (15%)	3 (7%)	4 (10%)	6 (21%)
Antibiotic treatment	84 (55%)	22 (56%)	41 (48%)	18 (41%)	18 (44%)	14 (48%)
Mean duration of hospitalization (d)	2.2	2.2	2.5	2.1	2.2	4.4

Conclusions:

When adjusted for age, the clinical presentation and outcomes appear to be similar between children hospitalized with influenza A and B infections. These findings underscore the importance of age as a crucial factor when analyzing clinical features of illnesses in children. The comparable clinical severity of influenza A and B infections supports the use of quadrivalent influenza vaccines that contain both influenza B strains circulating among humans.

Systematic Review Registration:

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ESPID19-0133
E-Poster Viewing - May 7-10 - E-Poster Hours

Upper respiratory infections and carriage studies

Impact of the 13-valent pneumococcal conjugate vaccine on incidences of acute otitis media (aom), recurrent aom and tympanostomy tube placements in children in turkey.

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Background and Aims:

The 13-valent pneumococcal conjugate vaccine (PCV13) was introduced into the Turkish National Immunization Programme (NIP) in late 2011. The aims of the study were to estimate the vaccine impact of PCV13 on incidences of acute otitis media (AOM), recurrent AOM and Tympanostomy tube (TT) placement in children between year 2011 and 2017 in Turkey.

Methods:

The study was conducted 2 big general hospitals pediatric and ear-nose-throat clinics located in each region of Istanbul, Turkey. The numbers of AOM diagnosed, recurrent AOM diagnosed and TT insertions, between years 2011 and 2017 were extracted from the Hospitals database. Yearly incidences were calculated, and trends of changes were evaluated.

Results:

Between year 2011 and 2017, the incidence of AOM gradually decreased from 10700 to 4712/100,000, in children under age of 5 years, on the other hand the incidence of AOM gradually increased from 1886 to 7410/100,000 in children age above 5 years. Moreover, for whole pediatric age period incidence of AOM slightly increased from 4067 to 4850/100,000 between years 2011 and 2014 and remained steable arround 4700/100,000 till year 2017. The incidence of reccurrent AOM gradually increased from 319 to 1000/100,000 between years 2011 and 2017 but the incidence of TT insertion decreased from 213 to 175/100,000 between years 2011 and 2017.

Conclusions:

The incidence of AOM have decreased in children under age of 5 years and the incidence of TT insertion fell in children in Turkey since the introduction of PCV13 into the NIP.

Systematic Review Registration:

None

ESPID19-0301
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Three years indian perspective of urinary tract infections in children: epidemiology, clinical profile, microbial spectrum and its antibacterial sensitivity pattern

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Background

The diagnosis of Urinary tract infections (UTI) is often clinically missed in children due to non-specific symptoms. Rapid evaluation and treatment of UTI is very crucial to prevent renal parenchymal damage and chronic renal failure. This prospective observational study was conducted to evaluate epidemiology, clinical profile, microbial spectrum and its antibacterial sensitivity pattern in urinary tract infections in children children in Bikaner, Northwestern India from January 2016 to December 2018.

Methods

This study included children aged 0-15 years presented with symptomatology suggestive of UTI. The diagnosis of UTI is based on positive culture of properly collected urine sample in a symptomatic child before starting antibiotics. Antibacterial sensitivity pattern of cultured microbial was noted. Data were analysed by student *t*-test.

Results

During study period, 328 children presented with culture proven UTI in which proportion of boys and girls was 25.21% and 74.78% respectively. Below one year age boys (14.67%) were predominantly affected than girls (5.05%), while after one year age girls (74.73%) preceded to boys (9.53%) ($p<0.01$). The common clinical manifestations were fever (91.17%), vomiting (71.20%), abdominal pain (66.92%), and poor weight gain (31.90%). The risk of UTI is higher in children with protein energy malnutrition and chronic diarrhea. The most prevalent cause of UTI was *E.coli* (68.12%), *Enterobacter* (14.12%), *Proteus* (10.11%) and *Klebsiella* (9.12%). *E.coli* was highly sensitive to nitrofurantoin (84.72%), levofloxacin (78.56%) and amikacin (68.62%) but highly resistant to cotrimoxazole (81.81%), ampicillin (76.19%), ceftriaxone (68.78%) and nalidixic acid (54.68%).

Conclusions

UTI was commonly seen in girls of age more than one years (boys in <1 year age); clinical presentation was nonspecific; *E.coli* was most prevalent microbial with highest sensitivity to nitrofurantoin and levofloxacin.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-1167
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Palmar rash in a teenager: what is hidden behind?

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Background

A palmar exanthema in paediatric population has a wide differential diagnosis and might represent a clinical challenge. In adolescence the omission of important clinical information can lead to diagnostic delays and misdiagnosis of easily treatable infectious diseases. The authors describe a case of a teenager with a palmar rash with no initial mention of genital involvement.

Case Presentation Summary

A 16-year-old male with no significant past or family medical history, presented to the paediatric emergency department with a 1-month history of a macular rash in both palms that in the following weeks spread to the face, trunk and all four extremities. He did not present fever or any other symptom. Clinical examination revealed a diffuse symmetric macular rash involving the face, the entire trunk and the extremities, including the palms and soles. Upon questioning, he mentioned a history of unprotected sexual intercourse and further examination revealed a mid-shaft 1 cm ulcer as well as a local macular rash and bilateral inguinal lymphadenopathy. Laboratory investigations confirmed the diagnosis of secondary syphilis with positive Venereal Disease Research Laboratory (VDRL) and Treponema pallidum hemagglutination assay (TPHA) tests. He was treated with penicillin 2.4 million units intramuscular and referred to the outpatient clinic. Screening for other sexually transmitted infections was negative. All partners were notified. Six months after diagnosis he presented a complete clinical resolution and a four-fold decline in VDRL titer.

Learning Points/Discussion

Despite being an uncommon disease in the paediatric setting, the incidence of syphilis has increased in the last years both in Europe and in the United States. Upon a suggestive palmar rash in adolescence, secondary syphilis must be considered and a complete sexual history is mandatory to avoid misdiagnosis and therapeutic delays.

ESPID19-1156
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Urinary tract infections due to esbl- and amp c- producing bacteria in derbyshire children: a retrospective review of cases between 2014 and 2018

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[2]Derbyshire children's hospital, Pediatrics, Derby, United Kingdom
[3]Derbyshire children's hospital, Pharmacy, Derby, United Kingdom

Background and Aims:

Urinary tract infection (UTI) in children caused by resistant organisms like extended-spectrum β-lactamase (ESBL) or AMP C producing bacteria poses a challenge for clinicians. Our aim was to use routinely reported laboratory data to describe the cases of UTI caused by these bacteria in Derbyshire children over a four- and half-year period.

Methods:

Children aged ≤16 years with urine culture positive for ESBL or an AMP C producing bacteria were identified from the records of the microbiology laboratory Derbyshire children's hospital during a 5.5-year period (1 April 2014 and 31 October 2018).

Results:

A total of 458 episodes of UTI was identified. The average number of episodes was 102 per year and did not vary significantly during the period; 53 in 2014, 105 in 2015, 105 in 2016, 101 in 207 and 94 in 2018. Median age of the cases was 5 years.

Most of the urine samples 411/458 (89.7%) were sent from General practitioners across the region whilst 47/458 (10.3%) were sent from hospital (in-patient clinical areas, n=40 and outpatient clinics, n=7). Most 278 (61%) were ESBL producing whereas 180 (39%) were AMP C producing. Most of the isolates were either *E. coli* 381/458 (83%) or *Enterobacter* spp. 35/458 (8%). Others were (*Citrobacte*r=16, *Morganella* =8, *Serratia*=7, *Klebsiella*=7, *Proteus*=3 and *Panthoa*=1).

The proportion of isolates reported as *E. coli* were higher in children ≥4 years of age 254/296 (86%) compared to those ≤3 years old 127/162 (78%) p=0.04.

Conclusions:

Most of the resistant UTI diagnosed in Derbyshire children hospital are from outside the hospital with *E. coli* the most common. Knowledge of these organisms provide an opportunity to review the factors associated with their occurrence and thus have impact on empiric antibiotics and prevention

Systematic Review Registration:

none

ESPID19-1051
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Condylomata lata: sencondary syphilis in a 15-year-old

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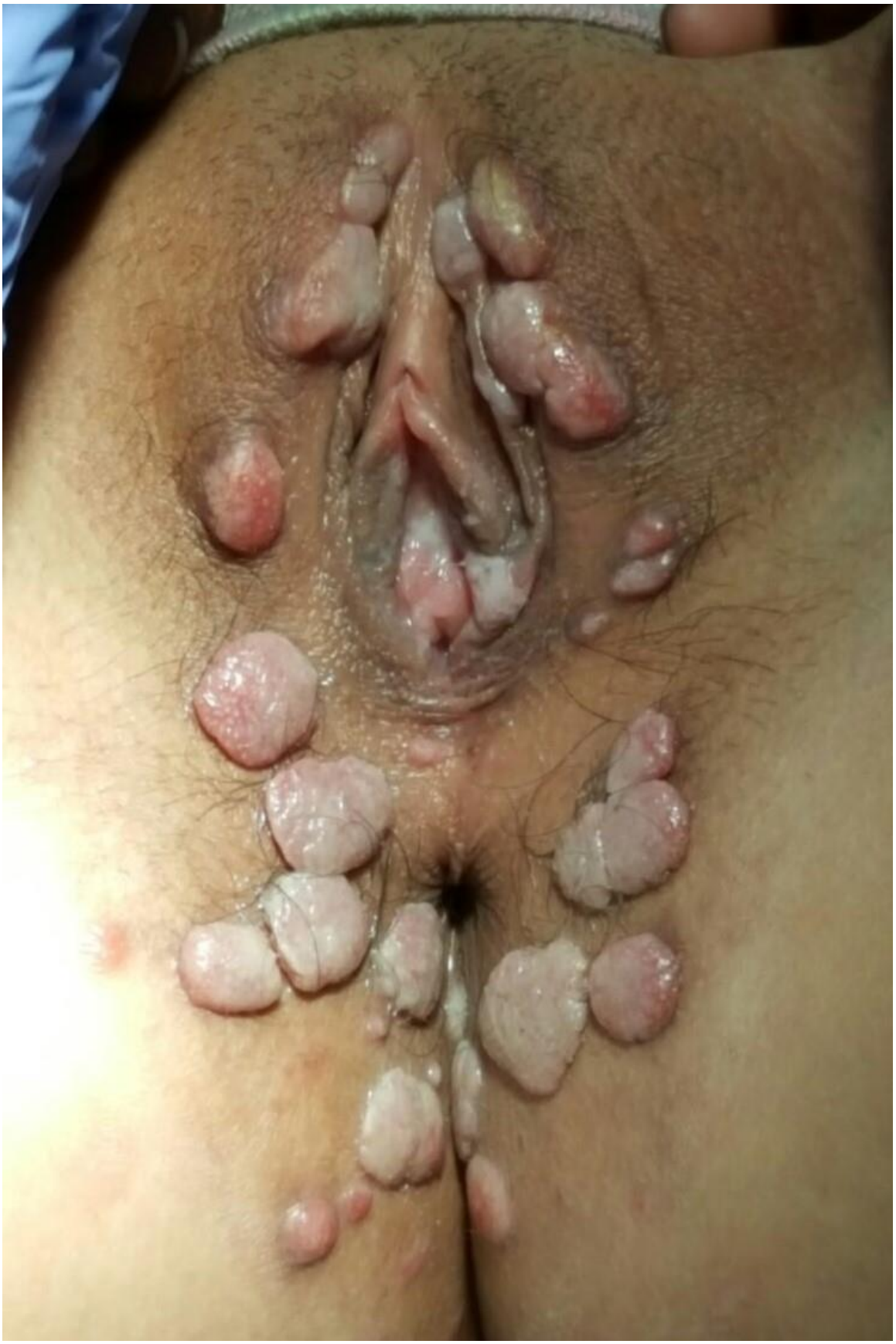
Background

Sexually transmitted diseases (STDs) are a major health problem affecting mostly young people. According to ECDE the incidence of Syphilis is increasing in Europe, with the trend rates on the rise since 2011. Usually, it's an easily treated infection, but in the absence of appropriate treatment, the disease progresses through different stages, with long term complications.

Case Presentation Summary

We present the case of 15 years old female, from an ethnic minority, previously healthy, admitted to the emergency room with a 5 months history of multiple vaginal and perianal lesions. She denied other symptoms. On examination the lesions were described as papular, small, flat, exudative, moist, wart-like. There were no other findings on examination.
She had all the vaccines from our national immunisation programme including the vaccine against Human papillomavirus (types 6, 11, 16, 18). She referred unprotected sexual practice with one partner.
Serologies for HIV, HBV and HCV were negative. Treponema pallidum antibody test and Rapid plasma regain test were positive.
Treatment with intramuscular benzathine penicillin G (2400000 U) led to complete remission of the lesions 4 weeks after the treatment.



Learning Points/Discussion

Condylomata lata is a well known presentation in secondary syphilis and should always be considered in differential diagnosis of genital and perianal lesions. Early diagnosis and treatment of Syphilis prevents the widespread of infection and reduce the risk of complications of late stages infection.

ESPID19-0740
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Which antibiotics should be used for urinary tract infection empirically in the post antibiotic era?

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Background and Aims:

In Asian countries, carbapenem resistant enterobacteriaceae (CRE), ESBL producing bacteria and vancomycin resistant enterococci were sometime detected in fecal culture. The organisms of urinary tract infection (UTI) were usually such enterobacteriaceae. But in some guideline for UTI, third cephalosporin and/or ampicillin was selected for empirical therapy. To reveal the organism of UTI is important for empiric therapy in post antibiotic era.

Methods:

We investigated the UTI organism in Kurume University Hospital from medical records between 2011 and 2016. We defined UTI as over 10^5 CFU/ml colony counts of urine cultures by clean catch, or over 10^4 CFU/ml colony counts by urethral catheterization.

Results:

One hundred seventy seven strains isolated from UTI cases. In these isolates of 106 were Gram Negative Rod (GNR) and 71 isolates were Gram Positive cocci (GPC). In the GNR isolates, E.coli were 67, K.pneumoniae were 19 and Enterobacter sp. were 7. In the those isolates 16 strains(15.1%) produced Extended-Spectrum Beta-Lactamase (ESBL). And 4 isolates (3.8%) produces Metallo-beta-lactamase. All GNR isolates were susceptible to aminoglycoside. In this study there was no VRE or VIE isolates.

Conclusions:

This study indicated that approximately 20% cases have possibilities of treatment failure with 3rd cephalosporin. Considering ESBL or Metallo-beta-lactamase producing GNR strains, aminoglycoside could be selected for the empiric therapy. Aminoglycoside has a side-effect of hearing disturbance especially for patients of mitochondrial A1555G mutation. Base on such antimicrobial resistant situation, the patients of UTI who have family histories of deafness can not choose but to be treated with carbapenem.

Systematic Review Registration:

N/A

ESPID19-0691
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Antibiotics and cure rates in childhood complicated urinary tract infections: a single-centre experience

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Background and Aims:

Urinary tract infections (UTIs) are common bacterial infections among children. Our aims were to describe the major causative pathogens, the antibiotic prescribing and the *in-vitro* resistance patterns vs *in-vivo* cure-rates in a single-centre retrospective study.

Methods:

All patients aged ≤18 years admitted to the Paediatric Department of Luigi Sacco Hospital, Milan, presenting with a complicated microbiologically-confirmed UTI requiring hospitalisation between 2016 and 2018 were included.

Results:

Fifty-five patients (0-15 years) were included. None of them presented with urosepsis. Fifty-six bacteria were isolated, of which 55/56 were Gram-negatives, with fifty-two antibiograms available. *Escherichia coli* resulted the main causative agent (44/56, 79%), followed by *Klebsiella* (4/56, 7%), *Enterobacter* (3/56, 5%), *Proteus* (2/56, 4%), and *Citrobacter* (2/56, 4%) species. The mostly prescribed antibiotics were co-amoxiclav (29/55, 53%), gentamicin (19/55, 35%) and ampicillin (6/55, 11%). A double regimen was initiated in thirteen patients (24%) and twenty-five received intravenous treatment (45%). Resistance rate against co-amoxiclav was 40% (21/52), 8% against gentamicin (4/52), and 11% against 3rd gen-cephalosporins (6/52). Among Gram-negatives, 7/51 (14%) were positive for extended-spectrum beta lactamases (ESBL). Although 13/55 (24%) patients received a discordant treatment in the first 48 hours, all children experienced a clinical resolution and microbiological response (urine sterilization) prior to switch to targeted treatment, which was performed in 9/13 (69%) of the resistant cases.

Conclusions:

We observed high treatment cure rates, regardless of the drug chosen, the initial treatment concordance/discordance with the antibiogram, and the route of administration. Treatments should be started oral and as narrow as possible, unless sepsis is suspected. Considering the increasing rates of antimicrobial resistance in children worldwide, future research should focus on children with multi-drug-resistant infections.

Systematic Review Registration:

N/A

ESPID19-0519
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Composition and properties of pathogens in urinary system infections in children

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Background

The incidence of urinary tract infections (UTI) in children is high (up to 1.8%). The etiological structure of UTI and resistance of the main pathogenic microorganisms (MO) requires dynamic evaluation. The analysis of the results of positive urine cultures was carried out in 82 patients aged from 1 month to 18 years. Resistance was assessed by determining the minimum inhibitory concentration (MIC). Clinical laboratory diagnostic standards were used (CLSI, 2015). Method of variation statistics was used.

Case Presentation Summary

15 types of MO caused UTI in children. Enterobacteriacea were cultured from 61.25% [49] urine samples; top three representatives of the family were Escherichia coli (63.28% [31]), Klebsiella pneumoniae (20.4% [10]) and Citrobacter freundi (6.12% [3]). Among the Enterococcaceae family (23.75% of all samples [19]) Enterococcus faecalis (68.4% [13]) and Enterococcus faecium (31.6% [6]) were identified. Pseudomonas aeruginosa was the leader (50% [4]) of the Pseudomonadales order (10% of all samples [8]). The Staphylococcaceae family constituted the smallest group (5% of the total number [4]). The results of the study confirm the dominant role of E.coli in etiology of uroinfections (38,75%). Enterococcus faecalis ranked second, itsshare was 16.25% of the cases. Klebsiella pneumoniae ranked third (12.5% of the cases). An assessment of sensitivity of E. coli, the leading pathogen, was performed.The highest resistance was found to ampicillin, ticarcillin, nalidixic acid and co-trimoxazole. The highest sensitivity was found to amikacin, nitrofurantoin, piperacillin / tazobactam, amoxicillin / clavulanate and cefoxitin, which justifies their use in the mode of empirical therapy of UTI.

Learning Points/Discussion

E.coli is the main uropathogen in UTI in children. E.coli exhibits variations in sensitivity and resistancewithin the group. Dynamic monitoring of uropathogenic species and theirproperties is required for the correct choiceof empirical therapy.

ESPID19-0345
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Urinary tract infection and its recurrence in the first year of life

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[3]Soroka University Medical Center, Pediatric Infectious Disease Unit, Beer-Sheva, Israel

Background and Aims:

Urinary tract infections (UTI) are common febrile illnesses in children with possible long-term morbidity. The characteristics of UTI – incidence, recurrence, epidemiologic and microbiologic data are sparse in our country.

Primary objectives: The analysis of the demographic, clinical and microbiological characteristics of the first and recurrent urinary tract infection in infants < 12 months and **secondary**: differences in first urine culture vs second or third episode on our study population.

Methods:

A retrospective study was conducted in Children Hospital Brasov during September 2014 - April 2018. We reviewed the clinical documents of all infants under the age of 12 months admitted with urinary tract infections. They were followed up 8 months.

Results:

227 infants were enrolled (87 boys/140 girls) with 189 cases of single UTI episodes. The highest prevalence was in the group 0-2 months. The most common symptoms at admission were fever (44.7%), vomiting (36.56%) and diarrhea (37.31%). 82 patients had negative urinary examination (stick). *Escherichia Coli* was isolated in 172 cases (75.10%), *Enterococcus Spp.* 28 cases (12.22%), *Proteus Mirabillis* 10 cases (4.36%) and *Staphylococcus aureus* 8 cases (3.49%). *Escherichia Coli* remained the most frequent pathogen in patients with both normal and abnormal ultrasound examination (69.67%/ 87.5%). 48 episodes of recurrent UTI were analyzed at 37 patients (16.2%) with *Escherichia Coli* the most frequent pathogen (49.41%). The patients did not receive any prophylactic antibiotics. The treatment consisted of third generation Cephalosporin, Ampicillin, Cefuroxime and Aminoglycosides according to antibiogram.

Conclusions:

1. *Escherichia Coli* was the most frequent pathogen in both initial and recurrent episodes of urinary tract infections.

2. To the best of our knowledge it is the first study in Romania to provide information regarding recurrent urinary tract infections at infant population.

Systematic Review Registration:

N/A

ESPID19-0323
E-Poster Viewing - May 7-10 - E-Poster Hours

Urogenital infections

Empirical antibiotics in urinary tract infections: is it time to change?
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[2]Centro Hospitalar de Lisboa Ocidental, Department of Clinical Pathology, Lisbon, Portugal
[3]Centro Hospitalar de Lisboa Ocidental,
Department of Infection and Antimicrobial Resistance Prevention and Control, Lisbon, Portugal
Background and Aims:

An adequate empirical antibiotic choice must be guided by surveillance data regarding local resistance patterns. Among uropathogens *Escherichia coli* (*E. coli*) accounts for 75% to 95% of all urinary tract infections (UTI) and several reports suggest an increasing resistance to first-line antibiotics. At our hospital, the first-line antibiotic for the treatment of UTI in children older than three months is amoxicillin/clavulanic acid.

Methods:

We conducted a retrospective cross-sectional chart review of all children older than three months discharged from our emergency department with positive urine cultures in 2017. Data analysis included patient demographics, symptoms, dipstick/urinalysis results, urine collection methods, isolated pathogens and their antimicrobial susceptibility patterns.

Results:

A total of 168 children, 78% males and 22% females, were enrolled in the study. The median age was five years. 34% had a previous history of UTI or urological disease. The most common agent was *E. coli* corresponding to 64% of cases, followed by *Proteus spp* (24%) and *Staphylococcus saprophyticus* (5%). Only one ESBL was identified. 41% of *E. coli* were resistant to amoxicillin, 23% to amoxicillin/clavulanic acid, 22% to trimethoprim-sulfamethoxazole and 1,9% to cefuroxime. 23% of *Proteus spp* were resistant to amoxicillin, 13% to amoxicillin/clavulanic acid, 23% to trimethoprim-sulfamethoxazole and 5% to cefuroxime. In 11% of the cases, the isolated uropathogen was resistant to the chosen empirical antibiotic.

Conclusions:

These results suggest that amoxicillin/clavulanic acid is currently not the best choice for the empirical treatment of community-acquired UTIs at our hospital. We emphasize the need for continuous monitoring of local bacterial resistance and the reviewing of treatment protocols.

Systematic Review Registration:

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ESPID19-0943
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Countering vaccination hesitancy in gender-neutral human papillomavirus vaccination programs: perspectives and experiences of experts in newly adopting countries

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[5]Harvard Medical School, Health Care Policy, Boston, USA

Background and Aims:

The growing recognition of the human papillomavirus (HPV)-related disease burden has prompted countries to establish gender-neutral HPV vaccination (GNV). However, the number of countries with GNV programs is significantly less than those with female-only programs. This study explored drivers and barriers to GNV program adoption and implementation.

Methods:

We conducted web-based and in-person interviews with HPV vaccine and policy experts in six countries with existing GNV programs (Argentina, Australia, Austria, Brazil, Canada, and Italy) using a semi-structured discussion guide designed to elicit expert perceptions of GNV program policy development and adoption. Thematic content analysis was conducted to identify factors participants considered important for GNV program development.

Results:

Eighteen experts participated in the study. A key theme emerging from the thematic analysis revealed rising negative attitudes towards vaccines, even in countries with historically positive perceptions such as Argentina, Brazil, and Italy. Experts identified several factors attributable to vaccine hesitancy, such as misinformation spread via social media, and a perception of diminished threat of vaccine-preventable diseases due to herd immunity. They also described specific factors affecting HPV vaccine receptivity, including stigma around sexual transmission, perception that it is a female-only vaccine, and safety concerns fueled by media attention.

Conclusions:

Multi-modal efforts that can strengthen HPV GNV program adaptation and implementation, and that are tailored to the needs and cultural considerations of specific country settings are warranted to counter negative perceptions of HPV vaccination and to ensure higher coverage rates.

Systematic Review Registration:

Not applicable

ESPID19-0901
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Assessing the impact of pneumococcal conjugate vaccines implementation: which methodological quality do we provide? A systematic review

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[2]Robert Debré Hospital, Emergency department, Paris, France
[3]National Reference Center for Pneumococci, Microbiology, Paris, France
[4]Necker Hospital, Emergency department, Paris, France

Background

Assessing the impact of pneumococcal conjugate vaccine (PCV) implementations at a population level over time is critical, and requires continuous population-based longitudinal surveys. To achieve this, several designs can be used, with interrupted time series (ITS) considered as the “next best choice” when randomization is not an option. We aimed to assess the methodological characteristics of the studies analyzing the epidemiological impact of PCV implementations on pneumococcal diseases.

Methods

We conducted a methodological systematic review of the literature, using Medline/Pubmed, Embase, and references of selected articles (last search January 7, 2019). Two reviewers (N.O and A.R) independently identified all non-randomized longitudinal studies assessing the epidemiological impact of PCV7, 10 or 13 implementations on invasive pneumococcal diseases, pneumonia, and/or acute otitis media, in children and/or adults, by title and abstract screening and full text examination. The main outcome was the design of the included studies, distinguishing before-after and ITS designs.

Results

Preliminary results showed that among the 241 included studies between 2001 and 2015, 200/241 (83%) used before-after design, while 36/241 (15%) used ITS. The percentage of ITS use increased from 2001 to 2015 (+1.4% per year, p=0.005), but remained low in 2015 (25%). Only 99/241 (41%) of studies took into account secular time trend before intervention when analyzing PCV impact, and only 22/241 (10%) took into account seasonality.

Conclusions

While before-after design provides a lower level of evidence than ITS, its use is much more frequent, even to date. Improving the level of evidence of longitudinal studies is critical to accurately assess the population level impact of PCV implementations over time.

Systematic Review Registration (Please input N/A if not registered)

Submission to Prospero January 6, 2019

ESPID19-0727
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Cost-effectiveness analysis of catch-up hepatitis a vaccination in the us: a dynamic model approach

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[2]Merck & Co.- Inc, Center of Observational and Real-World Evidence, Kenilworth, USA

Background and Aims:

Since 2006, hepatitis A (HepA) vaccination has been recommended routinely for children aged 1-2 years in the US. However, the vaccination coverage is below national targets and thus a substantial number of people remain unvaccinated and not protected from HepA. A cost-effectiveness of a routine HepA catch-up vaccination using a dynamic disease transmission model is used in formulating national policy.

Methods:

An age-structured population model of HepA transmission dynamics was developed to project the epidemiologic and economic impact in the US of catch-up vaccination interventions from 2 through 18 years compared to maintaining only the current routine 2-dose vaccination schedule starting at age 1-2 years. The number of outpatients, hospitalizations and deaths was calibrated using the latest US data on HepA. The structure is the same as the previous dynamic transmission model published in 2015.

Results:

The modelled catch-up vaccination program would reduce HepA diseases by approximately 20% (49K outpatients visits, 25K hospitalizations, and 589 deaths). Also, catch-up vaccination would have an impact on the unvaccinated cohort through herd protection. The incremental cost of a HepA vaccine catch-up program was $447,396 per QALY gained. Across different scenarios, 2nd dose catch-up coverage among previously vaccinated persons with one dose has the most impact on the results. The catch-up program is cost-savings if 2-doses of vaccine are administered to those who were never vaccinated..

Conclusions:

A catch-up vaccination program has the potential to protect directly a large number of unvaccinated children and adolescents, and also indirectly protect the entire US population during times of declining rates of HepA disease-acquired immunity. Our economic model suggests that a catch-up vaccination recommendation would be cost-effective or even cost-saving when it would be given to unvaccinated cohort.

Systematic Review Registration:

N/A

ESPID19-0430
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Evolution of penicillin non-susceptibility among emerging non-vaccine pneumococcal serotypes in carriage and co-colonization with haemophilus influenzae: a time series analysis of a 17-year prospective cohort.

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Background and Aims:

Pneumococcal conjugate vaccine (PCV) implementations led to major changes in serotype distribution and antibiotic resistance in carriage, accompanied by changes in antibiotics consumption. We aimed to analyze different dynamic patterns of penicillin non-susceptibility among emerging non-vaccine serotypes, and their respective association with *Haemophilus Influenzae* over time.

Methods:

We conducted a quasi-experimental interrupted time-series analysis based on a 17-year French nationwide prospective cohort. From 2001 to 2018, 121 pediatricians obtained nasopharyngeal swabs from children under 2 years with acute otitis media. Outcomes were analyzed by segmented regression.

Results:

We enrolled 10,204 children. Exposure to beta-lactams remained high over the study period (40% of children exposed within the 3 months before inclusion). Following PCV13 implementation, four patterns of penicillin non-susceptibility (PNSP) were observed among the main non-vaccine serotypes: serotypes already PNSP before PCV13, and remaining PNSP thereafter when emerging (pattern RàR), serotypes becoming PNSP after PCV13 when emerging (pattern SàR), serotypes remaining penicillin susceptible while emerging after PCV13 (Pattern SàS), and a serotype (15BC) becoming penicillin susceptible while emerging after PCV13 (Pattern RàS). Contrary to patterns RàR and SàR, for pattern SàS the rate of co-colonization with *H. influenzae* increased concomitant to their emergence. Even within serotype 15BC, among penicillin susceptible strains that emerged, the rate of co-colonization with *H. influenzae* increased concomitant to their emergence, whereas it remained stable for PNSP strains which did not emerged (Figure 1).

Conclusions:

In a context of continuing high antibiotic selective pressure, we highlighted an unexpected variability in dynamic patterns of penicillin susceptibility among emerging non-PCV13 serotypes, with serotypes emerging while remaining or even becoming penicillin-susceptible. Acquisition of antibiotic non-

susceptibility may not by itself explain adaptation to selective pressure, and co-colonization with *H. influenzae* may be involved.

Systematic Review Registration:

N/A

ESPID19-0865
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Relationship between psychosocial factors and women's decision to vaccinate against pertussis and influenza during pregnancy

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Background and Aims:

To investigate whether women's decision to vaccinate against pertussis or seasonal influenza during pregnancy is associated with psychosocial factors such as anxiety, depression, stress and emotional well-being in pregnancy.

Methods:

This prospective cohort study consisted of 1373 nulliparous women recruited in the Screening Tests to identify poor Outcomes in Pregnancy (STOP) study at two obstetric hospitals in South Australia between March 2015 and August 2018. Participating women completed lifestyle questionnaires at 14±2 weeks 'gestation and psychological scales were completed measuring perceived stress, depression, anxiety, and behavioural responses to pregnancy. Differences in baseline characteristics between vaccinated and unvaccinated participants were studied using the Chi-square test for categorical variables and Mann-Whitney U test for continuous variables.

Results:

Of 1373 women in the study, 75% and 39% received maternal pertussis and seasonal influenza vaccines respectively. Pregnant women with high perceived stress levels were significantly less likely to receive influenza vaccination during pregnancy (adjusted odds ratio, aOR 0.60; 95% CI 0.41–0.88, P-value<0.01). However, the association between receipt of pertussis vaccine and stress levels was not significant (aOR 0.83; 95% CI 0.54–1.25). Women who had received both pertussis and seasonal influenza vaccine during their pregnancy had decreased anxiety (aOR 0.69; 95% CI 0.45–1.07), depression (aOR 0.79; 95% CI 0.39–1.57) and limiting/resting behavior in pregnancy (aOR 0.83; 95% CI 0.53–1.31). Overall, low uptake of maternal pertussis and influenza vaccination was associated with unemployment, single parent household, household smoking, binge drinking other drug use pre-pregnancy.

Conclusions:

Our findings suggest psychosocial factors are associated with the decision to vaccinate against pertussis and influenza vaccines during pregnancy. Interventions that improve maternal vaccination uptake in women with psychological stressors should be designed and implemented in maternal immunisation programs.

Systematic Review Registration:

N/A

ESPID19-0858
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

20 years of varicella vaccination in the usa: insights for universal varicella vaccination implementation

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Background and Aims:

The US introduced 1-dose universal varicella vaccination (UVV) in 1996 for children 1- 12 years and 2-doses for those ≥13 without varicella disease history. Routine uptake among 1-2 year olds was slow, reaching 90% coverage after 10 years. A second routine dose was introduced in 2006, reaching 90% rapidly. The objective of this study is to estimate the impact of UVV in the US, evaluate possible alternative coverage uptake scenarios, and examine implications of these findings for implementation of UVV in other settings.

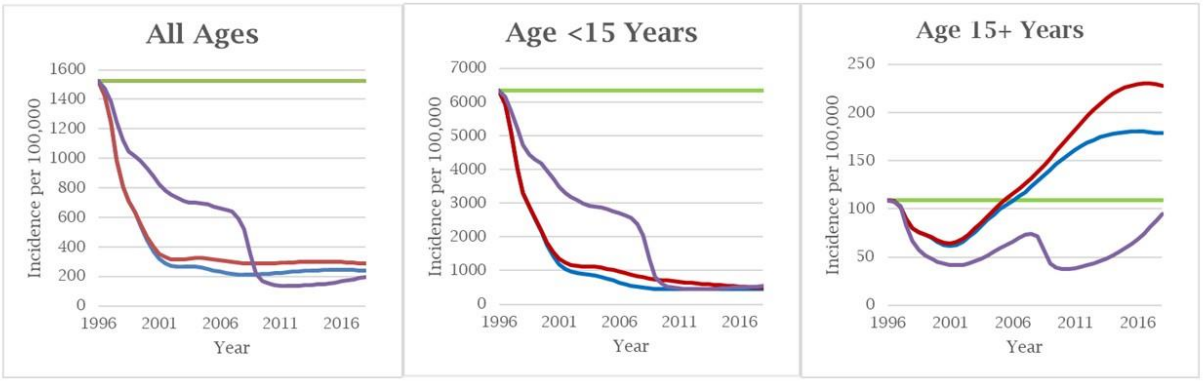
Methods:

A dynamic transmission model was used together with age-specific vaccine coverage from a commercial insurance claims database to evaluate three scenarios: (A) UVV given actual coverage , including catchup among pre-adolescents and older age groups; (B) UVV with a hypothetical two-dose program with rapid achievement of 95% 1st dose and 90% 2nd dose coverage, with both doses started together (no catchup vaccination); and (C), a hypothetical two dose UVV program with a ten year delay between the implementation of 1st and 2nd doses (no catchup vaccination).

Results:

Based on actual coverage (A), UVV between 1996-2018 prevented an estimated 68,745,397 varicella cases and 2023 deaths; the two dose program (B) with high coverage from the outset, and without teenage catch-up, would have resulted in 13,236,904 additional cases averted, however, the age-shift in varicella cases is estimated to result in 576 additional deaths.

Figure: Modelled impact of Universal Varicella Vaccination (UVV) in the United States, 1996-2016, by age groups.



No UVV
(A) Actual Coverage with Catchup
(B) 2 Dose (95%/90% Coverage) from 1996
(C) 1 Dose (95%) from 1996, 2nd Dose (90%) from 2006

Conclusions:

Vaccination of those outside the targeted age ranges (12-15 months and 4-6 years) for pediatric vaccination was an important component of preventing an age-shift in varicella incidence. Rapidly achieving high coverage with the first dose would have led to earlier sustained reductions in varicella incidence, and modelling can provide important insights for design of UVV.

Systematic Review Registration:

NA

ESPID19-0750
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Implementation and coverage of the first public sector introduction of typhoid conjugate vaccine navi mumbai, india

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Background

Typhoid fever poses a significant public health problem in India. In 2018, the first typhoid conjugate vaccine (TCV) was prequalified by the World Health Organization (WHO). In an effort to protect children from typhoid, the Navi Mumbai Municipal Corporation (NMMC) took a landmark decision to be the first in the world to implement a public sector TCV campaign. During July–August 2018, the first phase of the TCV campaign, targeting children 9 months to <15 years old in 11 urban primary health center (UPHC) areas, was conducted by NMMC with support from multiple governmental and non-governmental partners and Navi Mumbai paediatricians.

Methods

We describe planning and implementation from the first public sector vaccination campaign. During September–October 2018, we conducted a community-based coverage survey.

Results

In preparation for the campaign, workshops and trainings were conducted for medical officers, pediatricians, and UPHC staff. The campaign was implemented using existing NMMC immunization program resources through fixed posts. Overall, 1,210 vaccination booths (hospitals, clinics, schools, and other designated locations) were set up for a 10-day campaign and 3 days were used for mop-up rounds. According to NMMC reports, 113,420 children were vaccinated (administrative coverage=70%). A total of 1,368 households in 57 primary sampling units (PSUs), based on the polio microplan, were selected for the coverage survey. Among 956 eligible children (528 households), 719 (75%) received vaccine during the campaign (recall and vaccination card); 53 (6%) reported receiving TCV previously through the private sector.

Conclusions

The first public sector TCV campaign was successfully implemented by NMMC with technical support from partners. The campaign was well accepted with high coverage achieved in most targeted areas. Evaluations are ongoing to understand vaccine effectiveness and impact.

Clinical Trial Registration (Please input N/A if not registered)

NCT03554213

ESPID19-0566
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Exploring the evidence behind comparability of pcvs impact on overall pneumococcal disease

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Background and Objective

A decade after introduction, higher valent pneumococcal conjugate vaccines (HV-PCVs) have demonstrated significant impact on the burden of invasive pneumococcal disease (IPD) in children and at all population level. The overall impact of HV-PCVs is a combination of effectiveness against vaccine serotypes, protection against vaccine-related serotypes and potential impact on IPD caused by non-vaccine serotypes. Recent evidence suggests comparable overall impact of HV-PCVs despite some differences in their composition and formulation (included serotypes, carrier protein, conjugation method). Whys and wherefores are discussed herein.

Methods

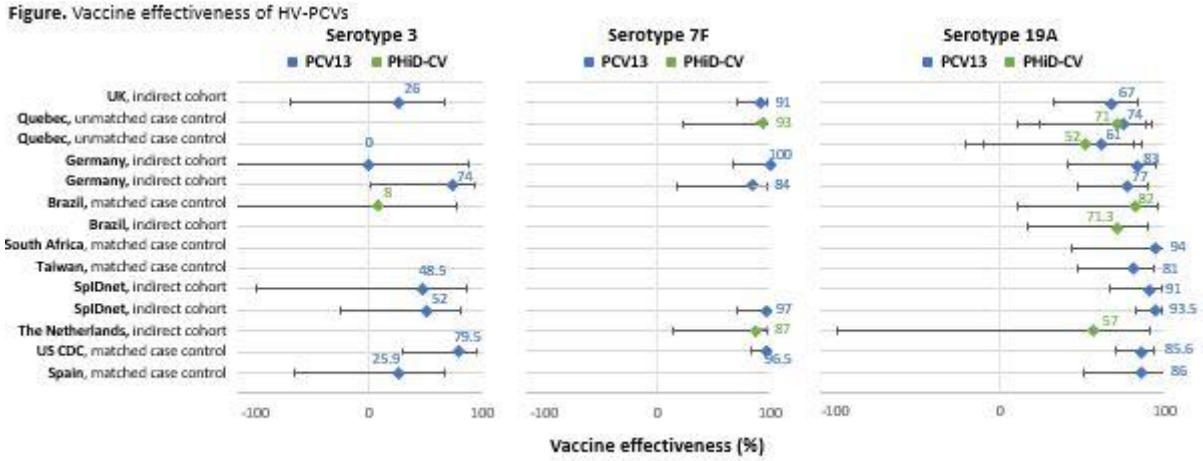
Literature data evaluating the effectiveness/impact of HV-PCVs (13-valent PCV [PCV13] and the pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine [PHiD-CV]) on IPD burden in children aged <5 years were reviewed and analysed by serotype from the selected surveillance sites. Selected data was limited to countries/regions with active IPD surveillance data before and after vaccine introduction up to December 2018.

Learning Points Discussion

• Serotype-specific vaccine effectiveness were mostly reported for the non-7-valent PCV serotypes (1, 3, 5, 6A, 7F, and 19A).
• While PHiD-CV does not contain serotype 19A, post-marketing data demonstrated cross-protection against this serotype in vaccinated population, although at a variable extent across different settings (Figure).
• Heterogeneous results of PCV13 effectiveness against serotype 3 have been observed due to limited sample size in the evaluated studies. Consequently, robust conclusions cannot be obtained with regards to IPD prevention.
• Variability in replacement disease has been observed among countries/region. One of the factors that may influence the observed difference is the HV-PCV formulation (PHiD-CV or PCV13) used in the national immunization program of each country/region.

Funding: GlaxoSmithKline Biologicals SA

Figure. Vaccine effectiveness of HV-PCVs



PCV13, 13-valent pneumococcal conjugate vaccine; **PHiD-CV**, pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine; **SpIDnet**, *Streptococcus pneumoniae* Invasive Disease network; **CDC**, Centers for Disease Control and Prevention.

ESPID19-0415
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine challenges

Increased carriage prevalence of pneumococcal serotype 19a carriage in belgian children following a pcv13-to-pcv10 vaccine switch

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Background

The predominantly “2+1” Belgian infant pneumococcal conjugate vaccine (PCV) programme changed from PCV13 to PCV10 in 2015-2016. A nationwide nasopharyngeal carriage study in children (6-30 months) attending day-care centres (DCC) or seeking care for acute otitis media (AOM) was initiated in January 2016. Carriage of *S. pneumoniae* (Sp) was evaluated over three sample collection periods.

Methods

Single nasopharyngeal swabs were taken yearly between January 2016 and May 2018. Sp was detected by culture and PCR; Sp-strains were serotyped by Quellung-reaction (all serotypes) and by real-time PCR (PCV13 vaccine serotypes). The presented increases are significant at a level <0.05 (Chi²/Fisher’s Exact Test).

Results

Over the three successive periods, samples from 2809 children attending DCCs and 366 children with AOM were collected. The proportion of children that were age-appropriately vaccinated exclusively with PCV10 increased to 75.9% (Figure 1A) and to 83.8% in the respective child populations. PCR-based carriage prevalence of serotypes 3, 6A and 19A increased from 1.2% to 7.0% in DCC-children, mainly caused by serotype 19A (Figure 1B); in AOM-children the increase from 0.0% to 5.9% was non-significant. Preliminary results of the other vaccine-serotypes are culture-based: carriage of all PCV13-serotypes increased from 5.4% to 10.4% among the DCC-carriers; among AOM-carriers, the increase was non-significant; from 7.4% to 9.7%. The dominating vaccine serotypes among DCC-carriers were 19F in period 1 (52.0% of all PCV13-serotypes) and 19A in the subsequent periods (50.0% and 68.1% in period 2 and 3), as was seen among AOM-carriers. Antimicrobial non-susceptibility against penicillin, levofloxacin, tetracycline, erythromycin or cotrimoxazole remained stable among Sp-strains (DCC:40%-43%; AOM: 48%-50%).

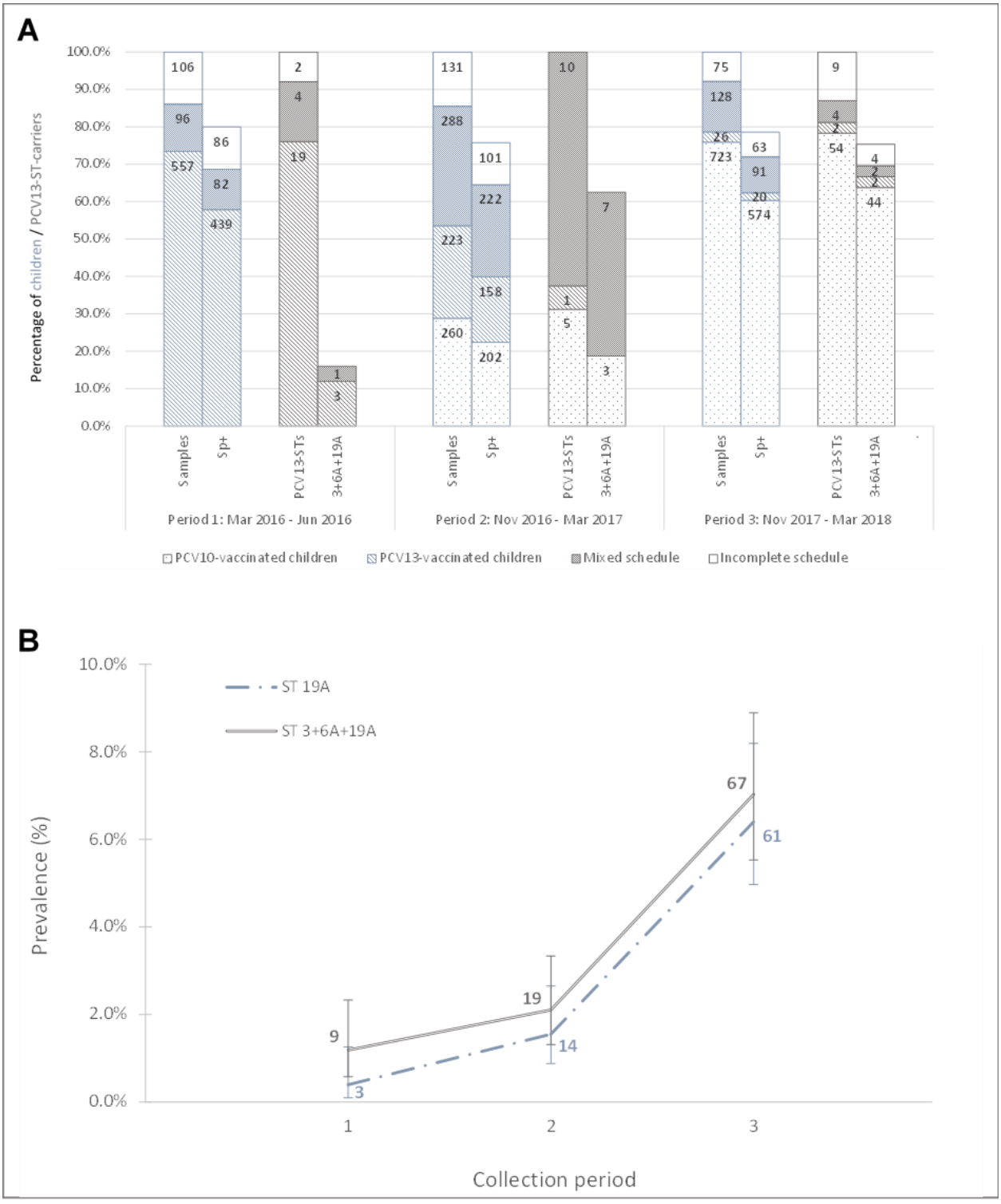

Figure 1. Carriage of *S. pneumoniae* (Sp) among children attending day-care centres in the consecutive collection periods; A – In blue/Two bars on the left within each period: PCR-based number of samples (bars) and carriage prevalence (Y-axis) per vaccination status, in grey/two bars on the right within each period: culture-based carriage of serotypes included in PCV13 (PCV13-STs) and the serotypes 3+6A+19A combined; Sp+ = positive for *S. pneumoniae*; B – PCR-based carriage of serotype 19A (blue dotted line) and the serotypes 3+6A+19A combined (grey line), error bars depict 95% confidence interval.

Conclusions

Carriage of PCV13-serotypes in DCC-children increased over the study period, mainly caused by serotype 19A. A similar, but non-significant trend was observed among AOM-children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0389
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine development (phase 1-2) - bacterial and all non-viral

What is the difference in the immune response elicited by the whole-cell versus acellular pertussis vaccine? A review of the role of t cell immunity

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Background and Objective

Despite high rates of pertussis vaccine coverage, there has been a recent resurgence in pertussis disease worldwide. The main reason proposed is the switch in infant primary immunisation from whole cell(wP) to acellular(aP) pertussis vaccines and the difference in the immune responses elicited, specifically those coordinated by T-cells. Our literature review aims to summarise current knowledge on pertussis-specific T-cell responses following disease and vaccination, as shown by studies in animal models (murine and baboon) and infected or vaccinated subjects.

Methods

We used a set of pre-specified terms to search PubMed and Google Scholar and meet our objective. Cross-referencing, the 'related articles' function and open search of the internet using Google engine were applied to expand the results. All relevant titles in English and French from January 1918 to December 2018 were extracted and reviewed.

Learning Points Discussion

As yet, there is no clear correlate of protection against pertussis; anti-pertussis toxin antibody is considered critical in reducing disease severity but the role of cell-mediated immunity is increasingly emphasised. Animal models have confirmed Th1 vs. Th2 polarisation according to the type of infant primary vaccine given, with Th1 subset shown to confer protective immunity. Furthermore, Th17 is important for protection against colonisation and subsequent transmission of infection, although this has not been demonstrated in infants.

Crucial gaps in knowledge were identified, including:
• Rigorous characterisation of pertussis-specific T-helper cell subsets, notably Th17, following aP vs. wP immunisation in infants.
• Contribution of T-cell immunity to qualitative and quantitative humoral responses, bridging the gap between the B- and T-cell compartments.

Therefore, further research is needed to inform the development of effective next-generation pertussis vaccines and of novel analytical approaches ('systems-based biology') that will fully elucidate pertussis vaccine immunogenicity and safety.

ESPID19-0604
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine development (phase 1-2) - bacterial and all non-viral

Maternal vaccination - patient perspectives and perceptions, kawempe hospital, uganda

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Background and Aims:

Group B streptococcus (GBS) is responsible for an estimated 90,000 infant deaths globally. Multivalent vaccines that could be delivered to pregnant women to protect their infants against GBS disease are being developed. A new maternal vaccine study site is being established in Uganda. The aim of this patient engagement project was to explore beliefs and practices regarding maternal immunisation including potential barriers and facilitators to uptake in this urban, high-burden setting in preparation for the implementation of vaccine studies.

Methods:

Women attending antenatal clinics at Kawempe Referral Hospital, Kampala were invited to participate in focus-group discussions. An interview guide was developed in collaboration with researchers from LSHTM Vaccine Confidence Project. During November 2018, two focus-group discussions were held. Seven women attended the first focus-group and eight women attended the second. The discussions were audio-taped, and the recordings translated and transcribed from Luganda into English. The transcriptions were analysed by two investigators.

Results:

The participants consulted numerous sources when making decisions regarding their pregnancy. These included their husbands, community-elders, healthcare workers and family. The majority of women accepted tetanus vaccination during previous pregnancies. Many of the respondents stated that they would accept a new vaccine against GBS but wanted reassurance from doctors about vaccine safety, especially safety for the developing fetus. Many women were autonomous decision makers, whilst others deferred to their husbands, elders or healthcare workers.

Conclusions:

Few studies have examined patient perceptions of maternal immunisation in low-resource settings. It is crucial that patient concerns are understood and addressed if vaccines are to be successfully implemented. Future work in Uganda should explore themes identified in these first focus-groups in more depth and engage other key decision-makers such as husbands and community elders.

Systematic Review Registration:

n/a

ESPID19-0981
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - bacterial and all non-viral

Effects of 13-valent pneumococcal conjugate vaccines on otitis media in 2 to 3 years old cameroonian children

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Background

Data on the effects of pneumococcal conjugate vaccines (PCVs) in low-income countries is scarce. We assessed the effect of these vaccines on otitis media (OM) in Cameroon where the 13-valent PCV (PCV13) was introduced in July 2011.

Methods

A community-based cross-sectional study design was used to assess 413 PCV13-vaccinated children aged 24 to 36 months. This was compared with a baseline cohort of PCV13-unvaccinated children. The diagnosis of OM was based on clinical inspection for chronic suppurative otitis media (CSOM), otoscopy for acute otitis media (AOM) and tympanometry for otitis media with effusion (OME). We defined CSOM as draining of the middle ear with duration of more than two weeks, AOM as otorrhea/bulged tympanic membrane and OME as a flat 'type B' tympanogram. Prevalence of OM and baseline characteristics in both cohorts were compared. Vaccine effectiveness (VE) was estimated by 1- Odds of vaccination against the Odds of no vaccination x 100.

Results

111 OM cases were detected including 42/433 (9.7%) in the PCV13-unvaccinated in 2013 and 69/413 (16.7%) in the PCV13-vaccinated in 2015. In the PCV13-unvaccinated, 3 (0.7%) children were identified with unilateral CSOM, 7 (1.6%) with bilateral OME and 31 (7.2%) with unilateral OME and 1 (0.2) with unilateral dry tympanic membrane perforation. In 2015, these figures were 9 (2.2%) of subjects with CSOM, 12 (2.9%) with bilateral OME and 48 (11.6%) with unilateral OME. In the stratified logistic regression analyses, a statistically significant association between OM and 'having previous history of OM' was found in the post-vaccine data, prevalence odds ratio (POR) = 4.24 (95%CI: 2.0 to 8.8), $p < 0.0001$. VE = -87% (95%CI: -181 to -24).

Conclusions

PCV13 effectiveness in preventing OM was statistically significant but negative.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0658
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - bacterial and all non-viral

Using administrative data to measure the impact of case physician on estimates of pertussis vaccine effectiveness

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Background and Aims:

Administrative data have been used to estimate vaccine effectiveness (VE) against laboratory-confirmed (LC) pertussis. An individual is, however, only eligible for inclusion in these datasets if testing is ordered. We explored the impact of matching on case physician on estimates of pertussis VE.

Methods:

We used a nested case-control design to analyze two controls groups (with different matching criteria). Patients with LC pertussis in Manitoba between April 1, 1992, and March 31, 2015 were identified from routinely collected health data and were matched to up to five population-based controls per group on age, gender, geography, and either i) physician seen most frequently in previous year or ii) number of physician visits in previous year. We assessed matching characteristics and estimated VE by control group for the acellular pertussis (aP) vaccine using conditional logistic regression models.

Results:

Of the 328 eligible cases, 123 (38%) and 7 (2%) were excluded from the physician and visit matched groups respectively based on inability to identify a suitable match. Data were available for 205 cases and 896 controls in the physician-matched group and 321 cases and 1503 controls in the visit-matched group. Pertussis VE estimates for up-to-date vaccination was 81% (65%-89%) for the physician-matched group compared to 82% (67%-90%) for the visit-matched group.

Conclusions:

Matching on the specific case physician led to the same pertussis VE estimates as matching on physician utilization and resulted in loss of a large proportion of eligible cases.

Systematic Review Registration:

N/A

ESPID19-0533
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - bacterial and all non-viral

Streptoccocus pneumoniae as a cause of acute otitis media in slovak children in pneumococcal vaccination era.

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Background and Aims:

S. pneumoniae is a leading bacterial pathogen causing acute otitis media (AOM) in Slovak republic. There is significant decrease of pneumococcal AOM after widespread vaccination with pnemococcal conjugate vaccines (PCV) although the replacement phenomenon has been observed by non-vaccine pnemococcal serotypes. In study area vaccination status of newborns is various due to various PCV vaccine availability (Synflorix or Prevenar 13).

Methods:

Goal of presenting study was to determinate AOM pathogens, detect antibiotic susceptibility and in case of *S.pneumoniae* performe serotyping by Quellung method. 295 patients in age 0-5 year were acquired in to the study with AOM. Middle-ear fluid was obtained by tympanocentesis or after spontaneous perforation for bacteriological testing. Time period of study was from January 2016 till Jun 2017 (16 months).

Results:

295 children with AOM were enrolled to the study. *S. pneumoniae*, 62%, *H. influenza* 23%, *S. pyogenes* 16% and *M. catarrhalis 2*% were identified respectively. Serotyping manifested dominant role of serotype 19A 41%, serotype 3 22%, although replacement phenomenon of non-vaccine serotypes increased dramatically (34 %).

Conclusions:

S. Pneumoniae, despite widespread of PCV vaccination is most common pathogen of AOM with dominant role of multi-resistant serotype 19A and serotype 3. However these are additional serotypes in 13-valent vaccine, but vaccination status of 13-valcent vaccine was only 22% in study group compare to 78% 10-valent vaccine with full vaccinated schedule 2+1 (68 %). 8% of children haven't received any PCV vaccine.

Systematic Review Registration:

Streptoccocus pneumoniae as a cause of acute otitis media in Slovak children in pneumococcal vaccination era.

ESPID19-0278
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - bacterial and all non-viral

Herd effect of higher-valent pneumococcal conjugate vaccines: a systematic literature review

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Background

Herd effect refers to a decreased disease incidence in unvaccinated groups due to pediatric vaccination programs that reduce pathogen transmission within a population. Recent analyses have shown a similar impact of higher-valent pneumococcal conjugate vaccines (HVPCVs: pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine, PHiD-CV, and 13-valent PCV, PCV13) on pneumococcal disease in vaccine-eligible age groups. We performed a literature review to assess available data on herd effect following PHiD-CV or PCV13 vaccination.

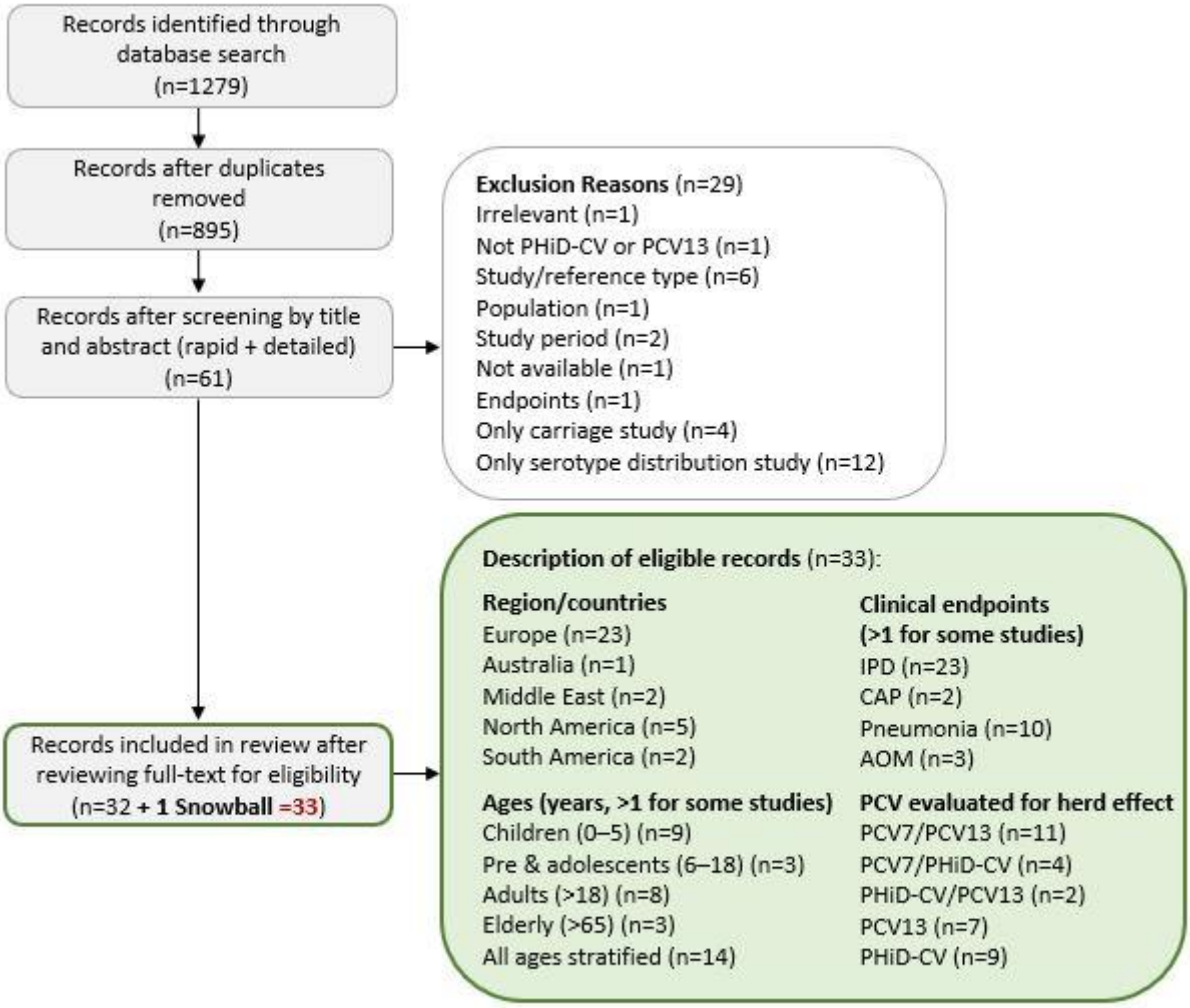
Methods

A systematic literature search was conducted from January 2006 to November 2018 in PubMed, EMBASE and Scopus databases. Primary research showing HVPCV impact through herd protection on morbidity caused by pneumococcal disease were included. Studies evaluating only carriage, serotype distribution and/or cost-effectiveness were excluded. Retrieved publications were screened by title/abstract and reviewed based on pre-defined criteria. Following quality assessment, integration and extraction of reviewed datasets, a descriptive analysis was performed.

Results

1279 articles were identified, of which 33 were included in our review (Figure). Eligible studies reported invasive pneumococcal diseases (IPD) and non-IPD outcomes in different age groups and countries routinely using either PHiD-CV or PCV13. Most studies included children (0-5 years) and/or adults (>18 years). Studies in older adults (>65 years) were limited. After HVPCV introduction in national immunization programs, overall reductions on IPD and pneumonia cases and hospitalizations were reported in children and adults not targeted for vaccination.

Figure. Systematic literature review flowchart and study descriptions



n, number of articles; **IPD**, invasive pneumococcal diseases; **CAP**, community acquired pneumonia; **AOM**, acute otitis media; **PCV7**, 7-valent pneumococcal conjugate vaccine; **PHiD-CV**, pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine; **PCV13**, 13-valent pneumococcal conjugated vaccine.

Conclusions

Evidence for herd effect due to HVPCVs was identified in unvaccinated children and adults, with few studies in older adults. Due to methodological limitations (e.g. short post-vaccination periods), more data and high-quality surveillance are needed to further assess the power and quantify herd effects generated by HVPCVs in different populations not targeted for vaccination.

Funding: GlaxoSmithKline Biologicals SA

Systematic Review Registration (Please input N/A if not registered)

N/A

ESPID19-1098
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - viral

Immunogenicity and safety of the new live attenuated varicella vaccine in healthy children aged 12 months to 12 years

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Background

In the Republic of Korea, varicella vaccine was launched in 1988 and included into the national immunization program in 2005. Thereafter, there has been continual efforts for the researches and developments of domestic varicella vaccines.

Methods

In this phase III double-blinded, multicenter study, healthy children aged 12 months to 12 years (randomized 1:1) received one dose of new R & D live varicella vaccine (SK bioscience, Pankyo, Korea) or Varivax® (Merck & Co.,Inc.) vaccine. The primary objective was to demonstrate non-inferiority of new vaccine compared to Varivax® vaccines in terms of immune responses by FAMA (fluorescent antibody to membrane antigen) assay and gpELISA (glycoprotein enzyme-linked immunosorbent assay), 6 weeks post-dose. Solicited symptoms (local and general) were recorded during 7 days, and unsolicited adverse events (AEs) during 6 weeks, after vaccination. Serious AEs (SAEs) were recorded during 26 weeks after vaccination.

Results

The immunogenicity of the new vaccine was non-inferior compared to Varivax® vaccine. Six weeks after vaccination, 211 of 212 subjects (99.53%) have seroconverted (FAMA VZV antibody titer <1:4 to ≥1:4) in new vaccine group, while 213 of 221 subjects (96.38%) have seroconverted in Varivax® group. There was no statistically significant difference in the incident rates of AEs between new vaccine group and Varivax® group (p = 0.7163). One hundred seventy one of 251 subjects (68.13%) who have received new varicella vaccine reported 449 AEs, and 172 among 247 subjects (69.64%) reported 411 AEs following vaccination of Varivax®.

Conclusions

The new varicella vaccine is highly immunogenic and safe, and this new varicella vaccine can be effectively used for preventing the varicella zoster virus infections.

Clinical Trial Registration (Please input N/A if not registered)

NCT03114943

ESPID19-0584
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - viral

The paradigm of using the same vaccine for the completion of multi-dose vaccination schedules: an example of mixed hpv vaccination program

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Background and Aims:

The objective of this review is to summaries the data used by the Quebec Immunization Committee (QIC) when recommending a mixed HPV vaccination with one dose of nonavalent (9vHPV) and one dose of bivalent vaccine (2vHPV) in school-based program.

Methods:

In 2014, the QIC recommended to conduct trials to assess the (I)immunogenicity of 1-dose of 9vHPV; (II)safety/immunogenicity of 9vHPV+2vHPV and (III)impact of different intervals between doses on vaccines immunogenicity.

By 2018, the results of 5 trials with mixed schedules were available. All have shown that the use of two vaccines in the same subject is safe and immunogenic. At least 2 other trials have shown that 1, 2 or 3 doses induce similar protection against infection for up to 7-11 years.

Results:

In 2018, the QIC concluded that 1 dose of HPV vaccine is likely sufficient. However, recognized that more robust data with 1-dose regimen will be available in the next years.

Until then, in order to optimize the vaccination program, two approaches were considered: (I)the use of a mixed 9vHPV+2vHPV schedule; and (II)the use of one dose of the 9vHPV in 9-10-year-olds with a second dose given several years later, if judged necessary.

The QIC recommended a mixed schedule. Being less costly, the mixed schedule allowed for the extension of HPV program.

Conclusions:

We conclude: (I)a review of the efficiency of vaccine programs should be periodically conducted; (II)the paradigm of using the same vaccine for the completion of multi-dose schedules should be challenged, and (III)public health stakeholders should be mindful of the negative impacts of vaccine monopoly. Availability of more than one product results in more accessible vaccine prices which allow more extensive programs, and diminishes the risk of vaccine shortages.

Systematic Review Registration:

N/A

ESPID19-0101
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine efficacy (phase 3) and effectiveness - viral

Trends in laboratory rotavirus detection in a medical center in northern taiwan from 2003 to 2016

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Background and Aims:

Two rotavirus vaccines were licensed in Taiwan since August, 2006 and only used in private sector. To evaluate the tendency of rotavirus activity in Taiwan between pre- and post-vaccine periods, we conducted this study.

Methods:

All stool specimens sent to CGMH virology laboratory for rotavirus detection by EIA method from 2003 to 2016 were included. The positivity rate of rotavirus was compared with pre-vaccine period (2003-2006), early vaccine period (2007-2011, vaccine uptake rate <30%), and late vaccine period (2013-2016, vaccine uptake rate around 60%) and also among different age groups.

Results:

During the 14-year period, 9055 out of 49994 specimen as positive results were included for final analysis. The overall positivity rate was 18.3%; if year 2012 excluded (positivity rate 7.2%, due to the norovirus epidemic), it would be 19.2%. It often reaches its peak in March (37.8%), followed by April (30.2%) and February (28.4%) while less than 10% between August to November, with the nadir (7.33%) in October. The positivity rate was 20.9% during pre-vaccine period, 21.3% during early vaccine period, and 14.4% during late vaccine period. It was highest for patients aged 4 (30.3%) and 3 years (30.2%), while 11.3% for patients aged < 1 year and 8.23% for aged >10 years. From pre-vaccine period to late vaccine period, the positive rate significantly decreased in patients aged 3 years or less while notably increased in patients aged 5-9 years.

Conclusions:

This study showed that on a hospital-based study, rotavirus activity was not remarkedly affected by the vaccines usage until the uptake rate reached certain level, which the younger age group (< 3 years old) was the benefit population.

Systematic Review Registration:

Linkou Chang Gung Memorial Hospital

ESPID19-0885
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Effects of childhood immunization on s. Aureus infection and carriage: a systematic review and metanalysis

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Background and Objective

The development and use of vaccines have had an important impact on rates of vaccine-preventable diseases. In the ecological niche of the nasopharynx, pathogens maintain a dynamic balance. Aim of this study was to investigate effects of childhood vaccinations on S*. aureus* carriage and infection.

Methods

We systematically reviewed the English literature for studies on the indirect effects of childhood vaccinations on *S. aureus* carriage and infection for outcomes published till December 2017. Data on pneumococcal vaccines, vaccines for *Haemophilus influenzae* and other pathogens were included. Metanalysis was performed for studies that provided comparison data from the pre- and post-vaccination period based on the random effect model and results were presented using forest plot charts. When only pre or post vaccination data was available a qualitative analysis was used.

Learning Points Discussion

A total of 30 studies were analyzed including randomized control trials and observational studies. Studies looking into vaccine effects on *S. aureus* carriage in infancy and childhood showed no significant changes in the carriage rate in the postvaccination period (17/20) apart from an increase at the age of 11-12 months (3/20) which was not sustained in later childhood. Data regarding nonpneumococcal vaccines was scarce. Relative increase in *S. aureus* infections (bacteremia, upper respiratory tract infections and septic arthritis) was noted in the postvaccination period (2000-2013). The observed changes are explained by the niche dynamic theory, integrating inter-species interactions and host immune responses. We conclude that immunizations can influence niche balances. Consideration of indirect effects on non-targeted pathogens is needed in future immunization planning.

ESPID19-0930
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Hexavalent formulation preference among italian hcps: preliminary results of a qualitative and quantitative survey

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Background and Aims:

In Italy, three hexavalent vaccines are available. While two are in pre-filled syringe (PFS), the third needs to be reconstituted with the Hib antigen. As demonstrated in literature, different formulations are related to time efficiency, safety and immunization errors.

Methods:

Experienced interviewers recruited by research company GfK Italy carried-out a quantitative and qualitative face-to-face survey to explore attitudes and preferences among Italian HCPs involved in vaccine administration (hygienists, nurses, pediatricians) in 9 Italian Regions.

The survey valuated advantages versus disadvantages of the two formulations. We analyzed the qualitative and quantitative preliminary results of the survey.

Results:

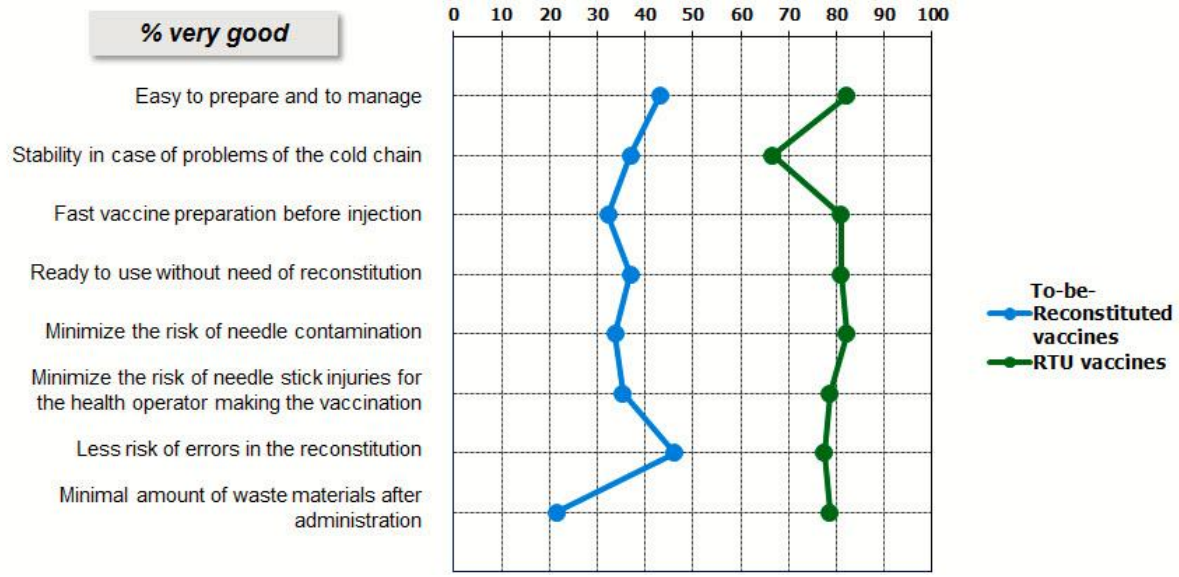
265 HCPs were interviewed. Satisfaction was measured using 1-10 scale, where 8-10 was very good. 80% of HCPs declared to be very good satisfied with the advantages of PFS hexavalent vaccines: easy preparation, no risk in the reconstitution, low risk of needle contamination and stick injuries. Only 40% of HCPs declared to be very good satisfied with the formulation to be reconstituted, due to more manipulations, higher risk of needle contamination and stick injuries (Figure). HCPs have large experience with both hexavalent formulations. Nevertheless, HCPs declared that the time saved in preparation of PFS can be effectively spent for vaccination counselling during the same visit.
Conclusions:

In line with the existing literature, our research demonstrated that HCPs preferred PFS formulation of hexavalents because it simplifies the preparation, minimizes the number of manipulations and errors risk. In particular, the risk of forgetting to reconstitute the Hib or not taking all the Hib antigen from the vial is avoided with the PFS. Finally, the time saved is relevant and can be spent with parents and the baby in a more productive way.

Systematic Review Registration:

N/A

Survey: preliminary results



ESPID19-0526
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Role of fully liquid or ready-to-use vaccines and vaccines requires reconstitution in minimization of vaccination errors: focused literature review

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Background and Objective

The optimization of immunization practices is crucial for the success of vaccination. Vaccination errors may decrease the impact of immunization on societal and individual levels. The reconstitution (dissolution of lyophilized vaccines by solvents or liquid vaccines) may lead to administration errors. The review's objective is to assess the quantity and quality of vaccination errors in vaccines requiring reconstitution versus fully liquid or ready-to-use vaccines.

Methods

Focused literature search of Embase, DOC Search, and hand searching of the bibliography of included studies and previously published reviews (including clinical and observational studies) was performed to identify studies on vaccination errors, preparation time, and health care professional (HCP) satisfaction.

Learning Points Discussion

Our literature search identified 24 relevant articles out of 1056 records initially found. After full-text screening, 12 articles that met the pre-defined criteria were included in this review. 5 articles were non-comparative studies in which data was retrieved from reporting databases, 2 were case reports/series, 1 was cross-sectional survey studies, and 4 were time-motion studies, including one randomized cross-over study.

7 of 12 articles reported vaccination errors. Only one published study directly compared fully liquid versus non-fully liquid vaccines, in this study fewer HCPs made mistakes preparing fully liquid vaccine. Preparation time was reported in 4 articles and was shown less for ready-to-use vaccines versus vaccines requiring reconstitution. 3 articles showed that HCPs preferred fully liquid vaccines over non-fully liquid vaccines.

Focused review suggests that fully liquid vaccines are associated with fewer vaccination errors, less preparation time, and higher satisfaction among HCPs than vaccine requiring reconstitution, more research in this area is required.

ESPID19-1023
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Delayed type hypersensitivity reactions to aluminium-adsorbed vaccines: a case series

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[2]Our Lady's Children's Hospital- Crumlin, Department of Infectious Diseases and Immunology, Dublin, Ireland
[3]Temple Street Children's University Hospital, General Paediatrics Department, Dublin, Ireland
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[5]Our Lady's Children's Hospital- Crumlin, Department of Histopathology, Dublin, Ireland

Background

Persistent pruritic subcutaneous nodules have been reported at the site of vaccination (vaccination granulomas) following the use of several aluminium-adsorbed vaccines. An incidence of 0.8-0.9% has been reported in the literature. Contact allergy to aluminium has been strongly associated with the presence of vaccination granulomas. During the aluminium adsorbed diphtheria-tetanus/acellular pertussis vaccine trials, hypersensitivity to aluminium was demonstrated in 77% of those with pruritic nodules. These nodules appear to be long-lasting but little is known regarding prognosis.

Case Presentation Summary

In this case series, we report twelve children who developed pruritic nodules at injection sites following vaccination and were referred to a tertiary paediatric Dermatology centre for assessment between 2010 and 2018. The median age at onset of symptoms was twelve (IQR: 6 – 19.5) months and the main presenting symptoms were pruritus in eight children (67%) and pain in three children. Six out of the seven children tested in the series for contact allergy for aluminium were positive (86%). One child was found to have developed cutaneous pseudolymphoma on biopsy, a potential adverse effect of vaccines containing aluminium hydroxide as an adjuvant. This is the first case described in a child following vaccination. Four of the eleven children had imaging studies, two of which were initially reported as venous malformations.

Learning Points/Discussion

Although an infrequent occurrence following vaccination with aluminium-adsorbed vaccines, the development of persistent pruritic nodules can cause significant distress and anxiety for parents and children and lead to unnecessary investigations and a delay in subsequent vaccination. Greater awareness among clinicians and primary health care providers of this potential adverse reaction is necessary.

ESPID19-0593
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Mmr vaccination in bitola, for or against

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[3]Protection and Rescue Directorate, Protection and Rescue Directorate, Skopje, FYR Macedonia

Background and Aims:

In Republic of Macedonia vaccination against measles, mumps and rubella is compulsory. The aim of the study is to evaluate MMR vaccine coverage among children in Municipality of Bitola.

Methods:

In this paper, a retrospective analysis was performed over the data for MMR primary vaccination and re-vaccination coverage among children in Bitola for the period of 2008 to 2018.

Results:

The study was conducted in the Health Center in Bitola. During the analyzed period, out of 10.757 children who are subject to the vaccination, 10.473 or 97.36% were actually vaccinated. The MMR vaccination coverage has been continuously declining over the years, ranging from 99.8% to 90% in 2018. From the total number of 11,443 children, 98.72% or 11.296 have been re-vaccinated. The coverage percentage range from 100% to 92.2% of children.

Conclusions:

In Bitola, the MMR coverage among children was over 95%, with a decline to 90% in the last two years. The re-vaccination range also declined, but in 2018 it was 97%. This data is in line with the general vaccine trend throughout the country, especially in recent years. The fact that parents are more often in dilemma whether to vaccinate children or not is upsetting. Despite the legal obligation, parents may choose not to vaccinate their child. In recent years, due to increased anti-vaccine campaigns, and the open question about the possible association of this vaccine with autism, parents are increasingly refusing to vaccinate their children. For higher coverage with compulsory vaccination and prevention of epidemics, it is of crucial importance for the health workers and the government to take proactive approach regarding health education.

Systematic Review Registration:

Not applicable.

ESPID19-0567
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Epidemiologic burden of meningococcal disease in latin america: a systematic literature review

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[3]*Pfizer Inc., Medical and Scientific Affairs, Sao Paulo, Brazil*
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Background and Objective

To evaluate the epidemiologic profile of invasive meningococcal disease (IMD), meningococcal meningitis and Neisseria meningitidis carriers in Latin America.

Methods

A systematic literature review was conducted for studies published in 2008-2018. Incidence, case fatality rate (CFR), and relative distribution of cases per serogroup by country were assessed.

Learning Points Discussion

Thirty-nine studies were selected. In 2006, IMD incidence rate per 100,000 inhabitants was higher in Brazil (1.9), followed by Uruguay (1.3), Chile (0.8), Argentina (0.7), Colombia and Venezuela (0.3 each), and Mexico (0.06). Brazil also reported the highest CFR among Latin America countries (20%), followed by Uruguay (15%), Chile (11%), and Venezuela and Argentina (10% each). In 2012, CFR in Chile increased to approximately 27%, the highest reported in the previous 20 years. The most frequent serogroups among IMD cases were C in Brazil (2007-2010) and Mexico (2005-2016), W in Chile (2012-2018), and B in Argentina (2012-2015). However, the true burden of IMD in Latin America is probably underestimated due to underreporting of cases.

ESPID19-0511
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Management of strong local postvaccinal reaction in children in belarus

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Background

Postvaccinal abscesses in children are serious local side effects after immunization and are subject to mandatory registration in Belarus. A retrospective analysis of the frequency of complications, diagnosis, methods and results of treatment, microbiological study of strong local postvaccinal reactions to combined vaccines with whole-cell pertussis component (DTP) in children in Minsk from 2015 to 2018 was carried out.

Case Presentation Summary

The number of vaccines administered amounted to 231653 (208127-DTP and 22701 – DTP+Hepatitis B+Hib). We registered 167 cases of abscesses of the thigh after the introduction of DTP. The age of patients ranged from 3 months to 3 years. 165 abscesses developed after the introduction of DTP vaccine and 2 after DTP+Hepatitis B+Hib (792.7 and 88.1 cases per 1,000,000 administered doses). The abscesses were manifested after immunization (minimum on the 1stday, maximum 3 months later, Me - 12 day). We performed an ultrasound examination of all the patients and found out a cavity with pus, which was an indication for surgery. We performed lancing and drainage of the abscess to 157 children. The volume of pus ranged from 0.2 to 7 ml (Me - 3 ml). All the patients were performed microbiological examination. Microbes were found out in 24 (14.5%) cases. We detected 9 types of microorganisms. Colony-forming unit in all the cases was less than 10^3. Local treatment consisted of dressings with hydrophilic ointment, 0.25% dimexide. No antibiotic therapy was performed. Hospitalization lasted 2.5±0.6 days. All the patients recovered.

Learning Points/Discussion

Detection of "sterile" abscesses often occurred later than the 7th day after immunization (85.5%). Differences in the frequency of abscesses depending on the type of vaccine were revealed. All cases of abscesses ended in recovery.

ESPID19-0470
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

General needs assessment of vaccination knowledge and communication skills of pediatric residents in ontario

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Background and Objective

The purpose of this paper is to describe the general needs assessment that I conducted to identify a potential learning gap related to paediatrics residents' knowledge of childhood vaccination in Ontario. The following parts of the paper will be explained: the potential learning gap, the questions that direct the needs assessment, identifying the methods used to gather information and conduct literature review, summarizing and discussing the findings of the review, and concluding with recommendations for future steps in developing the curriculum.

Methods

It is important to use a scholarly approach in obtaining information for the needs assessment, as it is more trustable by learners and other educators if the data is retrieved from up-to-date literature published in peer reviewed journals. Therefore, a literature review of already available information through three medical databases and one educational database was conducted. Then, the grey literature was reviewed. In order to cover this needs assessment, both the medical and educational aspects of it are considered

Table 1 *Outline of the Review of Literature*

Data	**Source**
Evidence-based systematic reviews	BEME & Cochrane
Reviews and original studies	Medline (Ovid), PsycINFO, ERIC
Clinical practice guidelines	Government health agencies
Expected core competencies	Recommendations or statements by accreditation agencies or professional organizations
Educational clearinghouses	MedEdPORTAL
Grey literature	Pertinent associations and societies' websites, and government publications
Incidence & prevalence of a problem	Public health statistics, clinical registry data, administrative claims data

Learning Points Discussion

The discussion will be organized in to two parts.

1. Different facets of the learning gap. The literature search clarified four different facets of our learning gap.

2. Addressing the focused research questions. The five focused research questions are addressed.

ESPID19-0317
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Bacillus calmette-guérin cervical lymphadenitis in a 6-year-old boy who had been on infliximab for very early-onset inflammatory bowel disease

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[4]University of Tennessee Health Science Center-, Department of Microbiology- Immunology- and Biochemistry, Memphis, USA

Background

Tumor Necrosis Factor-α (TNF-α) inhibitors play an important role in the treatment of inflammatory bowel diseases (IBD) in pediatric patients. However, it is also known that TNFα inhibitors increase the risk of mycobacterial infection by inhibiting the activity of macrophages. Bacillus Calmette-Guérin (BCG) vaccine, developed from *Mycobacterium bovis*, is generally safe, however serious infections due to the vaccine strain have been reported in immunocompromised patients. Nevertheless, there are only few reports regarding the relationship between TNFα inhibitors and serious BCG infection.

Case Presentation Summary

The case was a 19-month-old male diagnosed with very early-onset IBD. His humoral and cellular immunity screening exams were normal and no known genetic mutations accountable for primary immunodeficiency were identified by whole exome sequencing. He had received BCG vaccination at 4-months of age without any adverse events. In addition to daily azathioprine, bimonthly infliximab therapy was started at 23-months of age after confirming negative interferon gamma releasing assay and purified protein derivative skin test. He presented with fever and left cervical lymphadenitis at 6-years of age, and culture of the aspirate obtained from the lymph node abscess was identified as *Mycobacterium bovis* BCG by PCR. Infliximab was discontinued and at least 9-month course of anti-tuberculous therapy was started. His condition gradually improved with regression of the neck mass.

Learning Points/Discussion

BCG is contraindicated in patients who have recently received infliximab, due to case reports of disseminated BCG infection in infants exposed to infliximab in utero. Similarly, our case suggests that TNF-α inhibitors may provoke serious *Mycobacterium bovis* BCG infection even several years after BCG vaccination in children. Although underlying primary immunodeficiency was not diagnosed in our case, potential immune dysregulation associated with very early-onset IBD should raise additional caution.

ESPID19-0248
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Shedding of oral pentavalent bovine-human reassortant rotavirus vaccine indicates high uptake of vaccine and prominence of g-type g1

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Background

Shedding of live oral pentavalent bovine-human reassortant rotavirus (RV) vaccine RotaTeq®, as studied by RT-PCR, has been shown to be more common than initially reported, and includes formation of virulent vaccine-derived double-reassortant G1P[8] RVs. We studied the extent and duration of RotaTeq® vaccine virus shedding in 301 infants who received RotaTeq® vaccine according to Finnish schedule at 2, 3 and 5 months of age.

Methods

Stool samples were obtained from 292 infants 5-10 days after the first dose and from 247 infants 0-7 days before the third dose of the vaccine. Additional samples 6 and 12 weeks later were collected if the second stool sample was positive for RV. All stools were studied with RT-PCR for RV VP7, VP4 and VP6.

Results

We found that 93 % (271 of 292) of infants shed vaccine related viruses after the 1st dose and 20% (49 of 247) prior to the third vaccine dose. Prolonged shedding of G1 vaccine strain was detected in 10 children 6 weeks after 3rd vaccine dose, of these, 2 remained positive at the age of 8 months. Genotype G1 was the most commonly detected genotype, either alone or in association with P[8] or other VP7 or VP4 genotypes (in 81% of samples (220 of first 271 samples)), and was the only genotype found in prolonged shedding. G4 was also commonly detected (in 41% of samples after the 1st dose) whereas G2 and G3 were not.

Conclusions

Shedding of RotaTeq® vaccine-derived viruses is common and a sign for successful vaccination. Intense shedding of G1 suggests that pentavalent RV vaccine functions largely like a monovalent G1 vaccine. Shedding of G1 containing vaccine viruses may be prolonged up to 8 months of age.

Clinical Trial Registration (Please input N/A if not registered)

Eudra-CT:2014-004252-60

ESPID19-0227
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Identifying hpv vaccination coverage and assessing factors associated with parental decision-making starting the vaccination series in girls aged 11-14 in a provincial town

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Background and Aims:

Human papillomavirus(HPV) is considered the most common sexually transmitted agent worldwide. HPV vaccination programs for girls, and, more recently boys, is recommended by a number of health and scientific organizations. Most effective time of administration, is around the age of 11-12 but it may be given at 9y through 26y.The study objective was to determine the rate of vaccination starting age and assess the parental awareness of HPV.

Methods:

A simple anonymous questionnaire was distributed to parents of healthy girls aged 11-12 at the time of visit for the 1st dose. We have recorded age, parental knowledge and concerns about HPV and vaccination, sources of information and reasons for delayed vaccination(>12y).192 completed questionnaires were returned.

Results:

Table:age of 1st dose

	11-12y	12-13y	13-14y
1st dose	**81(42,2%)**	**57(29,7%)**	**54(28,1%)**

Awareness of HPV infection and vaccination(timetable-side effects) was reported by 64,1% parents whilst the most common sources of HPV knowledge(multiple choice question) were health services(88,5%), internet/social media(18,7%), friends/family(16,7%), other(1,6%). Reasons for delayed decision-making(multiple choice question) include unawareness of timetable(63,1%), inappropriate age(11,7%), fears of side effects of vaccines in general(19,8%) and of HPV vaccine(40,5%), demand for vaccine benefit(5,5%), unimportant vaccine(5,5%) and non-compliance(25,2%). 48,4% of parents believed that boys should also be vaccinated.

Conclusions:

At odds with parental awareness of HPV infection and vaccination, the initiation of vaccination at the recommended age and their positive opinion about male vaccination remains comparatively low.
As modifiable factors influence parental willingness regarding the HPV vaccine, public health actions(national education campaigns, together with advice and support from professionals) should be used in order to increase HPV awareness and knowledge in terms of changing attitudes toward vaccination's safety and parental hesitancy, improve vaccination uptake and narrow the gap of vaccination rates between males and females.

Systematic Review Registration:

N/A

ESPID19-0092
E-Poster Viewing - May 7-10 - E-Poster Hours

Vaccine safety (post licensure)

Ausvaxsafety active vaccine safety surveillance: monitoring events following pertussis booster vaccines in children

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Background and Aims:

In March 2016 an 18 month diphtheria-tetanus-acellular pertussis (DTPa) booster dose was re-introduced to the Australian National Immunisation Program (NIP). There was concern from immunisation providers about the likely occurrence of limb swelling reactions at both the 18 month and 4 year schedule points. We used the AusVaxSafety active vaccine safety surveillance system to monitor adverse events following immunisation (AEFI) with DTPa-containing booster vaccines in children.

Methods:

De-identified, parent-reported AEFI were collected through text message solicitation by the data monitoring platform SmartVax. Data were analysed for the period March 2016 – December 2018. Children were included in the analysis if they had received the NIP scheduled vaccines at either schedule point.

Results:

Among 37,421 children, limb swelling was reported at a rate of 5% at the 18 month schedule point (4th dose), lower than at the 4 year schedule point, either as a 4th or 5th DTPa dose (8% and 9%, respectively). Following 196 children who received doses at both 18 months and 4 years, 15 (8%) reported swelling after the 18 month dose and of these, 6 (32%) also reported swelling after the 4 year dose. In contrast, among the 181 (92%) without swelling after the 18 month dose, only 13 (7%) reported swelling after the 4 year dose.

Conclusions:

AusVaxSafety surveillance of DTPa-containing booster vaccines did not identify any unexpected AEFI. Limb swelling was more common in those receiving a 5th dose at the 4 year schedule point, but reactions requiring medical attention occurred rarely among all participants. This data can reassure both parent and immunisation providers about the frequency and severity of limb swelling reactions after DTPa-containing booster vaccines.

Systematic Review Registration:

N/A

ESPID19-1073
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Central line-associated bloodstream infection by new delhi metallo-beta-lactamase producing klebsiella pneumoniae in a preterm infant: a emerging carbapenem resistant infection.

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Background

Carbapenem-resistant *Klebsiella pneumoniae* (KP) infections, are a worldwide emerging threat. New Delhi metallo-beta-lactamase (NDM-1), is a newly described carbapenemase in Enterobacteriaceae producing community and health-care associated infections. NDM-1 producing KP infections in children reports are scarce. A case of an infant who developed a central line-associated bloodstream infection (CLABSI) by NMD-1 producing KP is presented.

Case Presentation Summary

A 4 month-old preterm infant (born at 27 weeks of gestation) admitted in the Neonatal Intensive Care Unit (NICU) in an Spanish hospital since birth, was on total parenteral nutrition (TPN) using a Hickman central line (HCL) due to a short bowel syndrome. He was colonized by NDM-1 producing KP after horizontal transmission from another colonized baby who was transferred to the NICU from Morocco. The patient developed sepsis 11 days after HCL insertion. CLABSI by NDM-1 producing KP was diagnosed by differential time to positivity from HCL and paired peripheral blood cultures. Targeted therapy with amikacin (MIC=8) and colistin (MIC=2), the only 2 susceptible antimicrobials in the antibiogram, was started. Although attempted, catheter removal was not possible (an alternative central line for TPN was not obtained), whilst a peripheral line was inserted and antibiotic central line lock therapy (ALLT) with amikacin was given. He was treated for 14 days after first negative blood culture (Total: 17 days) with blood cultures repeatedly negative during treatment and 72 hours after antibiotic discontinuation, retaining HCL for TPN. 8

Learning Points/Discussion

NDM-1 producing KP infections are challenging due to the lack of antimicrobial options. For CLABSI due to these pathogens adequate source control is necessary, however, when not feasible, combination therapy with active antimicrobials and ALLT could be an alternative as in the presented case.

ESPID19-0983
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Complications after surgery
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Background

Prosthetic joint infections (PJIs) are a group of high complexity infections that can have deep impact in our patients. Their management should combine three goals: eradication of the infection, reduce the pain and finally restore the joint´s function. It means orthopedic surgeons, infectious disease specialists, physiotherapists ...should choose together the best therapeutic decision.

Case Presentation Summary

We present a 15 years old boy attended in emergency room for fever (24 hours) and acute inflammation of surgical wound. He was operated 4 weeks before of tibia and fibula osteotomy and fixation with intramedullary legthening nail. Past medical history: right tibia shortening (5 cm). Congenital agenesis of 4th and 5th right toes. Rigth tarsal coalition. Shortening of Achilles tendon system. Firstly intervened at 8 years old with external fixator.

Physical examination at admission: Afebrile, normal bood-presure, 80 bpm. Keloid in proximal tibia: slightly edematous, no wound drainage, other two keloids without infectious signs. Lab test: 10.410 leukocytes/mm3 (Neu72,5%), Hb:13,8 gr/dl, CReative-Protein 82,1mg/L, ESR 33mm/h. Treatment with Ceftazidime and Vancomycin was started. After 3 days he continued with fever, increasing wound edema and it started to drain.US described pretibial abscesses. Aggressive surgical debridement was performed without removing prosthesis. Cultures (pre and during surgery) showed an *S. Aureus* Oxacilin-suspceptible,so treatment was modified to Cloxaciline; and Rifampin was added after 5 days. Wound improved progressively and fever disappeared. After 2 weeks of intravenous treatment he was discharged with levofloxacin and rifampin oral for 12 weeks, with excellent evolution.

Learning Points/Discussion

PJIs are one of the most serious complications of prosthetic implantation. Management includes prolonged courses of intravenous and oral antimicrobial therapies but also surgical interventions (debridement +/- retention of the prosthesis), so they require to be attended at multidisciplinary units.

ESPID19-0369
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Length of stay, cost, and mortality of healthcare-acquired bloodstream infections in children and neonates: a systematic review

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[3]National and Kapodistrian University of Athens- School of Medicine-
University General Hospital ATTIKON, Third Department of Pediatrics, Athens, Greece

Background

Healthcare-associated infections (HAIs) are associated with increased mortality, length of stay (LOS), and healthcare cost. Healthcare-acquired bloodstream infections (HA-BSIs) are the most common HAIs in children and neonates. The aim of this systematic review was to present the attributable mortality, LOS, and healthcare cost of pediatric and neonatal HA-BSIs.

Methods

A systematic search up to September 2018 was conducted in PubMed, Cochrane, and CINAHL databases. Moreover, cited references from selected articles were used to find additional studies that were not retrieved in the initial search. Studies eligible for inclusion were case-control or cohort studies published in English and available as full text that provided data for at least one of the following: attributable or excess mortality, healthcare cost, or LOS. Study quality was evaluated using the Critical Appraisal Skills Programme Tool (CASP) for cohort and case-control studies.

Results

Of 4660 papers identified in the search, 21 were included. Attributable mortality was presented in 7, attributable healthcare cost in 9, and attributable LOS in 16 studies. It was found that the attributable mortality rate ranged from 1.43% to 24%, and the attributable healthcare cost ranged from $1315 to $134279 USD per patient with HA-BSI. Finally, the attributable LOS ranged between 1.57 to 27.8 days. This wide range is due to the different demographic characteristics among the study populations. A meta-analysis is ongoing.

Conclusions

HA-BSIs in children and neonates are associated with higher mortality, LOS, and healthcare cost than is found among children and neonates without HA-BSI. This finding justifies and may enhance efforts to implement prevention strategies.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESPID19-0333
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Hospital acquired bacterial conjunctivitis in neonates needing intensive care

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Background and Aims:

Background: Bacterial conjunctivitis is one of the most frequent hospital-acquired infections in neonates, which if untreated, can lead to serious consequences such as blindness. However, it is less studied than potentially life-threatening infections.

Objectives: The aim of this study was to determine the incidence of hospital acquired bacterial conjunctivitis in the neonatal and paediatric intensive care unit in Malta.

Methods:

Method: Data were collected retrospectively from patient records and laboratory databases from 2012 to 2017. The Centers for Disease Control/National Healthcare Safety Network (CDC/NHSN) diagnostic criteria were used to define hospital-acquired conjunctivitis in neonates who acquired the infection >48 hours after admission to intensive care.

Results:

Results: Hospital acquired bacterial conjunctivitis was diagnosed in 33% (*n*= 120) of 368 neonates and children who had a conjunctival swab taken during the 5 year study period. Most of the episodes were in neonates (68%), with a mean age of 26 days. The mean annual incidence of conjunctivitis was 6.72/100 admissions to NPICU. The predominant pathogens were *Staphylococcus aureus* (37%), *Serratia marcescens* (12%), *Enterococcocus faecalis* (7.5%), and *Escherichia coli* (6%). Only two pathogens were multiresistant from the 125 isolates, one being ESBL positive and the other being carbpenemase positive. Analysis of the antibiogram showed that 93% of isolates were sensitive to gentamicin making this antibiotic the first line choice for empiric topical treatment for hospital acquired conjunctivitis.

Conclusions:

Conclusion: Hospital acquired bacterial conjunctivitis is an infection that may be prevented by implementing appropriate infection control measures.

Systematic Review Registration:

Nil

ESPID19-1169
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Clinical features, treatment and outcome of complicated pneumonia with pleural effusion in children in gipuzkoa (basque country, spain)

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[2]Donostia University Hospital, Department of Microbiology, San Sebastian, Spain

Background and Aims:

Parapneumonic effusion (PPE) is a common complication associated with community-acquired pneumonia (CAP). *Streptococcus Pneumoniae* is the most common pathogen isolated in pleural effusions and empyema. Its incidence seems to have grown recently attributed to the increase of serotypes of Pneumococcus 1, 3 and 19A, not included in the heptavalent vaccine, and to the appearance of different etiological agents such as *Staphylococcus Aureus*.

Methods:

The aim of the study was to evaluate the incidence, etiology, clinical features, treatment strategies and outcomes of CAP with PPE in children admited in a tertiary hospital in Gipuzkoa. We performed a cross-sectional and retrospective analysis of clinical and laboratory data of children<14 years with PPE due to CAP admitted to our Pediatric Intensive Care Unit (PICU) between January 2013-December 2018.

Results:

50 patients with PPE were admitted. Median-age 3 years (range0.8-13 years). In 100% a chest drainage was placed. 36 received intrapleural urokinase. Video-assisted-thoracoscopy was performed in 7(14%). There were 6-8cases/year (except in 2013 and 2018 with 12 and 10 cases,respectively). S.*pneumoniae* was isolated in 25 patients, followed by *S.pyogenes* (n=1) and *Mycoplasma pneumoniae* (n=1). No agent was isolated in 23(46%). We identified 9 cases by culture, but molecular PCR identified 40% (17/42) of culture-negative samples. Pleural fluid and blood cultures rentability was higher in patients without previous antibiotic (33%vs2,63%,p=0,0384) and(25%vs2,63%,p=0,0093).

Conclusions:

Streptococcus pneumoniae was the most common pathogen. The majority of cases had a favorable clinical course after chest drainage placement. Only 7 patients needed intensified treatment by performing videothoracoscopy due to unfavorable clinical course. The etiological diagnosis has improved considerably with the use of molecular diagnostic methods, given the low yield of traditional cultures, especially if the patient has received previous antimicrobial drug treatment.

Systematic Review Registration:

Ok

ESPID19-1139
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Clinical burden of coronavirus infections in children in gipuzkoa (basque country, spain)

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Background and Aims:

Human coronaviruses (HCoVs) are commonly detected in nasopharyngeal aspirates (NPAs) from children with respiratory tract infections (RTIs) but the real burden remains poorly defined. Six types of HCoVs have been discovered, the most recent one termed the Middle East respiratory syndrome coronavirus (MERS-CoV) . The aim of this study was to monitor the circulation of HCoV types in ours children.

Methods:

We analizad restropectively, nasopharyngeal aspirates collected from July 2015 through July 2018 from children<14 years in Gipuzkoa. We investigated the role that they played in those children who went to the emergency room with fever or acute respiratory symptoms. NPAs were analyzed with PCR tests for HCoV subtypes OC43,229E,NL63 and 13 other respiratory pathogens. We can not detect HCoV-HKU1, CoV MERS and SARS.

Results:

HCoVs was detected in 248/3891 children studied. 91(36.7%) were monoinfections (9 CoV-229E,26 CoV-NL63,56 CoV-OC43) which mainly occurred in winter (december-february 68/91). Cov-229E strains as a monoinfection were not found to circulate in 2017-2018. The mean-age of monoinfections was similar to coinfections(20.9±30.5/16.5±16.8months;p:NS). In addition to causing RTIs, we found that HCoV can present as croup, asthma-exacerbation, febrile-seizures and high-fever. 119/157(75.8%) were hospitalized. The hospitalization of monoinfections was similar to coinfections(46.6%vs48.7%) but they needed less respiratory-support (17.6%vs35.0%;p=0.004), aerosoltherapy (17.6%vs48.4%;p<0.001), corticotherapy (17.6%vs28.6%;p=NS), and PICU admissions (7.7% s10.8%;p=NS). CoV-229E hospitalized more frequently than CoV-OC43(88.9%/37.5%;p=0.008).

Conclusions:

HCoV cause a high proportion of illnesses among young infants in Gipuzkoa. HCoVs are associated with a substancial burden of RTIs in need of hospitalization, appearing with characteristic outbreak patterns, primarily in the winter. In our study, CoV-229E caused more hospitalizations than Cov-OC43. Coinfections of hCoVs and other respiratory viruses were associated with severe respiratory syndromes more frequently than hCoV single infections.

Systematic Review Registration:

I dont know

ESPID19-1123
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

An uncommon case of ascitic fluid infection in a patient with a vp shunt and csf overproduction.

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Background

We present a case of a 22-months-old child with a VP shunt and ascites due to CSF overproduction, who developed an acute ascitic fluid bacterial infection.

Case Presentation Summary

A 22-months-old child with a VP shunt for congenital hydrocephalus, was admitted to our Pediatric Unit with 1-month of progressive abdominal distention.

CT scans of the abdomen revealed a massive, non-loculated, fluid collection surrounding the shunt catheter, which was correctly placed within the peritoneal cavity. Common causes of ascites were ruled out. An abdominal drainage tube was placed with a drainage output of about 800 ml per day, suggesting a CSF overproduction. The cranial CT showed neither brain masses nor choroid plexus cysts.

Because of rapid reaccumulation of fluid, intermittent paracentesis was started. SAAG changed over time with values ranging from 1.7 g/dl to -2.4 g/dl. Cytologic evaluation of the peritoneal fluid revealed neutrophils, macrophages, lymphocytes and reactive mesothelial cells suggesting a reactive inflammatory process. Initial cultures were negative but after a month, the ascitic fluid culture turned out to be positive. Klebsiella Oxytoca and Pseudomonas Aeruginosa were isolated.

The patient started antibiotherapy based on the antibiogram results. Multiple shunt taps were performed with no findings of shunt infection or VP malfunction. After 2 weeks of antibiotic treatment, cultures returned negative. Ascites definitely resolved when the VP shunt was converted to a VA shunt.

Learning Points/Discussion

In our opinion our patient had a sterile CSF ascites due to CSF overproduction, complicated by a spontaneous bacterial peritonitis (SBP). As reported in literature, SPB is an uncommon complication in patients with VP shunt and ascites (Tchirkov 1979, Gaskill 1997). The pathophysiology of SBP in patients with VP shunt is not fully understood.

ESPID19-1062
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Hospital-acquired infection surveillance among 11 european countries. A ranin-kids survey

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Background and Aims:

Hospital-acquired infections (HAIs) are a major cause of morbidity and mortality in pediatric patients in Europe, but surveillance in this population is scarce and not systematic. An electronic survey was created and disseminated in order to gather data on the surveillance of pediatric HAIs in Europe, with the ultimate goal of creating a multinational collaborative consortium to design and implement a unified European surveillance mechanism for pediatric HAIs.

Methods:

RANIN-KIDS (Reducing Antimicrobial use and Nosocomial INfections in KIDS) is a collaborative European effort that aims to create a unified surveillance mechanism for pediatric HAIs and antibiotic use in Europe and to implement interventions to prevent HAIs and to promote antimicrobial stewardship

(ASP). In December 2018, an electronic survey that included questions on HAI surveillance and prevention practices was created and disseminated among members of the RANIN network.

Results:

18 teaching hospitals from 11 countries submitted data. All but two reported having formal infectious diseases (ID) teams. Only 1 reported having no infection control (IC) team. Surveillance programs for HAIs were reported as follows: CLABSI 50%, CAUTI 33%, and VAP 39%. Only 22% reported having surveillance programs for hospital-acquired viral infections (Table 1). Hand hygiene practices were monitored by 67% of hospitals. In almost 40% of hospitals, information related to multidrug-resistant organisms carriage is unavailable in at least half of transferring patients.

Table 1: Variability of surveillance mechanisms and methods among 18 hospitals in 11 countries (Estonia, Germany, Greece, Ireland, Italy, Portugal, Romania, Spain, Sweden, Switzerland, United Kingdom).

Existence of Surveillance for	Yes (active/PPS*)	%	No	%	NA/DK**	%
Hand hygiene	12	67%	5	28%	1	6%
Central line-associated infections	9	50%	7	39%	2	11%
Surgical site infections	9	50%	7	39%	2	11%
Catheter-associated urinary tract infections	6	33%	9	50%	3	17%
Ventilator-associated events/pneumonia	7	39%	9	50%	2	11%
Hospital-onset bacteremias	11	61%	5	28%	2	11%
Hospital-acquired viral infections	4	22%	11	61%	3	17%
Perioperative antibiotic prophylaxis	10	56%	6	33%	2	11%
Antimicrobial consumption	14	78%	2	11%	2	11%
Colonization Status						
Among patients with an MDRO admitted to your facility from another healthcare facility, please estimate how often your facility receives information from the transferring facility about the patient's MDRO status?	**N**					
none of the times	1	6%				
less than half the times	4	22%				
about half the times	2	11%				
more than half the times	7	39%				
all the time	3	17%				
Other Hospital Characteristics	**Yes (N)**		**No (N)**		**NA/DK** (N)**	
Is seasonal influenza vaccination mandatory at your institution?	2	11%	15	83%	1	6%
Do you have electronic health records at your hospital?	12	67%	5	28%	1	6%

* **PPS:** Point-prevalence survey
** **NA/DK:** No answer/Don't know

Conclusions:

Preliminary results on HAI surveillance practices showed that while the majority of hospitals surveyed have ID teams and IC nurses, surveillance of HAIs is significantly lacking. The results of this survey will be used to inform the creation of a unified surveillance mechanism for pediatric HAIs in Europe and to design preventative interventions.

Systematic Review Registration:

N/A

ESPID19-0624
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

A service evaluation of infection rates in neonates with peripherally inserted central catheters: more than 14 days dwell time compared to less than 14 days

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Background and Aims:

Peripherally inserted central catheter (PICC) lines are used for premature and unwell babies to allow administration of fluids, nutrition and medications, but are associated with risks including infection and necrotising enterocolitis (NEC). Research has suggested that the length of time a line remains in situ is not associated with an increased risk of infection or NEC. Our aim was to undertake a service evaluation to compare positive culture results in babies with PICC lines that remained in situ more than 14 days compared to those with lines in situ less than 14 days.

Methods:

We conducted a retrospective audit of all PICC lines inserted over a three-month period in a large tertiary neonatal unit. We evaluated the number of septic screens performed whilst the line was in situ and peripheral and line tip culture results and compared infection rates between the two groups.

Results:

Sixty-one PICC lines were inserted over a three-month period. The median duration of line insertion was 11 days. Only 14 (23%) lines were left in situ for over 14 days. A total of 57 septic screens were performed. There were three positive peripheral blood cultures, all in the less than 14 days group. There were two positive line tip cultures, one in each group.

Conclusions:

Confirmed line infections and bacteraemia were uncommon, also in babies with lines in situ for more than 14 days. Our results suggest that it is safe practice to leave PICC lines in situ for longer while ensuring sterile insertion technique and regularly reviewing the clinical need. Clinical judgment should be used to decide on removal of a long line, rather than a prescribed maximum duration of insertion.

Systematic Review Registration:

NA

ESPID19-0611
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Severe hand infection caused by an exceptional pathogen: bacillus pumilus

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Background

Bacillus *pumilus*is (BP) is a Gram-positive aerobic bacterium producing spores that are widespread in the soil and environment. Although infections associated with Bacillus *pumilus* seem exceptional, a few cases of anthrax-like, necrotic skin ulcers of the hand have been associated with this pathogen. We herein provide the clinical, imaging, and histopathological findings of a hand infection due to Bacillus *pumilus* in a healthy ten-year-old boy.

Case Presentation Summary

A ten-year-old previously healthy boy was admitted in our hospital with a prominent and rapidly progressive cellulitis of the right hand and fingers appearing less than 24 hours after sustaining a minor injury following a simple fall on the ground. Suspecting a pyogenic bacterial infection of the hand with rapid progression, the child underwent a prompt surgical exploration. At the bump incision, a transparent fluid came out from the subcutaneous fat which appeared abnormally soft and yellowish-coloured. Fluid aspiration and biopsy were obtained for microbiological and histopathological examination. The tendon sheath and operative site were copiously irrigated with physiological saline solution. Culture of the drainage fluid and fatty tissue yielded a massive growth of Bacillus *pumilus,* further confirmed by mass spectrometry (MALDI-TOF) and 16s rRNA sequencing. Histopathological analysis found septal eosinophilic panniculitis. The symptoms quickly resolved and the child was discharged from the hospital after receiving intravenous amoxicillin-clavulanate antibiotics for 48 hours. Oral treatment was administrated for eight more days. At the six weeks follow-up, the right hand had completely healed and no recurrence was further observed.

Learning Points/Discussion

This case emphasizes that *B. pumilus* should be considered as a cause of potentially severe hand infection in exposed skin areas after minor injury in healthy children and should not be discarded as a culture contaminant.

ESPID19-0528
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Helathcare-associated infections due to acinetobacter spp. In a pediatric intensive care unit: a single center experience

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Background and Aims:

To investigate the factors affecting mortality due to *Acinetobacter* infections in a pediatric intensive care unit (PICU).

Methods:

The patients who were hospitalized in PICU of Ankara University between January 2013 and September 2018 and had *Acinetobacter* infections were evaluated retrospectively.

Results:

82 patients who developed *Acinetobacter* infections were admitted to study. 53 (64.6%) of the patients were male. The mean age was 68.9 ± 74.6 months. The majority of patients had underlying disease. Most patients had a history of invasive procedures: mechanical ventilation (95.1%), central venous catheter (86.6%) and urinary catheter (62.2%). Ventilator-associated pneumonia was the most common infection (57.3%) followed by catheter-associated blood stream infection (14.6%), skin and soft tissue infection (6.1%). *Acinetobacter baumannii* (96.3%) was the most common strain. The majority of *Acinetobacter* species were resistant to carbapenems (93.9%). Colistin and meropenem were the most common antibiotics which were used in the treatment of patients and 15.8% of the isolates were resistant to colistin. The mortality rate on the 30th day of *Acinetobacter* infection was 35.3%. The mean age of the patients and the rate of invasive interventions were higher in the group of who died. The most common underlying diseases in the group of patients who died were neurometabolic diseases, solid tumors and immune deficiency, respectively. The most frequent infections in patients who died were ventilator-associated pneumonia and catheter-related blood stream infection. Most of the deceased patients were given antibiotics before the development of *Acinetobacter infection* and 34.4% of them were carbapenems. All of the patients who died were infected with a carbapenem-resistant strain.

Conclusions:

Acinetobacter infections cause high mortality in PICU. This risk is increased in the presence of underlying disease and invasive intervention and carbapenem resistance

Systematic Review Registration:

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ESPID19-0512
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

According to envin registry: microorganisms and resistances involved in healthcare-associated infections of paediatric intensive care units.

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Background and Aims:

To describe microorganisms responsible for healthcare-associated infections (HAI) and their resistance to antibiotics, in Paediatric Intensive Care Units (PICU) from the Spanish registry Paediatric-ENVIN-HELICS.

Methods:

Multicentre, prospective and observational study. There were 1983 patients admitted in 24 PICU. The infections were registered from April to June of 2017. The HAI included were: Ventilator-associated pneumonia accounted (17, 28.81%), catheter-associated urinary tract infections (14, 23.73%) and central line-associated blood stream infections (10, 16.95%). The ENVIN diagnostic criteria adapted to paediatrics were used, which is based on recommendations from the Centre of Prevention and Disease Control.

Results:

HAI diagnosed in 50 patients (2.6%). Microorganisms: 23 (69.7%) Gram negative (GN), 6 (18.2%) Gram positive (GP), 4 (12.1%) fungi.

GN: *Pseudomonas aeruginosa* (7; 21.2%), *Klebsiella pneumoniae* (5; 15.2%), *Enterobacter cloacae* (3; 9.1%), *Escherichia coli* (3; 9.1%). GP: *Staphylococcus epidermidis* (3, 9.1%). Fungal infections: Candida species.

Resistant bacteria: 7. *Klebsiella pneumoniae:* 2 (40%) ESBL, 1 (20%) also to amikacin, 4th generation cephalosporin and quinolones. *Enterobacter cloacae* resistant to 4th generation cephalosporin, piperacillin-tazobactam and quinolones (1, 33.3%). *E. coli* ESBL (1, 33.3%). Quinolone-resistant *Proteus mirabilis* (1). *Staphylococcus aureus* (2): 1 methicillin-resistant.

Conclusions:

Device-associated HAI during 2017 were low. The most frequently implicated microorganisms were GN bacteria, most of which were sensitive to the usual antibiotics. Surveillance is useful in order to detect rate resistant variations and outbreaks.

Systematic Review Registration:

N/A

ESPID19-0362
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Carbapenem-resistant enterobacterales bloodstream infection in spanish children. Mortality and survival analysis

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Background and Aims:

Carbapenem-resistant Enterobacterales (CRE) are a growing problem in pediatric population worldwide with high mortality rates (18.5-52%) in bloodstream infections (BSI). Carbapenem-containing combination therapy is associated with improved survival in severe infections in adults but children management has been extrapolated. The aim of this study is to evaluate predictors of 30-day mortality in CRE BSI in a pediatric cohort.

Methods:

Retrospective observational unicenter study (December 2005 - August 2018) was conducted. CRE BSI episodes in children 0 to 14 years were included. Demographic characteristics, underlying diseases, source of bacteremia, antimicrobial therapy and outcomes were collected from medical records. Microbiological identification (MALDI Biotyper) and antimicrobial susceptibility testing (Vitek2® and MicroScan panel NBC44) according to currently EUCAST breakpoints was performed. PCR OXVIKPND® were used to confirm genes OXA-48, VIM, KPC and NDM. Survival analysis to establish predictors of 30 day-mortality by Kaplan-Meier and log-rank test was performed.

Results:

Thirty-eight cases were included (mean age 2.2 years, DS 3.2; 55.3% female): nosocomial infections (76.3%) or related to healthcare (23.7%). VIM-producing carbapenemase was predominant mechanism (92%). Only 21.1% presented septic shock. Previous CRE colonization or infection rate was 52.6%. Gut (26%) and catheter (21%) were the predominant sources of infection. Crude mortality within 30 days was 18.4% (7/38). Directly related mortality: 10.5%. Conditions associated with 30-day mortality are shown in Table 1. Of note, including at least one active antibiotic in empiric therapy showed to decrease mortality in a 92.4%.

Variable	Survived N=31 (%)	Died N=7 (%)	Hazard ratio (95% CI)	P
Median Age (months)	17.64	4.32		
Male (%)	54.84	57.14		
Klebsiella isolated	19 (61.29)	6 (85.71)		NS
Source of infection Intestinal tract or hepatobiliar	13 (41.94)	3 (42.86)		NS
Catheter-related	7 (22.58)	1 (14.29)		NS
Urinary tract	3 (9.68)	0 (0)		NS
Pulmonary	2 (6.45)	0 (0)		NS
Peritoneal catheter	1 (3.23)	0 (0)		NS
Unknown	5 (16.13)	3 (42.86)		NS
Neonatal unit admission	3 (9.68)	4 (57.14)	0.197 (0.111-0.956)	**0.017**
Intensive care unit admission	10 (32.26)	6 (85.71)	0.13 (0-0.984)	**0.024**
Presentation as sepsis	26 (83.87)	6 (85.71)		NS
Presentation as septic shock	5 (16.13)	3 (42.86)		NS
Meropenem MIC >8	8 (25.81)	2 (28.57)		NS
No active antibiotic in empiric therapy	6 (19.35)	4 (57.14)	0.076 (0.012-0.494)	**0.001**
Meropenem in empiric therapy	19 (61.29)	4 (57.14)		NS
Aminoglycoside in empiric therapy	15 (48.39)	4 (57.14)		NS
Monotherapy in target treatment	16 (51.61)	2/6* (33.33)		NS
Meropenem in target therapy	14/30 (46.67)**	3/6* (50)		NS

TABLE 1. Univariate analysis of conditions associated with 30-day mortality. Non-significant (NS).
*One patient excluded due to death before knowing antibiogram.
**One case excluded because it was not possible to verify certainty that meropenem doses was adequate.

Conclusions:

The most important factor related to 30-day mortality in our CRE BSI cohort was success in empiric treatment with at least one active antibiotic. Combination antibiotic targeted treatment and a low meropenem MIC were not related to improved survival in our cohort.

Systematic Review Registration:

ESPID19-0237
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Clinical evaluation of biliary sepsis in biliary atresia patients undergoing kasai operation

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Background and Aims:

Biliary sepsis is a common complication in children with biliary atresia after the Kasai operation. In such children, it is difficult to differentiate biliary sepsis from other febrile diseases. It is important for early diagnosis and treatment to identify risk factors for biliary sepsis

Methods:

In order to characterize the laboratory data of biliary sepsis with cholangitis in patients who underwent Kasai operation, 170 patients with biliary atresia from 2006 to 2015 who underwent a Kasai operation in Severance hospital were studied. The follow-up period ranged 1 to 146 months. The laboratory data and results of bacterial cultures were analyzed retrospectively.

Results:

A total of 561 febrile episodes, including 517 of cholangitis and 44 non-cholangitis infections, were found in 133 patients. In the diagnostic evaluation factors such as hemoglobin, AST, ALT, bilirubin and GGT that showed statistically differences between cholangitis and non-cholangitis infection. There were statistical differences in hemoglobin, delta neutrophil and CRP between biliary sepsis and culture-negative cholangitis. The most causative pathogens of biliary sepsis are E. faecium (n=14, 27%) and E. coli (n=7, 14%), followed by K. pneumoniae (n=5, 10%) and E. cloacae (n=5, 10%). Antibiotic susceptibility results of the gram negative bacteria and the Enterococcus sp. are shown in figure.

Conclusions:

The laboratory factors, such as lower hemoglobin level, higher delta neutrophil, and higher CRP level can be early clues to suspect biliary sepsis in febrile children underwent Kasai operation. The increased emergence of resistant strains requires caution in antibiotic selection for treatment of the biliary sepsis patients.

Systematic Review Registration:

N/A

ESPID19-0204
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Which bug is to blame? Klebsiella and coagulase negative staphylococcal sepsis in a preterm neonate.

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Background

Klebsiella and coagulase negative staphylococcus (CONS) are both known causes of sepsis in preterm neonates. Specific risk factors include low birth weight, prematurity and birth in a resource poor setting. Outbreaks of klebsiella can also occur in Neobnatal units[1].

Case Presentation Summary

Infant F was born by emergency caesarean section at 23+6 weeks gestation weighing 0.56kg. Partial septic work up on day of life one was negative and antibiotics were discontinued after 36 hours. She subsequently developed pulmonary hemorrhage, pneumothorax requiring high frequency oscillatory ventilation, and ionotropes for hypotension.

Septic screen was performed on day of life (DOL) 16 for clinical decompensation, and teicoplanin, gentamycin and cefotaxime were commenced. Late onset sepsis was diagnosed based on a CRP of 32 and blood culture positive for klebsiella and CONS. Repeat blood culture taken 22 hours after first dose antibiotics again grew both klebsiella and CONS . Subsequent cultures on DOL 19, 21, and 28 were negative. Supportive management with re-intubation, fluid resuscitation and red cell transfusion were required. The infant recovered well and antibiotics were discontinued after 14 days.

Learning Points/Discussion

Klebsiella sepsis is an infrequent but recognised cause of neonatal sepsis, with an associated high mortality[2]. CONS is both a frequent cause of neonatal sepsis and also of blood culture contamination, and is often classified as a healthcare associate infection (HAI). It is difficult in this case to assess if CONS was pathogenic in the context of multiple organisms on blood culture incubation. Line sepsis is of particular concern in infants of extreme prematurity where intravenous access may be extremely difficult to obtain with limited alternatives.

ESPID19-0027
E-Poster Viewing - May 7-10 - E-Poster Hours

Ventriculoperitoneal shunt infections

Epidemiology and clinical features of healthcare associated viral infections in pediatric patients at a tertiary care center in thailand

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Background and Aims:

There is limited data of the epidemiology of healthcare associated viral infections (vHAI) in pediatric patients in developing countries.
Aims to evaluate the incidence and characteristic of pediatric vHAI at a large public tertiary care center in Bangkok, Thailand.

Methods:

vHAI is defined as a new illness caused by identifiable viruses with the onset of symptoms started after the hospitalization days that exceed the incubation period of the identified viruses. Cases of vHAI reported by hospital routine surveillance during 2014- 2018 were retrospectively analyzed for the incidence, clinical manifestation, treatment, and outcomes.

Results:

There were 190 vHAI episodes in 179 patients: 80 episodes of viral gastroenteritis (vGE), all were caused by rotavirus; 106 episodes of viral respiratory tract infection (vRTI) caused by RSV (49%), parainfluenza (39%), and influenza (7%); and 4 episodes of other viral infection; measles virus (1), varicella zoster virus (3). The incidence of vGE was 0.5, and vRTI was 0.66 episodes per 1000 patient-days. The peak incidence of RSV and influenza was in July-Sep, parainfluenza in April-Jun, and rotavius in Jan-Mar. There was no trend of change in incidence in the past 5 years. Most vHAI occurred in children aged < 5 years and 92% had underlying conditions. The median onset of vHAI was 20 days after hospitalization. RSV had the highest rate of requirement for respiratory support. Antibiotics were prescribed >80% of vRTI and 60% of vGE. One patient died with parainfluenza detection at the time of death.

Conclusions:

vHAI were mostly found in children <5 years of age. RSV and rotavirus were the major vHAI. The incidence of vHAI was persistent throughout the past 5 years reflected the need to improve infection control strategies to prevent vHAI.

Systematic Review Registration:

N/A

ESPID19-1159
Educational Track

ESPID Educational Symposium 10 - Healthcare associated infections in children

Colonisation and ways of transmission with gram-negative bacteria (gnb) in infants in the neonatal units (nnus) of the south-london neonatal network-the neohiec study

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Background

Infection is a major issue in the care of hospitalised neonates and its prevention is a priority. Multi-resistant Gram-negative bacterial (MRGNB) infections and outbreaks are of particular concern in NNUs and the emergence and spread of resistance complicates the treatment of neonatal infections. In order to devise strategies to prevent and control these infections the NeoHIEC Study was conducted.

Methods

The NeoHIEC Study is a large observational-cohort study, conducted in the south-London neonatal network, aiming to define the epidemiology of neonatal colonisation with MRGNB. Peri-anal swab samples were collected for 3 months and stored and analysed. All identified GNB underwent antibiotic susceptibility testing. MRGNB were defined as isolates resistant to 3 or more antibiotic classes. Whole genome sequencing was performed on all *Klebsiella* spp identified. These isolates were cultured and genomic DNA was extracted and sequenced on the Illumina MiSeq platform.

Results

782 samples were collected. Overall, 386 GNB were isolated, the majority (349, 90.4%) were *Enterobacteriaceae* (51% *Klebsiella* spp.). 19% of the isolates were MRGNB. Median-age at colonisation was 35.5 days (range: 3-216). Overall resistance to different antibiotics and specific resistance profiles for the most frequent isolates is shown in the Table. 175/179 stored *Klebsiella* spp were sequenced. Analysis suggests that some babies were colonised with the same isolates throughout the 3 month period. Multiple transmissions were also observed, corresponding with the movement of babies between NNU rooms.

Conclusions

Hospitalised neonates are frequently colonised with MRGNB of which the majority are *Enterobacteriaceae*. Resistance to gentamicin, the most commonly used antibiotic against GNB in the UK, remains low. Sequencing of isolates allows detailed analysis of transmission events and will assist in the development of interventions to prevent and control infections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0764
Educational Track

ESPID Educational Symposium 10 - Healthcare associated infections in children

Central line-associated bloodstream infections in pediatric hematology units in greece 2016-2018 - impact of an intervention bundle

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Background and Aims:

Healthcare-associated infections (HAI) are associated with increased morbidity and mortality and excess costs. Central line-associated bloodstream infections (CLABSIs) are the most common serious HAIs in neonates and children. The broad objectives of this study were to develop a CLABSI collaborative in pediatric oncology units in Greece and to implement an intervention to decrease CLABSI rates.

Methods:

Active surveillance for CLABSIs was conducted from June 2016 to June 2018 in six pediatric hematology oncology units (ONCs). Definitions of central line (CL), central line utilization (CLU) ratio, CLABSI event, and CLABSI rate based on the Centers for Disease Control and Preventions' National Healthcare Safety Network criteria from 2014. An intervention that included a care bundle for the insertion and maintenance of the central line, with on-site training and educational material posted in the unit environment, was implemented in March and April 2018.

Results:

In four units, there was a ≥10% decrease in CLABSI rates, with an increase ≥10% in only one unit. Post-intervention CLABSI rates had a median of 1.88 (IQR:0.75-2.5) compared to 2.48 (IQR:1.40-3.90) pre-intervention (Table 1).

The majority of the CLABSIs occurred more than seven days after the placement of the central line in both periods (97.1% pre-intervention and 100% post-intervention).

Table 1 – CLABSI rates in pediatric hematology oncology units in Greece before and after the implementation of an intervention in the form of a care bundle

	CLABSIs	CLABSIs <7d	CLABSIs ≥7d	CL days	Pts days	CLU ratio	CLABSI rate
Before intervention							
ONC 1	1	0	1	1592	1618	0.98	0.63
ONC 2	7	1	6	2490	3437	0.72	2.81
ONC 3	12	0	12	2580	2658	0.97	4.65
ONC 4	6	0	6	2784	3309	0.84	2.16
ONC 5	7	0	7	1916	2334	0.82	3.65
ONC 6	2	0	2	1210	1525	0.79	1.65
						Median (IQR)	**Median (IQR)**
ALL ONCs	35	1	34			0.83(0.78-0.97)	2.48(1.40-3.90)
After intervention							
ONC 1	1	0	1	2776	2905	0.96	**0.36**
ONC 2	4	0	4	4568	6757	0.68	**0.88**
ONC 3	6	0	6	3455	3671	0.94	**1.74**
ONC 4	14	0	14	6238	7235	0.86	2.24
ONC 5	5	0	5	2484	3111	0.80	**2.01**
ONC 6	10	0	10	2878	3021	0.95	3.48
						Median (IQR)	**Median (IQR)**
ALL ONCs	40	0	40			0.90 (0.77-0.95)	1.88 (0.75-2.55)

CLABSI: Central Line Associated Bloodstream Infection
Pts days: patient days **CL days:** central line days **CLU ratio:** CL days/ Pts days **CLABSI rate:** (CLABSIs/ CL days) x 1000
CLABSIs <7d: Number of CLABSIs that occurred in less than 7 days since placement of the central line
CLABSIs ≥7d: Number of CLABSIs that occurred in 7 days or more since placement of the central line
IQR: interquartile range **In green are the units with >10% decrease of CLABSI rates**

Conclusions:

An intervention in the form of a care bundle for the insertion and maintenance of central lines implemented in pediatric hematology oncology units in Greece led to a significant decrease in CLABSI rates. The experience gained and the material created can be used in other unit types across hospitals and countries.

Systematic Review Registration:

N/A

ESPID19-0546
Educational Track

ESPID Educational Symposium 10 - Healthcare associated infections in children

Healthcare-associated infection rates evolution in spanish paediatric intensive care units, from the envin-helics registry.

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Background and Aims:

To describe the rates of healthcare-associated infection (HAI) from the Paediatric Intensive Care Units (PICU) participating in the Paediatric-ENVIN-HELICS multicentre registry. To compare 2017 rates with 2013.

Methods:

Multicenter, prospective and observational study of 24 Spanish PICU. There were 1983 patients admitted from April to June 2017. The ENVIN diagnostic criteria adapted to paediatrics were used, based on CDC recommendations. The devide-related HAI registered were: ventilator associated pneumonia (VAP), catheter-associated urinary tract infections (CAUTI) and central line-associated blood stream infection (CLABSI). The statistical package Epidat 3.1 and 4.1 was used.

Results:

The patients' mean age was 5.4 years, 56.53% males. PICU admission due to medical pathology in 45.44% and 30.56% had comorbidities. Mortality rate was 1.77%. PICU HAI rate 5.4% (n=107), 2.52% (n=50) device-related HAI. PICU HAI rate decreased comparing with 2013 (2.69%, p=0.0018). Device utilization ratio: 0.30 mechanical ventilation (MV), 0.38 urinary catheter (UC) and 0.52 central venous catheter (CVC). Device-related infection rate/100 patients wih device that decreased compared with 2013 were: VAP rate (3,72%, p=0,0005) and CLABSI rate (1,71%, p= 0,0482); while CAUTI rate didn't show a significant decrease.

Conclusions:

Rates of HAI in Spanish PICU deceased in 2017 compared with 2013, due to VAP and CLABSI rate significant drop. Nevertheless HAI device-associated rates are higher than those referred in the international bibliography. Therefore, the HAI prevention measures in the participating units must be reviewed and reinforced.

Systematic Review Registration:

N/A

ESPID19-0028
Educational Track

Meet the Expert 01 - Complicated pneumonia (diagnostic and treatment approaches)

d. Unusual presentation of mycoplasma pneumonia in a young child

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Background

Mycoplasma pneumonia is a common cause of community acquired pneumonia (CAP) in school children. We report a case of pneumonia with empyema due to mycoplasma in a 2 year old child. This case is unusual due to 2 reasons, the young age of presentation and the unusual complication of empyema.

Case Presentation Summary

A 2 year old male child was brought with fever and cough since 8 days and breathlessness since 4 days. He had received oral amoxiclav for 4 days prior to admission. On admission,child had tachycardia of 170/min and tachypnea with reduced air entry on right side. CBC revealed Hb 8.7 ,total leucocyte count 9220 with 75% polymorphs. Xray chest showed right sided pneumonia with pleural effusion. USG chest reported consolidation with moderate pleural effusion, with no septations. USG guided pleural tap was suggestive of an exudate. Gram staining ,AFB staining and Genexpert for Myobacterium TB and culture were negative. The child was started on IV Ceftriaxone. After 48 hours, high grade fever persisted and tachypnea increased. USG done at 48 hours showed increase in the fluid collection. Intercostal drain(ICD) was inserted and 300 ml serous fluid was drained. Inj Vancomycin and Azithromycin were added. Over next three days, pleural fluid gradually decreased and ICD was removed on 6th day of insertion Mycoplasma IgM came positive (>27) by CLIA. Vancomycin was stopped and azithromycin given for total 6 days. Complete resolution occurred after treatment.

Learning Points/Discussion

Pediatricians need to be aware of mycoplasma pneumonia as causative agent of CAP in preschool children and also its presentation as empyema. Diagnostic testing is challenging especially in resource limited setting. Hence it should be a differential of a non responding pneumonia with standard regimens.

ESPID19-0626
Educational Track

Meet the Expert 01 - Complicated pneumonia (diagnostic and treatment approaches)

e. Extensive mycobacterium abscessus pneumonia in an immunocompetent infant

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Background

Pulmonary infections from non-tuberculous mycobacteria (NTM) typically present in patients with cystic fibrosis, underlying lung pathology, or immunodeficiency. Immunocompetent children typically have skin and soft tissue infection, cervical lymphadenitis, and rarely pulmonary infection. Although exact incidence is not known, NTM are an emerging pathogen. We describe the first extensive pneumonia with culture-confirmed *Mycobacterium abscessus* in an otherwise completely normal infant.

Case Presentation Summary

A 6-month old Hispanic female born at 38 weeks gestation via uncomplicated spontaneous vaginal delivery presented at age 4 months with 2-month history of cough and failure to thrive despite broad-spectrum antibiotic therapy. Our evaluation revealed an afebrile infant with heart rate 80 beats/min, respiratory rate 40 breaths/min with peripheral pulse oximetry of 98% on HFNC. She had nasal flaring, intercostal and subcostal retractions, but no wheezing nor rales. CT scan of the lungs showed large posterior bilateral perihilar opacities with sparing of pulmonary periphery and bases. Bronchoalveolar lavage and lung biopsy were performed as patient had no response to broad-spectrum antibiotic therapy. *Mycobacterium abscessus* was isolated from gastric aspirate and pleural fluid. Lung biopsy showed pleural and sub-pleural fibrosis, mixed focal neutrophilic aggregate, but no evidence of congenital lung malformation. Extensive immunologic testing, cystic fibrosis testing, and wide genetic testing by Dr. Holland's lab at NIH were negative. She responded to 12 months of clarithromycin and amikacin.

Learning Points/Discussion

Mycobacterium abscessus subsp. a*bscessus* can cause extensive pulmonary disease in young infants without immunodeficiency or underlying lung pathology, confirmed by culture, in this first case in English literature to our knowledge. We describe the first successful treatment of this presentation with combination antibiotic therapy without surgical intervention.

ESPID19-0444
Educational Track

Meet the Expert 02 - Endocarditis in children

d. Coxiella burnetii as a cause of negative blood culture endocarditis in a patient with congenital heart disease

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Background

Fever of unknown origin (FUO) is a challenge in Paediatrics. Q fever is caused by *Coxiella burnetti*, it is described as a cause of FUO, but it is rarely described in children.

Case Presentation Summary

Eight year-old boy admitted to Paediatric ID department because of FUO, temperature maximum 40ºC, daily, for the last 4 weeks. He developed petechiae on his legs, and hepatosplenomegaly, but nothing else remarkable on physical exam.

Past history: double out right ventricle, interventricular communication and pulmonary stenosis; after last surgery (18 months earlier), patient had a bovine pericardial patch and a prosthetic pulmonary valved conduit. No other relevant medical history; he lived in a rural area, in contact with animals.

Once admitted, blood tests were performed: normal full blood count, CRP 2.68 mg/dL, liver/renal functional test were normal, blood cultures and serologies were taken. Urine dipstick was normal. Chest X-ray was unremarkable, abdominal ultrasound showed homogeneous hepatosplenomegaly, blood cultures came back negative, and the echocardiography didn't revealed images suggesting endocarditis.

A body PET-CT revealed enhancement at prosthetic valve, serology for *C.burnetii* presented high title (>1/8912, phases I&II), and specific PCR for *C.burnetii* in blood was positive. A new echocardiography revealed vegetation at the prosthetic pulmonary valve. Patient started on doxycycline, plus hydroxychloroquine initially but switched to cotrimoxazole after 2 weeks due to gastrointestinal intolerance. He underwent valve replacement surgery and is still under antibiotics to date.

Learning Points/Discussion

Considering all causes of FUO, we should pay attention carefully to past history, physical exam and environmental exposures, especially cardiac surgery and petechiae, which could suggest endocarditis. *C.burnetii* causes negative blood cultures endocarditis and it should be taken into account if patients are exposed to animals or live in rural areas.

ESPID19-1054
Educational Track

Meet the Expert 02 - Endocarditis in children

e. Unusual infective endocarditis presentation: a 9-year-old boy with acalculous cholecystitis as an early symptom.

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Background

Infective endocarditis (IE) is an unusual, but potentially fatal disease in children. Modified Duke criteria are commonly used for clinical diagnosis. However, despite the current progress, its diagnosis continues to be difficult due to the numerous unspecific symptoms.

Case Presentation Summary

An 9-year-old boy with a minor interventricular communication (MIVC), presented with several days of fever, hepatosplenomegaly, acute phase reactants (APR) elevation and acalculous cholecystitis identified in an abdominal ultrasound. Two echocardiograms had been performed without pathological findings and blood cultures were negative. After five days of intravenous antibiotic therapy with cefotaxime and clindamycin for cholecystitis, he became afebrile, but started with acute glomerulonephritis symptoms (acute renal failure, arterial hypertension, hematuria, nephrotic-range proteinuria and generalized edema) that was handled symptomatically.

Antibiotic therapy was suspended after 10 days, relapsing fever 4 days later with increased APR and worsening of renal function. A new echocardiogram performed, revealed a vegetation on the right ventricle nearby the MIVC. Several new blood cultures were performed, and Methicillin-susceptible *Staphylococcus aureus* was isolated, confirming IE. Treatment with cloxacillin and daptomycin was started, but surgical excision s of the vegetation was decided after confirming septic pulmonary embolism in the 18F-FDG PET/CT and poor clinical and microbiological response to antimicrobials.

Symptoms and complications resolved after surgery and 6 weeks of antimicrobial treatment with a favorable evolution.**Learning Points/Discussion**

The diagnosis of IE is difficult, so we emphasize the importance of maintaining high index of suspicion in febrile children with any cardiological defect and unspecific symptoms. Acalculous cholecystitis is a rare but recognized complication of IE, particularly in *Staphylococcus aureus* bacteremia. 18F-FDG PET/CT should be considered when IE is suspected, and conventional diagnostic tools yield negative results.

ESPID19-0962
Educational Track

Meet the Expert 03 - Lyme disease – Diagnosis and management

d. Abdominal pain as presenting manifestation of neuroborreliosis in children

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Background

Lyme borreliosis is a tick-borne infection which affects the skin, joints, heart and nervous system. Children with a neuroborreliosis usually present with a facial nerve palsy or aseptic meningitis, but the spectrum of manifestations is wider.

Case Presentation Summary

PP, a 9- year-old male, was referred to our department with a 1-year history of abdominal pain, anorexia and loss of attention. He first presented severe continuos abdominal pain. A computed tomography (CT) scan of the abdomen, a gastroscopy and a colonoscopy were performed but no abnormalities were revealed. After 2 months the pain gradually remitted. Subsequently he presented anorexia with weight loss and poor scholar performance. At the physical examination reduced patellar reflexes were revealed. MRI showed leptomeningeal, cranial nerves and cauda equina contrast enhancement. A lumbar puncture was performed and a lymphocytic pleocytosis with hypoglycorrhachia and increased cerebro-spinal-fluid (CSF) protein level were found. Lyme neuroborreliosis was considered and IgG antibody test against Borrelia was positive in both serum and CSF. Intravenous ceftriaxone treatment 3 gr daily was given for 21 days. 8 weeks later a lumbar puncture showed normalised cell count and reduced protein concentration in the CSF. MRI was repeated showing a remarkable improvement. At the follow-up, 10 weeks after the end of the treatment, the patient gradually regained appetite and a slight improvement of the attention was observed.

Learning Points/Discussion

The early clinical symptoms of Lyme neuroborreliosis may be nonspecific and can point to a wide spectrum of disease. Although extremely rare in children, abdominal pain due to radiculitis could be the starting symptom of the infection.

ESPID19-1089
Educational Track

Meet the Expert 05 - Prevention of vertical transmission of HIV

e. An hiv-exposed, breastfeeding child of an hiv-viraemic mother presenting shortly after birth in zimbabwe

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Background

It is rare for paediatricians to encounter HIV-exposed infants who are breastfeeding and were not antiretroviral therapy (ART)-exposed in utero. Appropriate management is critical to prevent vertical HIV transmission; however, because cases are rare, what is classed as “appropriate management” may be controversial, especially surrounding breastfeeding recommendations when formula feeding is not “acceptable, feasible, affordable, sustainable and safe”.

Case Presentation Summary

An infant was brought to hospital in Harare, Zimbabwe by her mother shortly after birth. She was born by normal vaginal delivery and was clinically well. The mother was 16-years old and not in contact with the child’s father. She was known to be HIV-positive, but had not informed the HIV clinic that she was pregnant, and had stopped taking ART during pregnancy. At her last clinic appointment (>1 year prior to this presentation), she was taking a second-line combination ART regimen due to virologic failure. The infant was exclusively breastfeeding and was not taking ART prophylaxis.

The mother and infant were admitted to the inpatient ward. Prophylactic ART was commenced for the infant (zidovudine, lamivudine, nevirapine) and blood was sent for HIV PCR. The mother was commenced on ART, and was supported in giving medication to her child. An urgent maternal HIV PCR demonstrated a viral load >100,000 copies/mL.

Learning Points/Discussion

1. What ART regimen should be prescribed for the infant?
2. In settings where HIV-exposed infants are breastfed, which ART regimen should be prescribed for the mother to prevent postnatal transmission? With a late-pregnancy presentation and high viral load, an integrase inhibitor may be added to facilitate rapid HIV viral load reduction. Should an integrase inhibitor be added for the same reason during breastfeeding?
3. Should breastfeeding be paused until the maternal viral load has declined?

ESPID19-1036
Educational Track

Meet the Expert 05 - Prevention of vertical transmission of HIV

d. Hiv-infected infant born by a mother with negative anti-hiv testing during pregnancy - a case report

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Background

Mother-to-child transmission (MTCT) of HIV is the most common source of HIV infection in children. In Poland, all pregnant women should be screened towards HIV infection twice, in the first and the third trimester. In this case report we aimed to present an HIV-infected infant born by a woman with negative results of HIV-testing during pregnancy.

Case Presentation Summary

A male neonate was delivered at 39-week of gestation by natural labour with a birth weight 3365 g. He received 10 points in Apgar-score. His mother was tested towards HIV infection twice during pregnancy, in 1st trimester and at 36. week of gestation. Both results were negative. Short before delivery, the woman underwent a mononucleosis-like illness. At the age of 2 months, the infant was hospitalized due to gastroenteritis accompanied by dehydration, metabolic acidosis, and severe anaemia, requiring blood transfusion. At the age of 3 months, he was hospitalized with pneumonia, persistent anaemia, hepatitis, and maculopapular rash. Due to increasing cardiorespiratory failure, the infant required hospitalization in ICU. HIV-testing was performed as the child was 4 months old and it was positive. HIV viral load was >10.000.000 copies/mL. AIDS was diagnosed. Combined antiretroviral treatment (cART) was administered (ABC, 3TC, LPV/r regimen). The patient improved clinically after starting cART. His cardiorespiratory functions stabilized. After 8. months of therapy HIV viral load was 10.428 copies/mL. Patients physical and neurological development was normal**.** HIV infection was confirmed in the mother and her sexual partner.

Learning Points/Discussion

Woman acquired HIV in late pregnancy (mononucleosis-like illness). The second test towards HIV was wrought in window period. Thus, HIV infection should be considered in all infants with remittent or severe infections.

ESPID19-0988
Educational Track

Meet the Expert 06 - Tuberculosis – Still with us

d. Osteoarticular tuberculosis in children, a diagnostic challenge

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Background

Estimating tuberculosis disease (TB) data in children is complex since there is no standard case definition and definitive diagnosis is difficult to be established. Osteoarticular TB accounts for 10 to 20 percent of cases of extrapulmonary TB, however it is associated with high morbidity. While the majority of case reports of osteoarticular TB have been reported in highly endemic areas, here we present 3 cases of our hospital.

Case Presentation Summary

Case 1. 27-month-old girl with progressive loss of right hip function. She visited the emergency department in several occasions, all of them with normal clinical exploration and imaging tests. After 2 months without improvement she was admitted to our Unit.

Case 2. 36-month-old girl with frequent visits for hip and lower back pain. 6 months later, a progressive swelling in the lower back region appeared. Following another 6 months, an MRI was performed which showed a L2-L3 fracture and a retroperitoneal mass, so she was admitted to the Oncology department.

Case 3. 34-month-old boy with knee pain and swelling for 4 months. It was attributed to a mild fall. In the first visit, they suspected cellulitis and started oral antibiotics. After three days without improvement, he was admitted to his local hospital for intravenous antibiotics. 3 weeks later, the pain and swelling persisted, so he was transferred to our Unit.

A summary of clinical and laboratory parameters is presented in Table 1.

OSTEOARTICULAR TB	CASE 1	CASE 2	CASE 3
YEAR	2009	2014	2018
AGE	27 months	36 months	34 months
COUNTRY OF ORIGIN	Romania	Spain/Poland	Morocco
PRESENTING COMPLAINT	Limp	Limp, lumbar mass, hip and lower back pain	Limp, knee pain and swelling
FIRST CLINICAL SUSPICION	Transient synovitis of the hip	Neuroblastoma	Cellulitis
DIAGNOSIS DELAY	2 months	12 months	4 months
TUBERCULIN SKIN TEST	22 mm	20 mm	15 mm
HIV SEROLOGY	Negative	Negative	Negative
IMAGING TESTS	Chest X-ray: LUL consolidation	Chest CT: Calcified mediastinal nodes	Chest X-ray: RML consolidation
	Hip X-ray: Decreased bone density Hip US: Joint effusion	Lumbar MRI: L2-L3 fracture and right retroperitoneal mass (13x5x4 cm)	Knee X-ray: Soft tissue swelling and bone lytic lesions
MICROBIOLOGY TESTS	Gastric lavage smear and culture: Negative	Gastric lavage: Smear, PCR and culture: Negative	Gastric lavage: Smear, PCR and culture: Positive
	Joint effusion smear and culture: Positive	Bone biopsy smear, PCR and culture: Positive	Joint biopsy smear, PCR and culture: Positive
BIOPSY	-	Granulomas with caseous necrosis	Granulomas with caseous necrosis
DEFINITIVE DIAGNOSIS	TB hip arthritis	TB spondylitis (Pott disease)	TB knee arthritis
DRUG SUSCEPTIBILITY TESTING	Susceptible	Susceptible	Susceptible
TYPE OF DRUG AND DURATION OF TREATMENT	H+R+P+E: 1 month H+R+P: 2 months H+R: 9 months Total: 12 months	H+R+P: 2months H+R: 10 months Total: 12 months	-
SEQUELAE	No	Lumbar kyphosis	-

LUL: Left upper lobe, RML: Right middle lobe, MRI: Magnetic resonance imaging, PCR: Polymerase chain reaction, H: Isoniazid, R: Rifampicin, P: Pyrazinamide, E: Ethambutol

Learning Points/Discussion

Osteoarticular TB is uncommon in children and easily unperceived by clinicians. Delays in diagnosis and subsequent treatment are frequent. The country of origin and possible TB contacts are key questions in the history. A high index of suspicion is required to reach the diagnosis.

ESPID19-0683
Educational Track

Meet the Expert 07 - Diagnostic and treatment dilemmas in acute encephalitis

d. Coinfection with hepatitis a and e presenting as acute meningoencephalitis in an adolescent boy

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Background

Infections are still a major problem in the developing countries like India because of poor sewage disposal and economic restraints. Co-infection with hepatitis A and E is reported occasionally in the literature.We report an adolescent boy who presented with acute meningoencephalitis and coinfection with hepatitis A and E.

Case Presentation Summary

An 11 year old boy came to the emergency department of our hospital with complaints of fever,vomiting and headache 4 days and altered sensorium with one episode of uprolling of eye balls on the day of admission. On examination,child was responsive only to deep pain,neck rigidity and kernig's sign were positive.There was no pallor,cyanosis or icterus.Initially child was managed as a case of acute meningo encephalitis with ceftrioxone and acyclovir.Cerebrospinal fluid analysis revealed a total cell count of 80 cells/dl with all lymphocytes,proteins and sugar were normal.MRI brain done was also normal.Child's sensorium started improving but vomitings persisted and urine became dark colored.Thinking about acute viral hepatitis,liver function tests were done which revealed a SGOT-4262 U/L,SGPT-3698 U/L,total bilirubin-4.45 mg/dl,direct bilirubin-3.5 mg/dl.Viral markers were positive for hepatitis A and E.In absence of an alternative etiology,the aseptic meningitis was attributed to the co infection with hepatitis and E. Child's sensorium normalized and vomiting stopped.Repeat LFTs showed a falling trend in SGOT/PT and bilirubin levels.

Learning Points/Discussion

Isolated aseptic meningitis, unaccompanied by hepatitic features is an unusual presentation of a hepatotrophic viral infection. Co-infections should be kept in consideration when someone presents with atypical symptoms or unusual disease course like this presented case.Improving the sanitary conditions and vaccination against hepatitis A is a cost effective way of avoiding these diseases.

ESPID19-0860
Educational Track

Meet the Expert 07 - Diagnostic and treatment dilemmas in acute encephalitis

e. A rare cause of severe rhombencephalitis

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Background

Rhombencephalitis (RE) is a rare syndrome of multiple causes and variable prognosis. The etiologic categories of RE include infections, autoimmune diseases and paraneoplastic syndromes. Among viral agents, enterovirus 71 and herpes simplex virus (HSV) are the most common causes.

Case Presentation Summary

A previously healthy four-year old girl was admitted with fever for four days and somnolence and ataxia since few hours before medical observation. On admission, meningeal signs were suspected and a facial asymmetry was observed. In few hours, she developed flaccid paraparesis and arreflexia. Routine hemogram, blood gas and serum electrolytes were normal. Drug's use was excluded and CT was normal. LP was performed and CSF showed increased proteins (68,5mg/dL) and leukocyte count (263,2/mm^3, mainly mononuclear cells) with normal glucose and no organisms seen on the gram stain. Ceftriaxone and acyclovir were initiated. EEG was normal and MRI showed RE and extensive myelitis. Ampicillin and methylprednisolone were then started. CSF PCR for enterovirus and HSV were negative, as well as stool PCR for enterovirus. Three days after hospital admission, clinical worsening occurred with respiratory distress and dysphagia. Chest X-ray was normal and intravenous immunoglobulin was initiated, with clinical improvement. Epstein-Barr virus (EBV) serology was compatible with recent infection (IgG>200U/mL and IgM 0.4U/mL). CSF PCR for EBV was strongly positive. The patient started a rehabilitation program with mild improvement of the initial clinical condition.

Learning Points/Discussion

This case emphasizes the role of EBV in the pathogenesis of infectious neurologic disorders. The invasion of the nervous system by EBV-infected cells only occasionally produces significant neurologic disease and the highest mortality rate occurs among patients with isolated brainstem involvement. An adequate multidisciplinary rehabilitation program should be early initiated.

ESPID19-0843
Educational Track

Meet the Expert 09 - Diagnosis and management of osteomyelitis in children

d. Pediatric spondylodiscitis: a difficult diagnosis

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Background

Pediatric spondylodiscitis is an uncommon disorder. It is an infection of the spine involving the intervertebral disc and the vertebral body. The diagnosis is difficult and often delayed due to the non-specificity of clinical manifestations and children's inability to locate symptoms.

Case Presentation Summary

A 23-month-old girl presents to the Emergency Department (ED) for the fourth time in 10 days with a 2-week complain of abdominal pain and refusal to weight-bear. On physical examination, she had pain on palpation of lumbar spine and preferred to adopt side position. Laboratory showed 11300 leucocytes/mm3, ESR 91 mm/h, and CRP 1,9 mg/L. Lumbar X-ray showed a decreased height of the L1-L2 intervertebral disk. A bone scintigraphy revealed L1-L2 spondylodiscitis. She completed 11 days of intravenous flucloxacillin switching to oral for another 4 weeks. Two months later the x-ray showed L1-L2 narrowing space and after 1 year she was asymptomatic.

A 15-month-old boy was brought to the ED for the second time in 4 days with a 1 week complain of limping and refusal to sit. At the first visit, a lumbar x-ray was performed and read as normal. On physical examination, lower limbs were judged hypotonic. He was unable to remain sited and refused to weight-bear. Laboratory parameters were normal. A lumbar puncture showed no alterations in the CSF. A spine MRI revealed L5-S1 spondylodiscitis. Treatment with intravenous flucloxacillin was continued for 3 weeks and then switched to oral for another 2 weeks, with a significant clinical improvement.

Learning Points/Discussion

The diagnosis of spondylodiscitis should be suspected in children who present with reluctance to sit, stand or walk. The early use of appropriate imaging studies, such as MRI or scintigraphy, may avoid treatment delays and possibly prevent long-term problems.

ESPID19-0773
Educational Track

Meet the Expert 09 - Diagnosis and management of osteomyelitis in children

e. Complicated osteomyelitis caused by salmonella species in children with sickle cell disease

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Background

Osteomyelitis is an uncommon but important disease in childhood. Unlike in the general paediatric population, non-typhoid salmonella (NTS) species are major causative pathogens of osteomyelitis in children with sickle cell disease (SCD). The high susceptibility of SCD patients for NTS osteomyelitis is poorly understood, but asplenia, impaired blood circulation and excess iron are thought to contribute. Early diagnosis and appropriate management are key, particularly as distinguishing between bone infarction and infection is often a major challenge in this vulnerable patient group.

Case Presentation Summary

We report 3 cases of NTS osteomyelitis in children with SCD we encountered over the last 6 months. Patient 1, an 8-year-old boy with osteomyelitis of the sternal manubrium and a left anterior chest wall collection. Patient 2, a 14-year-old girl with extensive osteomyelitis of the right femur. Patient 3, a 7-year-old girl with multifocal osteomyelitis affecting the right scapula, both tibiae and tali bones. All patients presented with high-grade temperatures and markedly elevated CRP levels (> 150 mg/L). Only patient 2 had a recent travel history (Uganda). Salmonella species were detected by pan-bacterial 16s PCR (patient 1), and isolated from pus (patient 2 [*S. enteritidis*] and 3 [*S. typhimurium*]) and blood cultures (patient 3). All patients required 2 or more surgical interventions and antibiotic treatment for longer than 6 weeks, guided by inflammatory markers and clinical improvement.

Learning Points/Discussion

All 3 cases showed delayed response to antibiotic treatment and required multiple surgical interventions, highlighting the severity of NTS osteomyelitis in young SCD patients. Early diagnosis, multidisciplinary management and aggressive treatment are key to improving disease outcomes. Treatment duration and tools for disease monitoring are poorly-defined in this patient group, and require further research.

ESPID19-1177
Educational Track

Meet the Expert 12 - Kawasaki disease dilemmas

e. Kawasaki disease shock syndrome

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Background

Kawasaki disease (KD) is a systemic vasculitis effecting small and medium-sized arteries, especially the coronaries. It typically occurs between the ages of 6 months and 5 years.

Sporadic cases of Kawasaki Disease Shock Syndrome (KDSS) have been described in the literature and it is recognized that a subgroup of children with KD were admitted to Intensive Care Unit (ICU) in shock, prior to having signs of KD.

Case Presentation Summary

The authors describe a case of a 2-month-old boy who was transferred from another hospital to our ICU with a clinical picture compatible with shock, associated with 3-day fever. Physical examination revealed a maculopapular rash on the torso, palpebral oedema and non-exudative conjunctivitis.

Blood tests on admission revealed anaemia, raised C-reactive protein and a normal leucocyte count. KD was suspected, and an echocardiogram was performed on day 4 of illness, with no significant changes. Based on existent clinical and laboratory findings, the patient was initially treated empirically with antibiotics.

Because he maintained a persistently high fever at 14th day of illness and had rising inflammatory markers, with a maximum erythrocyte sedimentation rate of 16 mm/s, the echocardiogram was repeated revealing a 4.0mm aneurysm in the right coronary artery and a 3.8mm in the left coronary artery. The diagnosis of KD was confirmed and subsequently initiated treatment with Immunoglobulin 2g/kg/day, acetylsalicylic acid 100mg/kg/day and methylprednisolone 2mg/kg/day. Later, a doppler-ultrasound revealed bilateral axillary aneurysms.

Outpatient follow-up 6 months after discharge, the patient had near complete coronary aneurysm regression.

Learning Points/Discussion

KDSS is associated with more severe markers of inflammation and greater risk of coronary artery aneurysms.
Typical signs of KD may not be obvious in the early phase of KDSS making this syndrome challenging to diagnose.

ESPID19-1088
Educational Track

Meet the Expert 12 - Kawasaki disease dilemmas

d. Refractory kawasaki disease: the slovenian experience
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Background

Children who fail initial immunoglobulin (IVIG) and corticosteroid therapy in Kawasaki disease (KD) have increased risk for coronary artery (CA) aneurysms.

We report 5 cases of IVIG and corticosteroid resistant KD treated at University Children's Hospital in Ljubljana between 2006 and 2018.

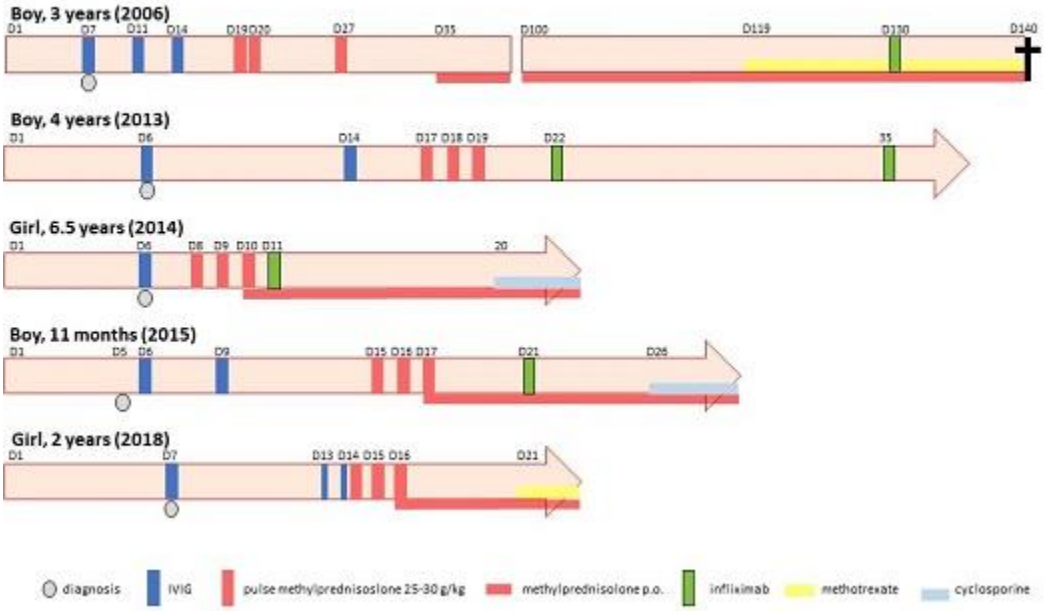
Case Presentation Summary

KD was diagnosed according to clinical criteria by the American Heart Association (AHA). All patients were initially treated according to AHA guidelines. Five children (2 female) with median age 3 years (0.9 – 6.5) and median 6 (5-7) days since the start of fever to diagnosis failed to respond to therapy with 1-3 doses of IVIG and pulse methylprednisolone.

Due to persistent inflammation 4 patients received infliximab 4-6 mg/kg, one needed a second dose after relapse. Two additionally received cyclosporine, first one with KD complicated by multiple organ failure and second one with changes on CA from D15. Two patients received methotrexate due to concomitant arthritis. One was a boy treated in 2006, who improved partially over weeks after IVIG and corticosteroid therapy. Low grade inflammation that persisted for weeks was attributed to arthritis. Echocardiography showed diffuse dilation of all CA. After exacerbation of inflammation he received infliximab on D130 with subsequent normalization of inflammatory parameters. However, due to complete CA fibrosis he died of cardiac arrest on D140.

Other patients recovered completely without cardiac or other sequelae. Detailed clinical courses of our patients are presented in Figure 1.

Figure 1. Clinical courses



Learning Points/Discussion

In refractory KD, timely aggressive immunomodulatory therapy is crucial to control the inflammation as early as possible. Anti-TNFα therapy had important influence on the outcome of disease in our patients. The only patient with prolonged disease and fatal outcome received anti-TNFα therapy late in the disease course.

ESPID19-0945
Educational Track

Meet the Expert 13 - Diagnostic approaches in paediatric infectious diseases (microbiology vs. host response)

d. Necrotizing granulomas in histopathology and a tricky differential diagnosis.
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Background

Granulomas are a common histopathology finding in several diseases such as tuberculosis, sarcoidosis, Crohn's disease and cat scratch's disease. Necrotizing granulomas can be found in infectious diseases, and, particularly in tuberculosis. However, this isn't always the case.

Case Presentation Summary

A 12 year-old boy was referred to our Pediatric Infectious Disease Unit. He had a personal history of IgA deficiency and cutaneous mastocytosis. He was diagnosed of necrotizing granulomatous mesenteric lymphadenitis after presenting with a low grade fever for two weeks associating abdominal pain in his right lower quadrant during the previous week. Abdominal ultrasound found enlarged mesenteric lymph nodes and the pathology showed necrotizing granulomas with acid fastness bacteria inside. He started treatment for tuberculosis that was discontinued after Mantoux, IGRAs and PCR came negative for *Mycobacterium.* Serology for *Bartonella henselae* was positive and he was subsequently started on azithromycin showing clinical and imaging improvement. Autoinflammatory conditions and malignancies were ruled out. Five months later, an ultrasound was performed that showed a colonic wall thickening. He was referred to our gastroenterology unit and diagnosed of Crohn's disease based on the colonoscopy findings.

Learning Points/Discussion

Granulomas are a common finding in several infectious and autoimmune and autoinflammatory conditions. Collaboration between an interdisciplinary team is the key to diagnose complex patients. Acid fast bacilli can be found accidentally in samples and are not always responsible for granulomas; therefore, a broad differential diagnosis other than infection needs to be kept in mind in case of atypical findings

ESPID19-0844
Educational Track

Meet the Expert 13 - Diagnostic approaches in paediatric infectious diseases (microbiology vs. host response)

e. An outbreak of acute paralysis affecting children: challenges in solving the puzzle of "why?"
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Background

Outbreaks of acute flaccid myelitis (AFM) predominantly affecting children have been associated with non-polio enterovirus infection. We report challenges in determining the infectious aetiology of AFM, despite the ability of polymerase chain reaction (PCR) to detect enterovirus in upper respiratory tract and faecal samples for several weeks following infection.

Case Presentation Summary

Four previously healthy children presented at a median (range) age of 3 (1-4) years old over a 6-week period with AFM following a febrile viral prodrome. Prodromal symptoms included coryza (n=4) and diarrhoea (n=2), and preceded paralysis by a median (range) of 4 (2-9) days. Paralysis involved all limbs (n=1), predominantly arms (n=1) or legs (n=2). Cerebrospinal fluid (CSF) analysis revealed: median (range) white cell count 14 (8-47) cells/mm^3; protein 0.74 (0.57-1.12) g/L; and negative PCR for viral pathogens. Multiplex PCR testing of upper respiratory tract and faecal samples was performed after a median (range) interval of 20 (12-35) days following viral prodrome onset, and was negative in all children, except one child in whom enterovirus D68 and coxsackievirus A6 were detected in both throat swab and faecal samples, as well as adenovirus and sapovirus in the same faecal sample. Magnetic resonance imaging revealed asymmetric spinal cord T2-hyperintensity (n=3) and cauda equina nerve root enhancement (n=1). Treatment included intravenous immunoglobulin (n=4) and corticosteroids (n=3). At three months after AFM onset, all children have residual neurological deficit requiring rehabilitation.

Learning Points/Discussion

AFM presents with asymmetrical paralysis following a febrile viral prodrome. Challenges in determining the infectious aetiology of AFM include the isolation of multiple viral pathogens, and the need to minimise false negative results due to delays in acquiring the appropriate samples. Current treatment approaches do not appear to prevent prolonged neurological deficit.

ESPID19-1154
Educational Track

Meet the Expert 14 - Invasive fungal infections in immunocompromised children

e. Invasive pulmonary aspergillosis in 15-months old child with mixed-phenotype acute leukemia and rapid metabolism of voriconazole

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Background

Invasive pulmonary aspergillosis (IPA) is one of the most common and serious complications occurring in immunocompromised children. Fast recognition, diagnostics and sufficient therapy are crucial. We report a case of IPA in a child with mixed-phenotype acute leukemia (MPAL) and genetic variant of *CYP2C19*17,* responsible for rapid voriconazole metabolism.

Case Presentation Summary

A 15-months old girl with MPAL, who was initially refractory to induction chemotherapy (ALL-BFM protocol) and then received AML-oriented intensification, was admitted to PICU due to respiratory failure. Laboratory results showed pancitopenia: leukocytes $0{,}1x10^9$/L, platelets $43x10^9$/L, hemoglobin 87 g/L and CRP 243 mg/L. Bone marrow aspiration revealed hypoplastic sample and discrete hemophagocytosis. High-resolution CT revealed bilateral difuse nodular (>1 cm) consolidations with necrotic components, massive pleural effusion (L<R) and small atelectasis in left apical region. Despite prophylaxis with Ambisome, PCR from BAL and pleural fluid confirmed *Aspergillus* spp infection. Broad antimicrobial coverage was initiated before ICU admission. We initiated treatment with voriconazole. Despite ascending voriconazole doses (max. 24 mg/kg/8 hours), we failed to reach terapeutic serum levels. We found that she is heterozygote for polymorphism of *CYP2C19*17* and consequentially a rapid metabolizer of voriconazole. We added fluconazole, a competitive inhibitor of CYP2C19. To overcome hyperinflammation due to hemphagocytosis we added anti IL-1 therapy with anakinra. During prolonged period of severe neutropenia she received 30 granulocyte transfusions. The child was discharged from ICU after 67 days. She was breathing with support of non-invasive mode of ventilation (CPAP/PS) through traheostomy.

Learning Points/Discussion

We present a child with refractory leukemia and pulmonary aspergillosis where genetic variant of *CYP2C19*17* was responsible for low serum concentrations of voriconazole. We successfuly overcame it with fluconazole as competitive inhibitor and granulocyte transfusions.

ESPID19-0694
Educational Track

Meet the Expert 14 - Invasive fungal infections in immunocompromised children

d. Invasive renal fungal infections in preterm- report on 3 cases

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Background

Preterm newborns have immature immune systems; there is a reduced production of cytokines which limits T cell activation that explain the increased risk of infection. Invasive fungal infections in preterm is more common and can lead to sever multiorgan affection with poor outcome. Aim: We present 3 cases with atypical urinary fungal infections.

Case Presentation Summary

Case 1: Triplet II born at 28 weeks referred from the Neonatal unit with clinical picture of acute abdomen at the age of 2 weeks. Imaging was inconclusive therefore he proceeded to an exploratory laparotomy, where a diagnosis of urinary ascites was made. Candida albicans infection was confirmed on urine culture. He was treated with antifungals and made a full recovery. Case 2: Triplet I presented to ED one month later with symptoms of respiratory infection. Commenced on empirical antibiotic medications but clinically deteriorated. Urine culture was positive for fungal infection so antifungal medication was commenced as well. Ultrasound scan demonstrated a right perinephric urinoma. This was drained percutaneously. Case 3: Preterm who received antibiotherapy for 3 weeks and developed fungal pyelonephritis with typical image on ultrasound, urine culture was negative but also with a good response after antifungal therapy.

Learning Points/Discussion

Fungal ball formation in urinary tract can cause obstruction leading to extravasation. Extravasation of urine and formation of urinoma is rare. Conclusions: Invasive fungal infections in preterm are common and extremely difficult to diagnose.Empirical treatment with antifungal therapy should be considered in high-risk, low-birth-weight infants who fail to quickly respond to empirical antibacterial treatment. Risk factors to consider when deciding to administer empirical antifungal therapy include: prior exposure to antibiotics, extreme prematurity, long term hospitalisation.

ESPID19-0269
Educational Track

Meet the Expert 15 - Invasive bacterial infections

d. Streptococcus pyogenes endocarditis with rupture of mitral valve chordae tendineae following varicella associated necrotising fasciitis – case report and review of the literature

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Background

Varicella-zoster virus (VZV) may cause serious and potentially lethal complications such as Group A Streptococcus (GAS) associated necrotizing fasciitis. GAS is rarely described as a cause of infective endocarditis (IE).

Case Presentation Summary

A 5-year-old previously healthy boy presented with varicella and painful livid discoloration on the left buttock on day 3 of illness. Inflammatory markers were elevated. Cefuroxime and Clindamycin i.v. were started. Blood cultures grew *S. pyogenes.* CT suggested fasciitis of the gluteal muscle and urgent surgical debridement was performed confirming necrotising fasciitis. Two further debridements were necessary and vacuum assisted closure was applied. On day 5 of hospitalisation respiratory distress and a systolic murmur were noted. Echocardiography revealed mitral valve prolapse with regurgitation. The child deteriorated further and echocardiography 2 days later showed progressive prolapse of the mitral valve, assuming rupture of the chordae tendineae. Cardiac surgery confirmed IE, the mitral valve was reconstructed and neo-chordae were implanted. No growth of other pathogens was noted. Treatment was adjusted to Amoxicillin and continued for four weeks. He survived.

Learning Points/Discussion

IE is rare in childhood, especially in children without congenital or valvular heart disease. GAS associated IE as a complication of VZV and fasciitis has rarely been described in children. In the past 80 years only 15 cases of IE caused by GAS in children were reported. Acute deterioration secondary to rupture of mitral valve chordae tendineae, as described in our case, has not been reported in the literature yet. Serious complications like these could be prevented by an universal varicella childhood immunization programme which unfortunately is currently not in place in Switzerland.

ESPID19-0632
Educational Track

Meet the Expert 15 - Invasive bacterial infections

e. Listeria meningoencephalitis in an immunocompetent child

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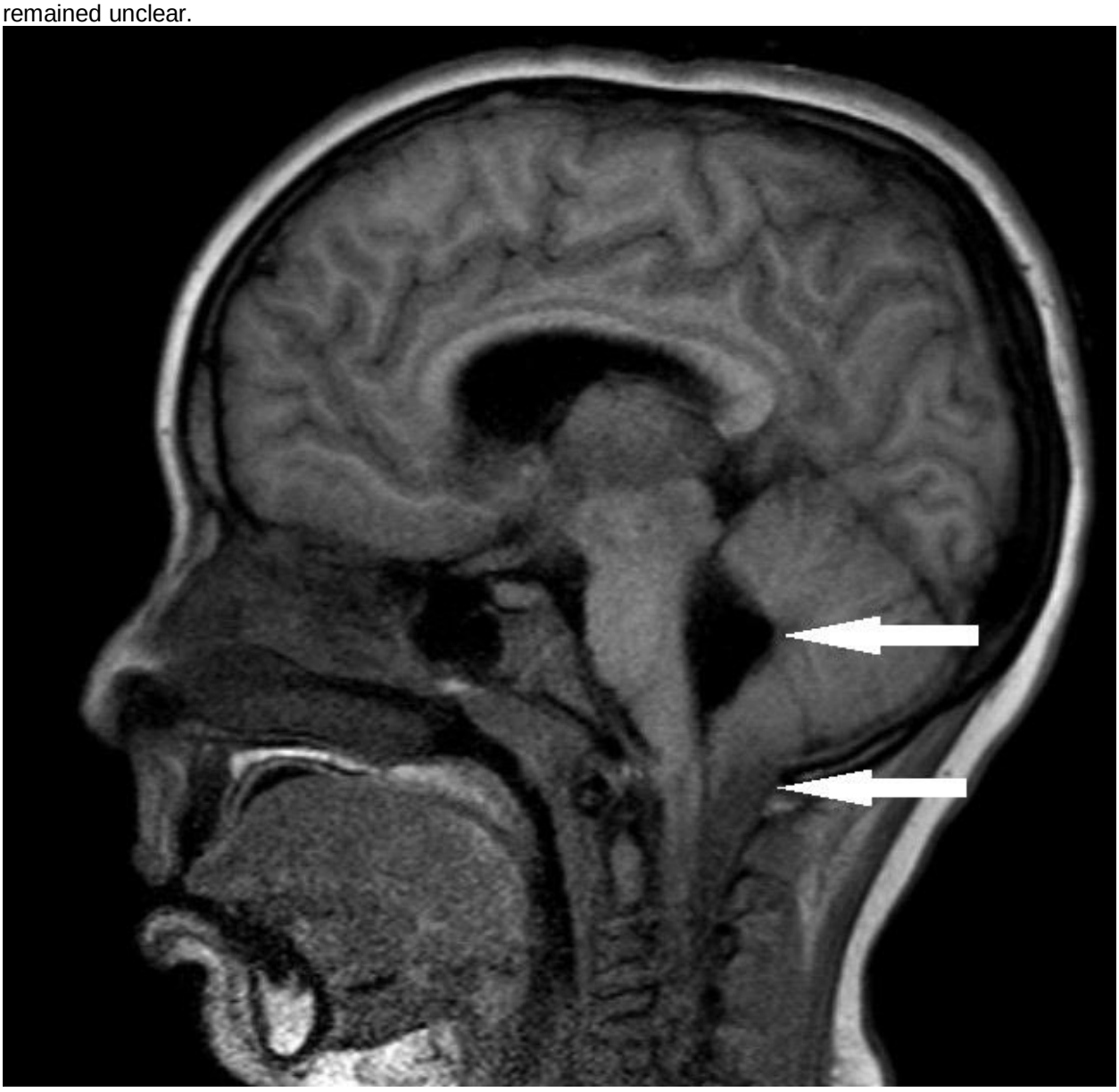
Background

Listeria is an important cause of severe meningitis/encephalitis in elderly, neonates and patients with immunosuppression. CNS infections due to listeria are rare in immunocompetent children. We present a 7-year old previously healthy female patient with acute meningitis/encephalitis and hydrocephalus due to Listeria.

Case Presentation Summary

A 7-year old healthy girl presented to a local emergency room with one day history of fever, headache and vomiting. Lumbar puncture (LP) was unsuccessful. Vancomyin, ceftriaxone and acyclovir were initiated and the patient was transferred to another institution. On the second day of hospitalization (day 2), she developed altered mental status and LP was attempted again. CSF results showed glucose at 2 mg/dl, protein at 246 mg/dl, leucocytes at 199/mm^3 with 66% lymphocytes. MRI of the brain showed acute ischemia in left parieto-occipital lobe. Blood culture grew *Staphylococcus capitis,* considered as contaminant. On day 5, the patient had developed apnea leading to intubation. Head CT showed new-onset hydrocephalus at which point the patient was transferred to our facility for neurosurgical intervention. CSF's Gram stain results were then reported by the outside facility as Gram-positive rods followed by initiation of ampicillin and gentamicin. Patient received external ventriculostomy and later posterior fossa decompression for brain stem herniation and worsening obstructive hydrocephalus (figure, arrows). Final CSF cultures showed *Listeria monocytogenes*. She was treated with ampicillin/genatmicin for total 3-4 weeks. She suffered impaired mobility and cognition. The definitive source of Listeria

remained unclear.



Learning Points/Discussion

Listeria is a rare but possible cause of meningoencephalitis in immunocompetent children. It's important to add ampicillin empirically in suspected bacterial meningoencephalitis patients not responding to conventional therapy. Although hydrocephalus is usually a late complication of bacterial meningitis, it can occur in the acute phase in listeria meningitis.

ESPID19-1102
Educational Track

Meet the Expert 16 - CMV infection in the neonate

d. Postnatally acquired cytomegalovirus infection: the unpausterized human milk dillema
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Background

Postnatally acquired cytomegalovirus infection (CMV) in preterm infants through unpasteurized human milk (UHM) can manifest with sepsis-like symptoms, often self-limited, but some might require antiviral treatment.

Case Presentation Summary

Case 1: A 745g male was born at gestational age of 25-weeks due to premature labor and rupture of membranes. The mother seroconverted for CMV during 2nd trimester of pregnancy, amniocentesis tested negative for CMV-PCR and all initial screening of the newborn, including urine CMV-PCR, were negative, making congenital infection less likely. During hospitalization, he was fed with UHM. At 6 weeks of life he presented with abdominal distension and hepatosplenomegaly. During investigation, acute CMV infection (IgM and IgG positive) was diagnosed, and he was successfully treated with a 21 days ganciclovir/valganciclovir course.

Case 2: A 2400g male was born at gestational age of 35-weeks. Three days before delivery, the mother presented fever, hepatitis and thrombocytopenia and was diagnosed with acute CMV infection (IgM positive and IgG inconclusive). C-section was performed due to oligohydramnios. The infant was born with no clinical signs of CMV infection and initial screening revealed IgM negative and IgG positive (close to indeterminate range). UHM and breast feeding was not authorized.

Learning Points/Discussion

CMV is shed in UHM in up to 96% of CMV seropositive mothers. Preterm infants can be infected through UHM. The main risk factors for symptomatic disease are extremely low birth weight, early transmission and low gestational age (<32 weeks), as in case1.

Several reports found an association between high CMV viral load in UHM and transmission risk, hence our cautions about feeding case 2 with UHM.
Effective prevention of CMV transmission can be achieved through pasteurization of human milk, but can lead to nutritional loss.

ESPID19-1104
Educational Track

Meet the Expert 16 - CMV infection in the neonate

e. Asymptomatic congenital cmv in a hiv positive newborn: clinical dilemmas
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Background

There is consensus in the benefit of treating symptomatic congenital cytomegalovirus (cCMV) infection according to international guidelines, however, recommendations for asymptomatic cCMV, especially in HIV exposed newborns, are lacking.

Case Presentation Summary

Full term infant, born from a 23 years old mother, HIV diagnosed during pregnancy in stage N1, starting ART at 16 weeks gestation with emtricitabina + tenofovir + raltegravir, decreasing HIV viral load (VL) to 52 copies/mL at week 36. Elective C section was performed at week 38 with fully completed prevention of mother-to-child transmission (PMTCT) protocol (mother:intrapartum ZDV, newborn: oral ZDV and breastfeeding contraindication). HIV blood PCR and urine CMV isolation were positive within 48 hrs of life. CMV disease was assessed in the newborn by CSF analysis, CBC, liver function tests, brain and abdominal ultrasound, ophthalmoscopy, and BERA, resulting all normal. Case was categorized as asymptomatic cCMV. CMV blood VL was 990 copies/ml (Log 3), and negative in CSF before starting treatment at day 24 of age, with valganciclovir for 6 weeks. CMV VL of 88 copies/mL (Log 1.5) was achieved after two-weeks of treatment. HIV was confirmed with a second positive PCR. Infant was classified on stage B1 (CD4 count 2550 cel/ul – 39%) and other opportunists were ruled out. ART started at 6 weeks of age with AZT+3TC+LPV/rtv. Satisfactory evolution and remain asymptomatic at 4 months of age with appropriate response to therapy.

Learning Points/Discussion

Fulfillment of PMTCP protocol decreases the risk of HIV acquisition to 1-2%. CMV infection may lead to more rapid progression of infant HIV infection, which was the reason to prescribe CMV antiviral treatment, despite being asymptomatic. There are still many questions regarding appropriate timing and length of treatment in cCMV and HIV coinfection.

ESPID19-0903
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Bcg vaccination in babies born to parents coming from high risk countries

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Background and Aims:

The World Health Organization in its 2017 global tuberculosis (TB) report advises that in countries with a low incidence of TB, neonates born to parents coming from countries with a high TB burden (>40 cases/100,000 persons per year), should be vaccinated with the Bacillus Calmette-Guérin (BCG) vaccine as soon as possible after birth. We aimed to assess the success of the current BCG vaccination programme in Malta.

Methods:

Data were collected from January 2014 until December 2016 from the obstetric wards at Mater Dei Hospital (MDH), Malta, and from the Floriana health centre where the BCG vaccine was administered.

The data were then analysed to assess the age when the BCG vaccine was being administered, the uptake rate and the main originating countries of those parents at high risk of TB.

Results:

Over the three-year study period, there were 13,725 live births in MDH, of these 13.4% (1,785) were born to parents originating from countries at high risk of TB. The uptake of the vaccine in these babies was 71.7%, the mean age of vaccine administration was 94.6 days (95% CI: 90.4-98.7). Babies were more frequently born to parents coming from Libya (10.9%), Syria (8.3%), Bulgaria (6.6%), Russia (6.3%) and Somalia (5.4%).

Conclusions:

In order to have a successful BCG vaccination programme more measures need to be in place to provide timely immunisation and increase the uptake of the BCG vaccine in babies born to parents coming from countries with high TB incidence rates.

Systematic Review Registration:

N/A

ESPID19-0848
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Multiple serotype and genotype colonisation of group b streptococcus in pregnant women and infants

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Background

Group B *Streptococcus* is a leading cause of neonatal meningitis and sepsis. Maternal colonisation is the primary source of transmission in neonatal GBS infections. Currently, there are 10 different GBS serotypes (Ia, Ib, II – IX) with serotypes III and Ia more commonly associated with disease. Serotype co-colonisation in pregnant women has not yet been fully characterised.

Methods

We analysed a pilot study of 31 rectovaginal, nasopharyngeal and breast milk swabs from 5 GBS positive mother-infant pairs to investigate GBS co-colonisation. GBS was cultured using LIM and CHROMagar and species identification was confirmed using MALDI-TOF. We isolated upto 20 GBS colonies per swab and analysed each colony with RAPD PCR to detect potential genetic diversity within samples. Each different RAPD PCR pattern was then serotyped by multiplex PCR.

Results

We identified 8/31 swabs were co-colonised with ≥2 serotypes with serotype Ia found in 6/8 of the co-colonised samples. A maximum of four different serotypes were found co-colonising a single swab. Serotypes Ia, Ib, II-V were also represented in this cohort. The RAPD patterns loosely correlated with the different number of serotypes. For the swab with four co-colonising serotypes there were a maximum of four different RAPD patterns. Diverse RAPD patterns were more commonly seen in infant samples than in mothers.

Conclusions

Our study is the first to show GBS co-colonisation in Gambian pregnant women and is important in informing serotype-specific vaccine targets. We confirm there is multiple serotype co-colonisation in pregnant women and paired infant in our pilot study, suggesting that more than one GBS colony should be tested to have a better representation of the diversity of colonising serotypes. Further investigation into a bigger sample size is currently ongoing.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESPID19-0838
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Seroepidemiology of measles, mumps and rubella on bonaire, st. Eustatius and saba: the first population-based serosurveillance study in the caribbean netherlands

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Background

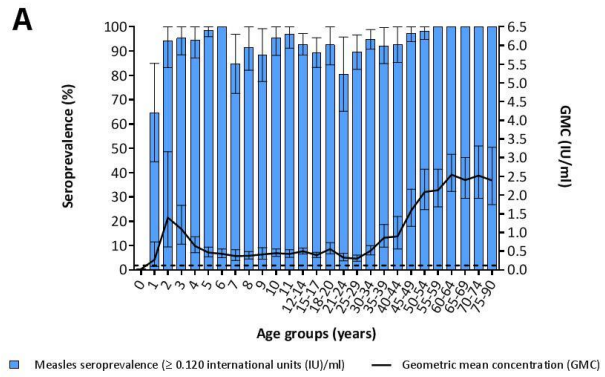
The National Immunization Program (NIP) on Bonaire, St. Eustatius and Saba (i.e., Caribbean Netherlands (CN)) includes the measles-mumps-rubella (MMR) vaccine since 1988. Seroepidemiological data is an important tool to evaluate the NIP, however has not been available yet for CN. Hence, a large cross-sectional population-based serosurveillance study was conducted in 2017 and here we report data on MMR.

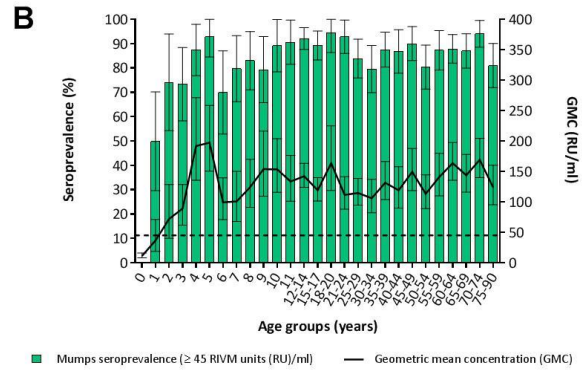
Methods

Participants (n=1,829, aged 0-90 years, randomly selected from the population registry) donated a blood sample and completed a health-related questionnaire. IgG antibodies against MMR were tested using a bead-based multiplex immunoassay and risk factors were analysed separately using logistic regression models.

Results

Weighted overall seroprevalence did not differ significantly between islands, and was 93.8% (95% confidence interval (CI) 92.3-95.2) for measles, 85.0% (95% CI 83.0-87.0) for mumps and 82.6% (95% CI 82.4-86.6) for rubella (Figure). Lowest seroprevalence for MMR was found in infants too young to be vaccinated. Seropositivity for measles in NIP-eligible age groups ranged overall between 80.5-100.0% and was lowest in those aged < 20 years originating from Latin America and former Netherlands Antilles (LANA). Mumps seroprevalence was lowest in children aged < 10 years, highest in 10-24 year-olds, and was negatively associated with not or once being vaccinated (vs. twice). Seropositivity for rubella was generally high among NIP-eligible age groups, however – contrary to measles – declined steadily thereafter, and was negatively associated with originating from LANA.





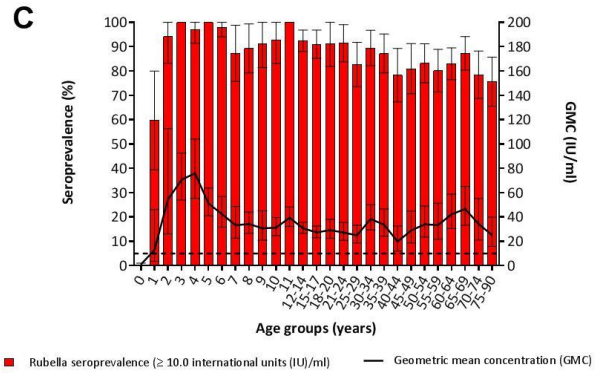


Figure. Weighted age-specific overall seroprevalence and geometric mean concentrations (GMC) (with 95% confidence intervals (CI)) of measles (A), mumps (B) and rubella (C) IgG antibodies in the general population of Caribbean Netherlands, 2017. Note: antibody concentration of ≥ 0.120 international units (IU)/ml for measles, of ≥ 45 RIVM units (RU)/ml for mumps, and of ≥ 10.0 IU/ml for rubella were considered seropositive (see dotted lines).

Conclusions

These seroepidemiological data enabled us to show that immunity against MMR is generally good in CN. Nonetheless, potential gaps in immunity were found in infants and residents from LANA. Additionally, although no measles cases have been reported in CN, healthcare workers should be on the alert as outbreaks remain ongoing in the Americas.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0690
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Immature platelet fraction (ipf) as a predictor for recovery of platelets in children with dengue fever

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Background and Aims:

Thrombocytopenia associated with dengue fever is one of the predictors of severity of dengue fever. Immature platelets reflect activity of platelet production in the bone marrow. Prediction of recovery of platelet using immature platelet fraction (IPF) may help in avoiding unnecessary platelet transfusions. Objective-:To study the pattern of platelet recovery using IPF as a predictor of recovery of platelets in children with dengue fever

Methods:

A prospective observational study was conducted in children (6months to 18 years)with serologically diagnosed dengue fever .Serial monitoring of platelet count and immature platelet fraction was done on daily basis .Samples were analysed by Sysmex XN-1000.Data analysis was done with univariant analysis, ROC and logistic regression analysis.

Results:

It was found that IPF increased 1-2 days before the platelet count increased. Sensitivity, specificity and positive predictive value (PPV) was 76.08%, 89.02% and 88.23% for association of IPF and platelet recovery. In 74.28% of cases platelet recovery occured within 24 hours of achieving a single IPF value of 10% and 88.57% showed platelet recovery within 24-48 hours of achieving a single IPF value of 10%.In the present study 72% of patients showed recovery within 24 hand the rest between 24 and 48 h after attaining peak IPF of 5.7%.It was also found that 93% of cases showed platelet recovery with falling trend of IPF from peak IPF value.

Conclusions:

IPF is a very sensitive and specific test in predicting recovery of platelet count in dengue fever. IPF helps in avoiding unnecessary platelet transfusion in dengue fever, if recovery of platelet count is anticipated as evidenced by trend of IPF.

Systematic Review Registration:

Not applicable

ESPID19-0659
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Distribution of alpha-like protein genes in streptococcus agalactiae isolated from invasive infections in a korean population

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Background

Group B Streptococcus (GBS) is a prominent pathogen in sepsis and meningitis. Vaccination is the most promising approach to prevent GBS infections. However, vaccines targeting capsular polysaccharides (CPS) for encapsulated bacteria are limited owing to their serotype-specific immunity. One of the surface proteins, alpha-like protein (Alp), which mediate adhesion to human mucosal cells, has attracted attention as a universal vaccine candidate. Therefore, this study aimed to elucidate *alp* gene distribution and their association with their serotypes of invasive strains in Korea.

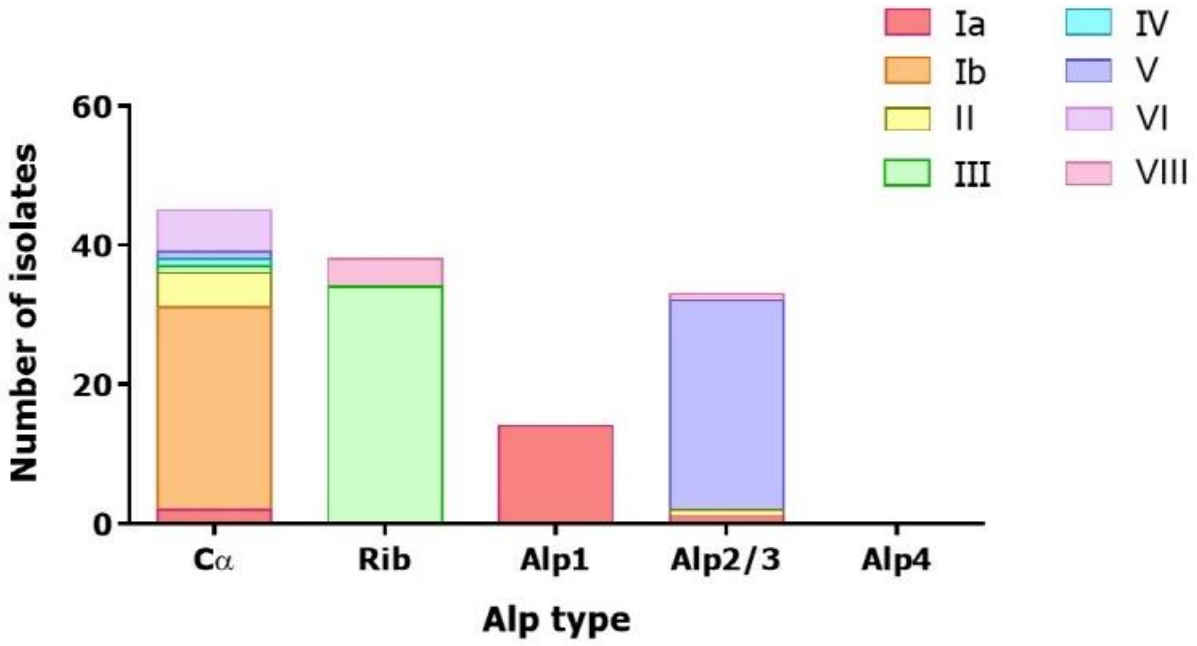
Methods

In total, 130 GBS strains were collected from blood, cerebrospinal fluid, and other sterile body sites in patients with an invasive GBS infection in Korea. *Alp* genes (*alpha-C, rib, alp1, alp2/3,* and *alp4*) in all isolates were assessed via multiplex PCR.

Results

The *alp* genes were detected in all 130 strains, *alpha C*, with the highest frequency, accounting for 34.6% (45), followed by *rib* (38, 29.2%), *alp2/3* (33, 25.4%), and *alp1* (14, 10.8%), with no *alp4* isolates detected herein (Figure 1). Serotype IV, VI, and VIII, which were not considered when developing the CPS target vaccine accounted for 9.2% (12/130); however, most of them (11/12) contained the target antigen of the Alp vaccine.

Figure 1. Distribution of the alpha-like protein (alp) genes and serotypes among the invasive Group B Streptococcal strains



Conclusions

The Alp vaccine is expected to serve as a universal protein vaccine to prevent GBS infections. Further studies are required to determine the Alp expression-associated genotype and Alp cross-immunogenicity among Alps.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0646
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Influenza virus infection factors: 19 years' active surveillance in a pediatric hospital

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Background and Aims:

Influenza is an important cause of acute lower respiratory tract infection (ALRI), hospitalization and mortality in children. The aims of this study were to describe the clinical-epidemiologic pattern and infection factors associated with influenza, and to compare case features of influenza A and B.

Methods:

A prospective, cross-sectional study of patients admitted for ALRI 2000–2018, diagnosed with respiratory syncytial virus, adenovirus, influenza, or parainfluenza by fluorescent antibody (FA) or real-time polymerase chain reaction (RT-PCR) assay of nasopharyngeal aspirates.

Results:

From a total of 16,018 patients included, 13,545 were tested for respiratory viruses and 44.6% (6,047) had positive samples identifying Influenza in 7.5% (456; 89%[406] influenza A, 11%[50] influenza B). Influenza frequency followed a seasonal epidemic pattern (May-July, the lowest average temperature months). The median age of influenza cases was 12 months (IQR: 6-23 months); 21% <6 months, 47% <1yo, 76% <2yo, 90% <5yo; 55.7% of cases were male. The most frequent clinical presentation was consolidated pneumonia (58.1%). Almost half of influenza cases had previous admissions for respiratory causes; 9% were readmissions; 61.2% had comorbidities; 25.7% (115/447) had complications. The average case fatality rate was 2% (9/450). The following were independent predictors for influenza infection: age ≥6 months, odds ratio(OR): 1.8(95% CI: 1.4-2.4); p<0.001; presence of chronic neurologic disease, OR:1.4 (95%CI: 1.0-2.1); p=0.04; previous admissions for respiratory causes, OR:1.5 (95%CI: 1.2-1.9); p<0.001; readmissions, OR:1.70 (95%CI: 1.2-2.4); p=0.005; clinical pneumonia, OR:1.6 (95% CI: 1.3-1.9); p<0.001; immunodeficiency, OR:1.7(95%CI:1.1-2.7); p=0.02. No significant association was found when comparing cases of both influenza A and B infection.

Conclusions:

Influenza infection showed an epidemic seasonal pattern (May-July), with higher risk in children aged ≥6 months, pneumonia, previous admissions for respiratory causes or certain comorbidities.

Systematic Review Registration:

N/A

ESPID19-0469
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Surveillance and evaluation the rapid antigen detection test of influenza-like illness among outpatient children during 2015-2018 in shanghai, china

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Background

Respiratory tract infection is the most common illness in childhood worldwide. Rapid antigen detection tests (RADTs) are increasingly used to detect influenza viruses in hospital setting in China. We carried out a prospective surveillance among outpatient children visiting hospital for ILI between January 2015 and May 2018, primarily aiming to understand the recent epidemiological trend of influenza and to evaluate the diagnostic value of BinaxNOW® Influenza A&B assay for rapid identification of influenza virus A and B.

Methods

A total of 2056 patients with ILI were enrolled, influenza viruses and other respiratory viruses including respiratory syncytial virus (RSV), parainfluenza virus (PIV1-4), enterovirus (EV) and adenovirus (ADV) were also detected by multiplex real-time PCR. 1114 swabs were also tested by RADTs.

Results

Among them, 1143 (55.6%) had at least one virus detected by PCR; 590 (28.7%) were positive for influenza viruses. Three outbreaks of influenza were observed. EV, RSV, ADV, PIV-3, PIV-1, PIV-2 and PIV-4, were detected in 12.6%, 1.8%, 8.7%, 8.4%, 5.4%, 1.6% and 0.2% of ILI cases, respectively. Compared to PCR assay, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of o BinaxNOW® Influenza A&B assay were 55%, 95%, 72% and 91% for influenza A virus, respectively, and were 41%, 96%, 71% and 88% for influenza B, respectively.

Conclusions

Influenza virus remained the most common pathogen causing pediatric ILI in Shanghai. A mismatch of influenza B sublineage between trivalent influenza vaccine strain and circulating strains contributed to a large influenza outbreak in 2017-2018 influenza seaosn. It is necessary to improve the coverage of influenza vaccination among children and introduce quadrivalent influenza vaccine. RADTs has an ideal specificity for field rapid confirmation of influenza virus A and B.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0398
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Pharmaceutical use during the primary pertussis immunisation period for hosptialised pertussis vaccine failure cases: a case series study

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Background

Descriptions of host factors for pertussis vaccine failure cases outside known risk groups, such as solid organ transplant recipients, are extremely limited. Host pharmaceutical use during the primary pertussis immunisation period may increase the risk of vaccine failure. We describe pharmaceutical dispensing events during the primary pertussis immunisation period for hospitalised pertussis vaccine failure cases.

Case Presentation Summary

A case series study design with data obtained from three large linked national data sets was used to describe prescription drug dispensing events between birth and two weeks after administration of third pertussis vaccination for all hospitalised cases of pertussis vaccine failure occurring in New Zealand between 2006 and 2016 (n=85). Dispensing events were described using the Anatomical Therapeutic Chemical classification system. More than three quarters of hospitalised cases had at least one pharmaceutical dispensing event. The greatest proportion of dispensing events were from the *alimentary tract and metabolism* group, accounting for one quarter of all dispensing events during this period. This was substantially higher than *alimentary tract and metabolism* dispensing events observed in a reference population (this has not yet been statistically tested). Half of the *alimentary tract and metabolism* pharmaceuticals dispensed to cases are indicated for treatment of gastroesophageal reflux symptoms. Gastric acid suppressants for example Omeprazole, were dispensed more than antacids.

Learning Points/Discussion

Our results indicate *alimentary tract and metabolism* pharmaceuticals, particularly gastric acid suppressant use during immunisation are of interest for further pertussis vaccine failure research. Existing literature describes a relationship between gastrointestinal microbiota and vaccine effectiveness; alteration of gastric pH such as through the use of gastric acid suppressants influences gastrointestinal microbiota and therefore potentially pertussis vaccine failure risk. Follow-up work is being undertake to statistically test this hypothesis.

ESPID19-0770
Science and Educational Track

E-Poster discussion session 01 - Global paediatric health - Station 01

Respiratory syncytial virus (rsv) in preterm infants: epidemiology, clinical pattern and risk factors in a pediatric hospital in argentina.

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Background and Aims:

Preterm infants(PT) have a higher risk of hospitalization and complications associated with RSV infection. The aim of this study was to describe epidemiology, clinical pattern and risk factors associated to RSV infection in PT infants.

Methods:

Prospective, cross sectional study of patients admitted for ALRI, 2000-2018. Virological diagnosis was made by fluorescent antibody assay of nasopharyngeal aspirates or RT-PCR. We compared epidemiological and clinical features, complications and lethality between full term (FT) and PT infants. Logistic regression was performed to establish lethality risk factors in PT.

Results:

A total 16,018 patients with ALRI, 13,545(84.6%) were tested for respiratory viruses, 6047(45%) were positive: RSV 81.1%(4907), all through the study period showing a seasonal epidemic pattern (May-July); 14%(686) were PT.

	PT	FT	OR	**IC95%**	**2-tailed p**
Gender(male)	58.2%	56.1%	1.1	0.9-1.3	0.28
Age(median)	7(4-13)	7(3-12)	<0.001		
Bronchiolitis	60.7%	61.6%	0.9	0.8-1.1	0.65
Comorbidities	56.3%	38.6%	2.1	1.7-2.4	<0.001
Perinatal respiratory history	46.7%	5.4%	15.3	12.6-18.8	<0.001
Cardiopathy	8.4%	5.7%	1.5	1.1-2.0	0.005
Malnourishment	9.9%	3.7%	2.8	2.1-3.8	<0.001
Chronic Respiratory Disease	41.5%	28.9%	1.7	1.5-2.1	<0.001
Bronchopulmonary Displasia	7%	0,07%	98.7	32.2-401	<0.001
Immunosupression	1%	2.1%	0.5	0.2-1.1	0.06
Previous ALRI hospitalization	42.6%	24%	2.3	1.9-2.7	<0.001
Chronic Neurological Disease	7.4%	3.6%	2.1	1.5-2.9	<0.001
Re-admission	4.8%	3.1%	1.6	1.1-2.3	0.02

During hospitalization PT had more requirement of intensive care (11% vs 7.7%;p<0.01) and stayed longer (7 vs 8 days;p<0.01). Lethality rate was higher in PT (2.9% vs 1.5%;p<0.01). Independent predictors of VSR lethality in PT: congenital cardiopathy OR3.67(1.25-10.8);p=0.01.**Conclusions:**

RSV showed an epidemic pattern and affected PT with certain comorbidities, severe disease, complications during hospitalization and higher lethality than FT. RSV lethality in PT was more associated with congenital cardiopathy.

Systematic Review Registration:

N/A

ESPID19-0944
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Public health impact and cost-effectiveness of nine-valent gender neutral hpv vaccination in slovenia

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Background

In Slovenia, human papillomavirus (HPV) vaccination is included in the national immunization program among 11-year-old girls in school since 2009/2010; the nine-valent vaccine is available since 2016. The objectives of the study were to assess the public health impact and cost-effectiveness of switching from current girls-only vaccination program to gender neutral nine-valent vaccination (GNV) program.

Methods

A published HPV disease transmission dynamic model accounting for herd protection effects has been adapted and calibrated to Slovenia. It was used to simulate population-level impact of nine-valent GNV over a 100-year period. The model provided health and economic outcomes such as cases of disease, quality-adjusted life years (QALY), costs and incremental cost-effectiveness ratio (ICER). It assumed a 55% vaccination coverage rate (VCR) and lifelong duration of vaccine protection. Deterministic sensitivity analyses were performed.

Results

Over 100 years, in Slovenia, the nine-valent GNV program would result in an additional reduction of 406 and 175 additional cervical cancer cases and deaths, 4,921 and 8,155 additional CIN 1 and CIN 2/3 cases, 84 and 28 additional anal cancer cases and deaths, 1,094 and 511 additional head and neck cancer cases and deaths, 71 and 19 additional penile cancer cases and deaths, and 1,123 additional genital warts versus a girls-only program. These results correspond to substantial additional reduction in HPV-related diseases incidence and mortality. (Table 1) The ICER was estimated at 5,774€/QALY. Base case results were most sensitive to VCR, discount rate and duration of protection.

Table 1. Additional reduction in HPV 6/11/16/18/31/33/45/52/58-related diseases cases and deaths with nine-valent gender-neutral vaccination program versus girls-only program over 100 years

HPV-related disease	Disease events avoided with GNV program *vs* girls-only program	Cumulative reduction in HPV 6/11/16/18/31/33/45/52/58-related disease incident cases	Deaths avoided with GNV program *vs* girls-only program	Cumulative reduction in HPV 6/11/16/18/31/33/45/52/58-related deaths
Genital warts (females)	407	12.5%		
Genital warts (males)	716	19.8%		
CIN 1	4,921	11.3%		
CIN 2/3	8,155	10.7%		
Cervical cancer	406	5.2%	175	4.8%
Anal cancer (females)	30	5.7%	10	5.3%
Anal cancer (males)	54	14.2%	18	13.6%
Head and neck cancer (females)	65	5.3%	23	5.0%
Head and neck cancer (males)	1,029	16.2%	488	15.4%
Penile cancer	71	19.9%	19	19.0%

Conclusions

In Slovenia, GNV has a significant impact in terms of public health benefits and is considered cost-effective compared to girls only vaccination, even with conservative assumptions such as low VCR (20%) and a duration of protection of 20 years.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0922
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Safety and immunogenicity of a quadrivalent meningococcal conjugate vaccine (menacyw-tt) administered in healthy meningococcal vaccine naïve and menc vaccine primed toddlers (12-23 months)

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Background

MenACYW-TT (tetanus toxoid,TT) is an investigational quadrivalent meningococcal conjugate vaccine intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT compared to a licensed quadrivalent conjugate meningococcal vaccine (MCV4-TT; Nimenrix®) in toddlers (12-23 months) in Europe.

Methods

In a modified double blind Phase III study, 918 toddlers were randomized to receive one dose of either MenACYW-TT vaccine or MCV4-TT vaccine. Serum bactericidal assays with human (hSBA) and baby rabbit (rSBA) complement were used to evaluate antibodies against representative meningococcal serogroup strains. Safety data were collected up to 30 days post-vaccination.

Results

Based on the percentages of participants achieving hSBA ≥ 1:8 at Day 30, non-inferiority of immune responses for all four serogroups was demonstrated for MenACYW-TT vs MCV4-TT in the combined meningococcal vaccine naïve and MenC vaccine primed participants and, also in meningococcal vaccine naïve participants. In the naïve population, post vaccination hSBA GMTs were higher for MenACYW-TT recipients than the MCV4-TT recipients. GMT ratios (MenACYW-TT/ MCV4-TT) were 1.03, 16.5, 1.34 and 1.18 for serogroups A, C, W and Y respectively in the naïve subjects. Percentages of participants with post vaccination rSBA ≥ 1:128 were comparable (overlapping 95% confidence intervals) between the study groups for the combined population. Overall, the safety profiles of MenACYW-TT and MCV4-TT were comparable. Reactogenicity at the injection sites of MenACYW-TT and MCV4-TT was higher in Meningococcal vaccine naïve than in MenC vaccine primed participants. Post-vaccination rates of severe reactions were low for both vaccines.

Conclusions

MenACYW-TT vaccine was well tolerated and demonstrated a non-inferior immune response compared to the licensed MCV4-TT vaccine when administered as a single dose to MenC vaccine primed and/or meningococcal vaccine naïve toddlers.

Clinical Trial Registration (Please input N/A if not registered)

EudraCT# 2016-000749-30

ESPID19-0890
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Long-term hepatitis b immunity after different immunization schedules with sanofi pasteur hexavalent dtap-ipv-hb-prp~t vaccine: a review

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Background and Objective

Standalone hepatitis B (HB) vaccines have demonstrated long-term persistence of immunity for up to 40 years and no boosters are recommended in the general population. Objective is to review all published literature on the long-term persistence of immunity against the HB component of Sanofi Pasteur's DTaP-IPV-HB-PRP~T vaccine (Hexyon®, Hexacima®, Hexaxim®).

Methods

All published clinical trials with DTaP-IPV-HB-PRP~T vaccine were considered, and the results of 4 clinical trials performed in 3 three different geographical regions were reviewed for data on persistence of anti-HBs antibodies and on persistence of memory upon HB re-vaccination challenge.

Learning Points Discussion

Data on persistence of anti-HBs antibodies were available following four different primary immunization schedules: HB standalone vaccine at birth followed by 3 infants doses with DTaP-IPV-HB-PRP~T at 2, 4 and 6 months, followed or not by a toddler dose at 12-24 months, or 3 infants doses with DTaP-IPV-HB-PRP~T at 6, 10, 14 weeks and a toddler dose at 15-18 months preceded or not by HB standalone vaccine at birth. Vaccinees were followed until 9-10 years of age in one study and up to 4.5 years of age in two studies.

Anti-HBs antibodies declined after primary vaccination but were above the seroprotective level (10 mIU/mL) in 73.3%-96.1% of children at 4.5 years of age. 49.3% of children had anti-HBs antibodies ≥ 10 mIU/mL at 9-10 years of age (versus 42.9% of children after comparative DTPa-HBV-IPV/Hib vaccine, Infanrix® hexa); 92.8% of subjects in this group demonstrated a booster response after re-vaccination challenge with HB vaccine.

Good long-term persistence of anti-HBs antibodies has been demonstrated irrespective of the primary vaccination schedule during the first 2 years of life.

ESPID19-1033
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Assessment of selected gaia outcome definitions for potential aefi in pregnant women and their infants in developed countries

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Background and Aims:

Case definitions (CD) are necessary to accurately evaluate adverse events following immunization (AEFI) during pregnancy. The Brighton Collaboration (BC) Global Alignment of Immunization Safety in Pregnancy (GAIA) project developed CD for AEFI assessment in mothers and infants following maternal immunization.

Methods:

We developed data collection forms to retrospectively abstract the key elements of the GAIA CD from clinical and research records for 5 neonatal (preterm birth, low birth weight, small for gestational age, respiratory distress, microcephaly), 5 maternal (preterm labor, fetal growth restriction, pre-eclampsia, non-reassuring fetal status, dysfunctional labor) outcomes, and gestational age. The ability to assign LOC for each outcome, as well as the positive predictive value (PPV) for their respective ICD-9/10 codes, were evaluated at seven study sites (4 US, 2 European, 1 Australian).

Results:

1248 cases were abstracted, 624 neonatal (578 clinical, 46 research records), and 622 maternal (583 clinical, 39 research records). Gestational age was not assessable in 114/624 (18.3%) neonatal records and in 13/622 (2.1%) maternal records. Except for pre-eclampsia and fetal growth restriction, a higher percentage of maternal outcomes was non-assessable for LOC compared to neonatal outcomes, which were more likely to be assessed and classified, except for microcephaly. The range in PPV was large for all definitions across sites and could not be extrapolated. (Table)

Conclusions:

The applicability of the GAIA CD to retrospectively identify and classify maternal and neonatal outcomes was variable in developed countries sites. It is likely that the GAIA CD are more applicable for the prospective evaluation of maternal vaccine safety. Retrospective studies should consider limiting factors

such as the source and completeness of data in clinical and research records and the need for consistency in the methods of data abstraction.

Systematic Review Registration:

NVPO

ESPID19-0837
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

A review of immunogenicity and safety of menacwy-tt immunization in infants and toddlers

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Background

The quadrivalent meningococcal conjugate vaccine MenACWY-TT is licensed to protect those ≥6 weeks of age against serogroup A, C, W, or Y meningococcal disease. Four clinical studies in infants and toddlers established the immunogenicity and safety of MenACWY-TT administered with or without routine childhood vaccines, summarized herein.

Methods

In 4 phase II, III, or IIIb studies, infants aged 6–12 weeks (NCT01144663, NCT01340898) and toddlers aged 12–14 or 15 months (NCT01939158, NCT01994629) received MenACWY-TT given on various primary and booster schedules with or without routine childhood vaccines. Coadministered vaccines included a 10- or 13-valent pneumococcal polysaccharide conjugate vaccine (PCV10 or PCV13) and DTPa-IPV/Hib or DTPa-HBV-IPV/Hib. Immunogenicity was measured by serum bactericidal assays using rabbit complement (rSBA) to evaluate percentages of subjects achieving titers ≥1:8 1 month after the last primary and booster doses. Safety was assessed.

Results

In total, 2845 infants and 1003 toddlers were vaccinated (**Table**). Among infants given MenACWY-TT on a 2+1 or 3+1 schedule, ≥93.1% of subjects had rSBA titers ≥1:8 for all serogroups after the last primary dose; for other infant groups evaluating a 3+1 or 1+1 schedule, ≥93.9% had rSBA titers ≥1:8 for all serogroups after the last primary dose. In all groups, immune responses to a booster dose were robust. Among toddlers receiving 1 or 2 doses of MenACWY-TT, ≥89.0% of single-dose recipients and ≥98.0% of 2-dose recipients had rSBA titers ≥1:8 for all serogroups 1 month after the last dose. Coadministration of MenACWY-TT with other vaccines did not affect immunogenicity of MenACWY-TT or the other vaccines, and all studies reported acceptable safety profiles.

Table. Summary of Characteristics of 4 Clinical Studies Evaluating the Safety and Immunogenicity of MenACWY-TT.

Clinical Trial Registration	Reference	Age Group	Study Design	Comparator Vaccine	Coadministered Vaccine	Dose Schedule	Number Vaccinated
NCT01144663	Arribas *Pediatr Infect Dis J* 36 (2017) e98–e107 Arribas *Pediatr Infect Dis J* 37 (2018) 704–714	6–12 wk	Phase III Open-label Randomized	MenC-CRM MenC-TT	PCV10 DTPa-HBV-IPV/Hib	MenACWY-TT 2+1 (2, 4 mo and 12 mo) 3+1 (2, 3, 4 mo and 12 mo) MenC-CRM or MenC-TT 2+1 (2, 4 mo and 12 mo) PCV10+DTPa-HBV-IPV/Hib 3+1 (2, 3, 4 mo and 12 mo)	2095
NCT01340898	Dbaibo *Vaccine* 36 (2018) 4102–4111	6–12 wk	Phase IIIb Open-label Randomized	-	PCV10 DTPa-IPV/Hib	MenACWY-TT 3+1 (2, 4, 6 mo and 15–18 mo) 1+1 (6 mo and 15–18 mo) 1 (15–18 mo) PCV10+DTPa-IPV/Hib 3+1 (2, 4, 6 mo and 15–18 mo)	750
NCT01994629	Bona *Vaccine* 34 (2016) 3363–3370	12–15 mo	Phase II Observer-blinded Randomized	MenACWY-CRM	-	1 dose at 12–15 mo	201
NCT01939158	Cutland *Vaccine* 36 (2018) 1908–1916	12–14 mo	Phase III Open-label Randomized	-	PCV13	MenACWY-TT 1 dose: month 0 2 doses: months 0 and 2 MenACWY-TT+PCV13 Coadministered at month 0 PCV13, MenACWY-TT PCV13: month 0 MenACWY-TT: month 2	802

DTPa-HBV-IPV/Hib=combined diphtheria-tetanus-acellular pertussis-hepatits B, inactivated poliomyelitis and *H influenzae* type b vaccine; DTPa-IPV/Hib=combined diphtheria-tetanus-acellular pertussis, inactivated poliomyelitis and *H influenzae* type b vaccine; MenACWY-CRM=quadrivalent meningococcal conjugate vaccine using CRM_{197} as a carrier; MenACWY-TT=quadrivalent meningococcal conjugate vaccine using tetanus toxoid as a carrier; MenC-CRM=meningococcal serogroup C vaccine using CRM_{197} as a carrier; MenC-TT=meningococcal serogroup C vaccine using tetanus toxoid as a carrier; PCV10=10-valent pneumococcal conjugate vaccine administered as the 10-valent pneumococcal nontypeable *Haemophilus influenzae* protein D conjugate vaccine; PCV13=13-valent pneumococcal conjugate vaccine.

Conclusions

MenACWY-TT is immunogenic and safe in infants and toddlers with or without coadministration of routine childhood vaccinations.

Funded by Pfizer.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0550
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

False vaccine contraindications among healthcare workers in europe

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Background and Aims:

Healthcare workers (HCW) would often delay or hold immunization when a child comes to an immunization visit with a comorbid condition. These false vaccine contraindications are a significant contributor to the number of unvaccinated children in Europe.

Methods:

We surveyed members of the European Society of Pediatric Infectious Diseases (www.espid.org, ESPID), last June 2018 to assess the knowledge of vaccinators on the contraindication for immunization. Ten (10) cases were presented to which the healthcare provider had to determine whether to vaccinate, to delay, or to hold (contraindication) to immunization.

Results:

Among all responses, we found that 23.4% (1186/5074) of the answers were wrong: in 21% (900/4096) the physician would unnecessarily postpone or contraindicate the vaccination, and in 29.0% (286/978) the patient would be vaccinated despite the existence of a true contraindication or reason to delay vaccination

There was a huge proportion of vaccinators who would specifically delay vaccinating infants with fever (75.7%, 389/514). Vaccines could have been delayed in infants on antibiotics at 37.5% (192/512) and on steroids at 33.1% (171/516).On patients with recent chemotherapy, 4.6% (23/500) of the vaccinators would continue with the scheduled shots and 34.4% (172/500) would not offer immunization.

Only 6.4% (33/573) of the respondents have correct answers on all the case scenarios.

Conclusions:

In this era of declining immunization coverage and eroding vaccine confidence, the education and training of frontline healthcare workers on vaccines and vaccine safety are crucial in promoting its use. We identified significant gaps in the knowledge of vaccine contraindications among healthcare workers in Europe. Rectifying these may result to increase vaccine confidence and immunization uptake in the region.

Systematic Review Registration:

Prospective survey

ESPID19-0504
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Indirect impact of the national ten-valent pneumococcal conjugate vaccine programme on tympanostomy tube placement in finland

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Background and Aims:

Otitis media is the most common reason for antimicrobial use in children; tympanostomy tube placement (TTP) is the most common reason for surgery requiring general anesthesia in many high-income countries. Infant ten-valent pneumococcal conjugate vaccine (PCV10) was introduced into the national vaccination programme (NVP) began in 2010 with vaccinations at 3, 5 and 12 months of age (2+1 Nordic schedule without catch-up). To estimate indirect programme impact, we evaluated changes in TTP procedures in unvaccinated children.

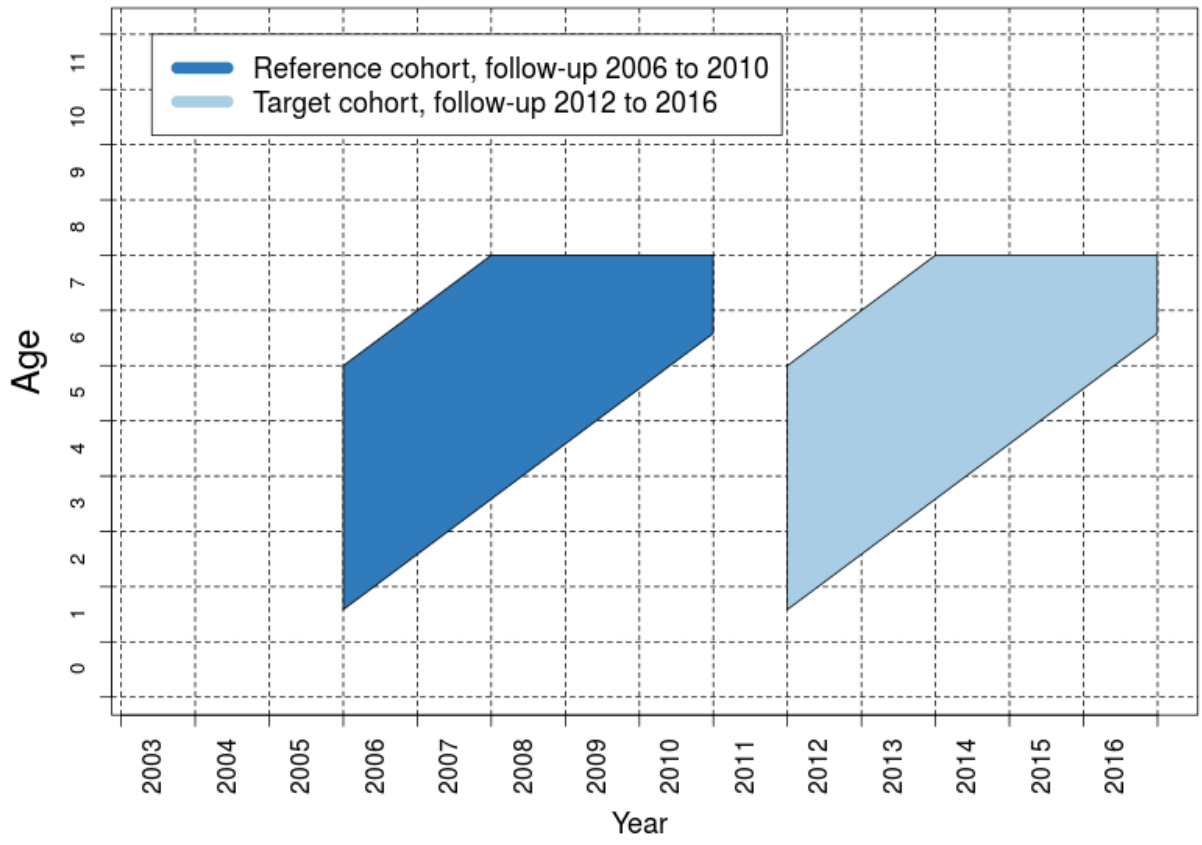
Methods:

Unvaccinated children ineligible for NVP (born 01/2006-05/2010) were followed-up during 2012-2016 (target cohort, age 1.5-7 years). Children who received PCV10 in FinIP trial during 20092010 (N=30,972) were excluded. Using before-after design, the target cohort was compared with an age- and season-matched reference cohort (born 01/2000-05/2004) during 2006-2010 (Figure). Data on TTP procedures were obtained from the national hospital discharge register and the Social Insurance Institution of Finland benefits register to collect both public hospital and private outpatient procedures.

Results:

Altogether 16997 TTP procedures were identified in the reference cohort, 53% were conducted at the public hospitals. The TTP rate per 100 person-years was 1.66 in the unvaccinated reference cohort compared with 1.61 in the target cohort; relative rate reduction, 2.6% (95%CI 0.5 to 4.8); absolute rate reduction, 0.04 per 100 person-years. While 6% (95%CI 3 to 8%) reduction was observed in public hospitals, no reduction in private outpatient procedures was seen (-1%, 95%CI -4 to

2).



Conclusions:

Although considerable reductions have been observed in unvaccinated children for antimicrobial consumption (surrogate for otitis media), the indirect impact against TTP was minor, with no effect seen in the private sector.

Systematic Review Registration:

ESPID19-0474
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Implementation of two different recommendations regarding pneumococcal vaccination for preterm (3+1) and term (2+1) infants in germany (birth cohort 2016)

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Background and Aims:

In August 2015, the German Standing Committee on Vaccination (STIKO) changed the pneumococcal conjugate vaccination (PCV) schedule for term infants (TI) from a 3+1 scheme (2, 3, 4, and 11-14 months of age) to a 2+1 scheme (2, 4 and 11-14 months of age). For preterm infants (PI) the 3+1 schedule remained. The study aim was to assess vaccination rates and timeliness (as recommended by STIKO) for the PCV in TI and PI after the change of recommendations based on real world data.

Methods:

We conducted a retrospective claims data analysis using the InGef research database containing a representative sample of the statutory health insured population in Germany. The study population consisted of all infants in this database born in 2016 who were followed-up for an individual timeframe of 9 months. Hexavalent combination vaccination (HEXA) with a consistent 3+1 recommendation for TI and PI was analyzed as reference vaccination.

Results:

After follow-up of 9 months, 73.3% of PI and 78.0% of TI received the three recommended HEXA vaccinations. At the same age, 43.3% of PI obtained the three recommended PCV doses and 77.6% of TI received the two recommended PCV doses. 9.1% of PI and 11.1% of TI obtained no PCV at all. Regarding the PCV vaccinated infants, 45.7% of PI and 51.5% of TI received the first dose on time as recommended.

Conclusions:

Although STIKO still recommends a 3+1 PCV schedule for PI in Germany, only 43.3% received the three recommended doses within 9 months of age compared to 73.3% who obtained three (recommended) doses of HEXA. Vaccinations were often delayed; about 10% of all infants remained unvaccinated. Further analyses especially regarding the booster dose will follow with data availability.

Systematic Review Registration:

ESPID19-0220
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Review of effectiveness and impact of higher-valency pneumococcal conjugate vaccines on otitis media: is there a difference?

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Background and Objective

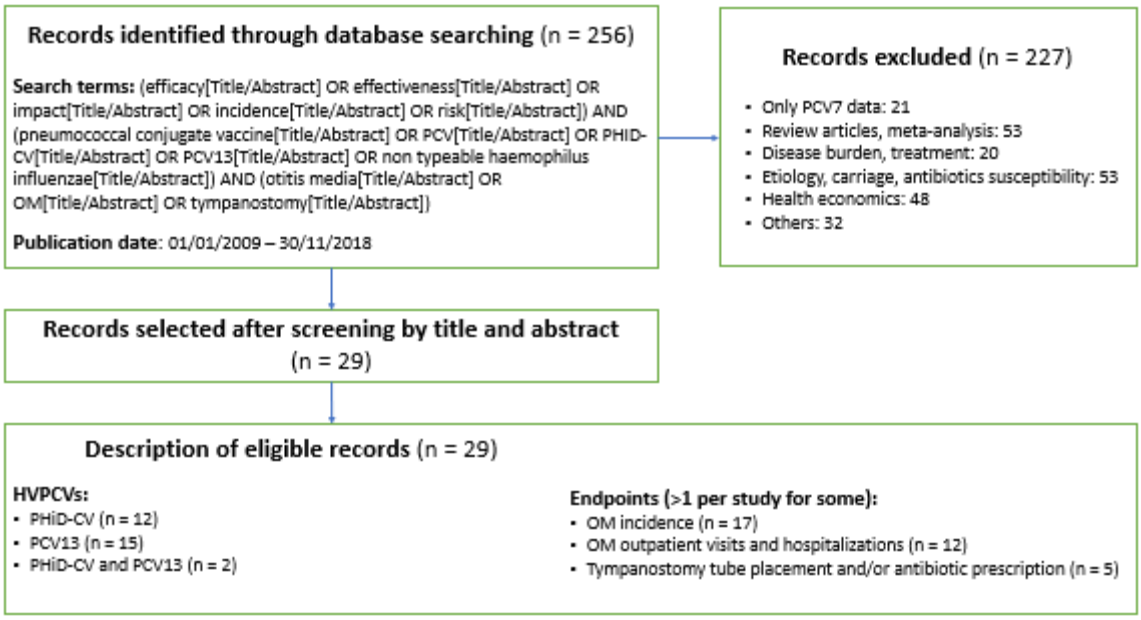
The higher-valency pneumococcal conjugate vaccines (HVPCVs) PHiD-CV (pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate) and PCV13 (13-valent PCV) have demonstrated high effectiveness against invasive pneumococcal disease with no consistent evidence of a difference in their overall impact. Moreover, both vaccines have shown an impact on pneumonia and otitis media (OM). Vaccine effectiveness against OM may impact HVPCV cost-effectiveness and play a key role in reducing antibiotic use. We aim to review the available efficacy and effectiveness data on OM and assess any differences between HVPCVs.

Methods

We conducted a literature search in Pubmed database (01/01/2009-30/11/2018; flowchart). All articles reporting efficacy, effectiveness or impact data relevant to PHiD-CV and/or PCV13 on OM or surrogate endpoints (OM hospitalization, tympanostomy tube placement, antibiotic prescription etc.) were included. Sequential use of PCV7 and HVPCVs were considered but articles reporting only PCV7-related data were excluded.

Learning Points Discussion

- 29 eligible articles reported effectiveness/impact of PHiD-CV (12/29; 4 randomized controlled trials [RCTs]), PCV13 (15/29; no RCTs) or both (2/29) (flowchart).
- Both HVPCVs have shown effectiveness and impact against pneumococcal and all-cause OM, and/or all surrogate endpoints considered.
- Comparing studies is difficult due to the high heterogeneity of study designs, age groups, disease endpoints and case definitions, and follow-up time.
- Two studies provided a comparative analysis of OM trends following PHiD-CV and PCV13: a national observational study in Sweden found a more pronounced decrease of outpatient AOM and ventilation tube insertions after PHiD-CV, while a study of community-based cross-sectional surveys of OM in Australia found no significant differences in the ear health.
- To understand the differences between HVPCVs in terms of OM prevention, randomized controlled head-to-head studies are required.



Funding: GlaxoSmithKline Biologicals SA

ESPID19-0124
Science and Educational Track

E-Poster discussion session 02 - Vaccines - Station 03

Immunogenicity and safety of tetravalent influenza vaccine: a phase iii, double-blind, randomized and controlled multicenter study in korean children aged six months to three years

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Background

This study evaluated the immunogenicity and safety of a novel tetravalent influenza vaccine containing two influenza A and two influenza B strains developed in Korea: GC3110A tetravalent pre-filled flu vaccine (GC Pharma, Yong In, Korea) in healthy children aged six months to three years.

Methods

A double-blind, controlled multicenter clinical trial was carried out involving healthy Korean children aged six months to three years. The subjects were randomized into a test(GC3110A) and a control(trivalent vaccine) group in 4:1 ratio. In the cases where the subject had never been injected with an influenza vaccine before, injections were given twice at an interval of four weeks. To investigate the immunogenicity, HI titers of the subjects' blood sample, collected at baseline and 4–5 weeks after vaccination, were measured and compared. For safety assessments, the solicited events until the seventh day of injection, the unsolicited events until the 28th day and the serious adverse events until the 180th day were examined.

Results

A total of 200 subjects were randomized into a test group (160 subjects) and a control group (40 subjects). The analysis for immunogenicity and safety was carried out on 191 subjects and 199 subjects respectively. In the test group, the seroconversion rates of the HI were A/H1N1 76.3%, A/H3N2 78.9%, B Yamagata 73.0% and B Victoria 82.2%. The seroprotection rates were A/H1N1 80.3%, A/H3N2 84.9%, B Yamagata 79.6% and B Victoria 85.5%. All the study participants well tolerated both the vaccines.

Conclusions

The new tetravalent flu vaccine, GC3110A is expected to prove clinically effective and safe for the prevention of seasonal influenza infection in young aged Korean children as well as overseas, in the future.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1147
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Neonatal toxoplasma serology in infants born to mothers with toxoplasma primary infection in pregnancy; interpretation remains a challenge

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Background and Aims:

Toxoplasmosis is usually an asymptomatic parasitic human infection, however primary infection during pregnancy can result in miscarriage/stillbirth or serious visual, motor or cognitive problems in the infant.

Methods:

We performed a retrospective case note review of patients presenting with positive maternal serology between 2013 and 2018. Serological testing included: screening latex test for total antibody; toxoplasma Dye test for IgG; and enzyme linked immunosorbent(ELISA), and immunosorbent agglutination(ISAGA) assays for toxoplasma IgA andIgM.

Results:

29 children were reviewed, 6 with confirmed congenital toxoplasmosis and end organ disease. 3/6 had ocular disease with scarring, none had abnormal hearing. All 6 infants had abnormal MRI-brain findings – 2 hydrocephalus, 4 extensive white matter changes. Maternal infection was identified in the first trimester in 3/6 infants and second trimester in 2/6, data unavailable for 1/6. All children were treated with 12 months pyrimethamine, sulfadiazine and folinic acid, despite this, they remain under paediatric review with poor neurodevelopmental outcomes.

14/23 presumed uninfected children were regularly reviewed until serological tests (dye and latex) converted to negative. They remained IgM and IgA antibody negative throughout. Negative serology was confirmed in 20% at 6 months, 67% at 9 months and 94% at 1 year. There was no linear correlation between the titer of dye test IgG at birth and the time to negative results(Figure1). Of interest, the children treated for confirmed congenital toxoplasmosis followed a similar serological pattern, presenting with positive serology, converting to negative serology on treatment, with only 2/6 developing positive IgA at 18 months and no IgM positive**Conclusions:**

This highlights that serological results alone cannot be used for diagnosis of congenital infection, and close clinical and ophthalmological review, and low threshold for MRI scanning are warranted.

Systematic Review Registration:

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ESPID19-0879
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Serratia marcescens infections in a neonatal intensive care unit

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Background and Aims:

Serratia marcescens (SM) is a gram-negative bacterium recognized as a cause of healthcare-related outbreaks in neonatal intensive care units (NICU).

Methods:

We performed a retrospective, descriptive study including all infections caused by SM in neonates admitted to a level III NICU from 2013 to 2018. Clinical and microbiological characteristics were reviewed.

Results:

From January 2013 to December 2018, we detected 32 neonates with nosocomial SM infection (14 males). The overall incidence rate was 5.37 per 1,000 inpatients. The mean age at the time of diagnosis was 15.7 days, the mean time from admission until infection was 16.2 days (range of 1 to 62 days) and the median gestational age at birth was 33 weeks (range of 25 to 41 weeks). More than half of the cases had birth weight less than 2,000gr, required prior endotracheal intubation or central catheter devices. No significant seasonal variation in incidence rates was observed. The most common infections were conjunctivitis (13/32), blood stream (16/32) and CNS infections (2/32). A cluster of cases was observed between February 2015 and March 2016 (period 1) involving 22/32 neonates. Antibiotic susceptibility patterns did not change during the study period (95%CI RR 0.61-1.79, p 0.58). All isolates were resistant to ampicillin, amoxicillin/clavulanate, cefoxitin and amikacin and susceptible to carbapenems and ciprofloxacin (32/32). Resistance to gentamicin and piperacillin/tazobactam was observed in 23/32 of strains (71.8%). The case fatality rate was 6.25%, all deaths occurred in period 1.

Conclusions:

Serratia marcescens can cause recurrent outbreaks in NICU despite infection control measures. We emphasize the importance of hygiene and surveillance measures to minimize transmission of nosocomial infections.

Systematic Review Registration:

N/A

ESPID19-0381
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

An approach to the investigation and management of the infant with suspected congenital toxoplasmosis

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[2]MRC The Gambia at The London School of Hygiene and Tropical Medicine, Vaccine and Immunity Theme, Banjul, The Gambia
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Background and Objective

Congenital toxoplasmosis(CT) occurs when *Toxoplasma gondii(T.gondii)* crosses the placenta from a mother who acquires or reactivates infection during pregnancy. Irrespective of symptom status at birth, children with congenital infection may develop serious long-term sequelae, including learning disability, hydrocephalus, motor and hearing deficits, chorioretinitis, and retinal scarring with impaired vision. We aim to outline a structured approach for paediatricians managing infants born to mothers with positive *T.gondii* serology in pregnancy, including key aspects of the antenatal history, interpretation and timing of investigations, indications for treatment, and follow-up.

Methods

There is no national guideline for suspected CT in the UK. Our recommendations are based on current evidence in the literature, including recent US, Canadian and Australian guidelines, and consensus from two UK paediatric infectious diseases centres and a specialist *Toxoplasma* reference unit.

Learning Points Discussion

•Positive IgM and IgG in pregnancy does not necessarily equate to subsequent CT and further assessment is required.

•Thorough postnatal examination is key, although the majority of newborns are asymptomatic initially; ophthalmology review and neuroimaging may detect subclinical disease.

•*T.gondii* PCR (on amniotic fluid, placental tissue, infant blood or CSF)and serial infant serology are helpful in making a diagnosis, but there are important caveats to interpreting laboratory results.

•Data on comparative efficacy of different infant treatment options is limited and protocols are not internationally standardised. The preferred regimen in the UK is sulfadiazine, pyrimethamine and folinic acid for 12months. Any decision to start treatment must include careful discussion of benefits and risks of therapy with the multidisciplinary team and parents.

•Close monitoring for medication toxicity, therapeutic response and disease recurrence is critical. Congenital disease, particularly ocular lesions, can present beyond the neonatal period and, therefore, suspected cases must be followed up appropriately.

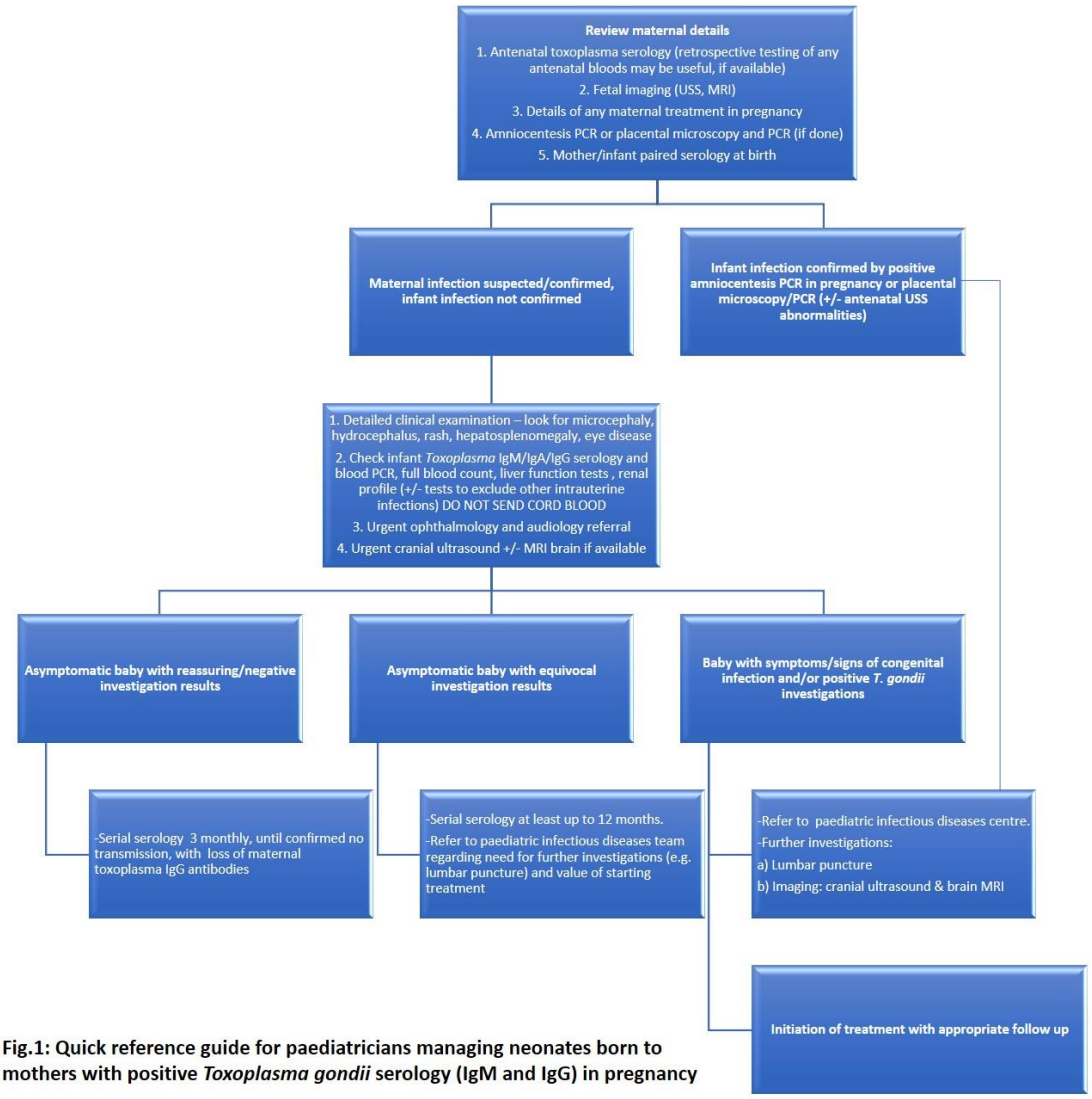

Fig.1: Quick reference guide for paediatricians managing neonates born to mothers with positive *Toxoplasma gondii* serology (IgM and IgG) in pregnancy

ESPID19-1059
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Epidemiology and management of neonatal sepsis in gaborone, botswana

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[2]The Botswana-UPenn Partnership, Department of Pediatrics, Gaborone, Botswana
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Background and Aims:

Sepsis is a leading cause of neonatal mortality, particularly in low-to-middle income countries. The rise of antimicrobial resistance had lead to a shift in both the epidemiology of both early- and late-onset sepsis, in addition to management challenges. This prospective study aimed to define the current epidemiology and mortality burden of neonatal sepsis at a neonatal nursery unit (NNU) in a large referral center in Gaborone, Botswana.

Methods:

From June 2018–October 2018 we conducted a prospective cohort study on all neonatal patients admitted to Princess Marina Hospital, Gaborone, Botswana. After parental consent was obtained, demographic, clinical, microbiologic and antibiotic data were collected. Data was summarized using descriptive statistics in Stata v15. Analyses revealed the results outlined below.

Results:

A total of 243 patients were enrolled with a median gestational age of 35 weeks and weight of 2.1kg. Cohort was 56% male, 27% were HIV exposed. Neonatal sepsis was the most common reason for admission; 45% of cases. Approximately 80% had a blood culture ordered with 11% positivity rate. The majority of positive cultures were due to Klebsiella pneumoniae, Coagulase-negative staphylococci and Staphylococcus aureus. Overall, mortality was 42%; of which 30% were attributable to confirmed infection. In the entire cohort, 66% were prescribed at least one antibiotic, of which 50% were deemed inappropriate. Antibiotic dosing issues were frequently noted, particularly with the most commonly prescribed antibiotic ampicillin. Additional barriers to inappropriate antibiotic use included frequent antibiotic shortages.

Conclusions:

Neonatal sepsis represents a disproportionate amount of NNU admissions and mortality. A heavy burden of antibiotic use was observed, with approximately 50% being deemed inappropriate. Antimicrobial stewardship initiatives are needed to address this, in addition to dosing issues and drug shortages which hampered appropriate administration.

Systematic Review Registration:

ESPID19-0780
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Should syphilis be included in routine congenital infection screen? A south east england experience

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Background

The recent increase in the diagnosis of syphilis in adults in England could result in an increase in the incidence of congenital syphilis. While vertical transmission can occur throughout pregnancy, this is more common in the last two trimesters. We report on 3 cases of congenital syphilis to raise awareness amongst clinicians and highlight our observation of a changing risk profile for mothers infected during pregnancy.

Case Presentation Summary

Three cases of congenital syphilis were managed by the paediatric infectious diseases team at Southampton Children's Hospital, UK (2016-2018). Two cases were diagnosed in the first 2 months of life while the third case was a retrospective diagnosis at 15 months following positive maternal syphilis testing during a subsequent pregnancy. All three children received standard therapy as per the BASHH guidelines with good outcomes. All three mothers were white caucasian and had negative syphilis serology at booking. None was retested for syphilis or assessed for change in risk status during the pregnancy. One of the younger children had a negative 'TORCH' screen which meant that the clinical team did not consider the possibility of syphilis which was not included in the acronym determined 'TORCH' screen.

Learning Points/Discussion

Although the guidelines recommend retesting of high risk mothers in pregnancy, it is hard to identify these women as questions exploring change in risk status (e.g. new partner) are not routinely asked during pregnancy. We recommend a relabelling of the 'TORCH screen' to 'congenital infection screen' to include syphilis, which is now our local practice. This will enable clinicians think widely about other infections outside the scope of the current infections tested for and is likely to lead to earlier diagnosis and management.

ESPID19-0480
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Reducing antimicrobial use through audit at a large tertiary neonatal unit in harare, zimbabwe

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Background and Aims:

In low-income settings, effective antimicrobial stewardship interventions are challenging. We aimed to improve antimicrobial prescribing practices through audit at Harare Central Hospital Neonatal Unit, Zimbabwe, a tertiary-level teaching hospital.

Methods:

Primary prospective audit of babies admitted over 4 weeks using local guidelines (based on World Health Organization 2016 evidence) as the gold standard. Data were collected daily from medical records until all babies reached their final outcome. All babies admitted from 8.5.18-5.6.18 were included. Results were fed back to unit staff with subsequent training and consultant-led ward-rounds reinforcing antimicrobial stewardship and differentiating between babies 'at risk of' versus clinically suspected sepsis, observing asymptomatic babies with one risk factor. Repeat retrospective audit was carried out(29.10.18-11.11.18). Analysis adjusting for case-mix is ongoing.

Results:

648 babies were included, 459 in the primary and 189 in the repeat audit (Table).

Sepsis was the most common admitting diagnosis at both time points but reduced significantly at repeat audit (82% versus 59%, p<0.0001). There was a reduction in mortality of borderline significance: 95(21%) versus 26(14%), p=0.047. Antibiotic use at admission reduced significantly: 449(98%) versus 96(51%), p<0.001 commenced antibiotics at admission and inpatient days of therapy reduced from 1243 to 1110/1000 patient days. The median duration of therapy reduced from 6 days(IQR 5-9) to 3 days (IQR 2-5, p<0.001). Prescription of seven days of oral amoxicillin at discharge reduced from 349/354(99%) to 1/161(1%, p<0.001).

Table showing characteristics and outcome of 650 babies admitted to Harare Central Hospital at initial and repeat audit with unadjusted comparison of key features

	INITIAL AUDIT			REPEAT AUDIT			
	Number of patients (unless otherwise specified)	Percentage	IQR	Number of patients (unless otherwise specified)	Percentage	IQR	P Value (Fisher's Exact Test, t-test or Wilcoxon rank-sum test)
	n=459			n=189			
FEMALE	225	49		79	42		0.100
BIRTH WEIGHT IN KG	2.8		2-3.4	2.9		2.3-3.25	1.000
INBORN	369	80		153	80		1.000
CAESAREAN SECTION	115	25		48	25		1.000
MOST COMMON DIAGNOSES AT ADMISSION							
HYPOXIC ISCHAEMIC ENCEPHALOPATHY	71	15		42	22		0.053
MECONIUM EXPOSURE/ASPIRATION	95	21		28	15		0.080
PREMATURITY (<37 WEEKS)	133	29		56	29		0.925
RESPIRATORY DISTRESS	207	45		90	47		0.605
SEPSIS	371	81		113	59		<0.0001
KNOWN MATERNAL HIV INFECTION	60	13		26	14		0.899
OUTCOMES							
DISCHARGED HOME	361	79		161	84		0.082
DIED	95	20		26	14		0.047
TRANSFERRED TO ANOTHER HOSPITAL	2	0.4		0	0		1.000
UNKNOWN	1	0.2		2	1		0.205
DURATION OF ADMISSION IN DAYS (MEDIAN)	3		2.0-6.0	2		1.0-4.3	<0.0001

Conclusions:

A substantial decrease in antibiotic use was achieved with inexpensive interventions, although some disparity in results may be due to differing methods and duration of audit (adjusted analysis ongoing). High antibiotic use can be reduced by performance feedback, training and leadership, although ongoing performance review will be key to ensuring sustainability.

Systematic Review Registration:

N/A

ESPID19-0346
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Incidence and morbidity of viral respiratory infections in the premature infant

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Background and Aims:

The real incidence of viral respiratory infections (VRI) in the Neonatal Intensive Care Unit (NICU) is unknown. Neonates who suffer VRI do not show classic symptoms of cold therefore discrimination between viral and bacterial infections is rather difficult. Premature infants are at particular risk of VRI outbreaks that associate increased morbidity and mortality in this vulnerable population

Methods:

Observational, prospective study on preterm infants below 32 weeks of gestation admitted at the NICU. Prospective collection of nasopharyngeal aspirates (NPA) within the first 3 days of life, then weekly until discharge and if clinically indicated due to respiratory events or suspected bacterial sepsis.

Results:

During the two-years study period, 925 NPA were collected from 148 infants. Thirty nine per cent of infants presented at least a positive sample and 43% had symptomatic infection, increased rate of desaturations (77.4%) and apnea episodes (48.4%) being the most prevalent symptoms. Type of viruses identified were rhinovirus (56.4%), adenovirus (32.7%) and coronavirus (5.5%). Positive NPA were associated with greater immaturity ($p= 0.021$), prolonged need of supplementary oxygen ($p< 0.003$), increased rate of bronchopulmonary displasia (BPD) ($p< 0.001$), and longer length of stay ($p< 0.05$). Symptomatic infection associated male gender (66.7%, $p= 0.016$), BPD (81.5%, $p= 0.035$) and prolonged need of supplementary oxygen (58 vs 38 days, $p=0.038$). Apnea and use of non-invasive ventilation was more frequent among the non-rhinovirus infections. BPD was an independent risk factor for VRI.

Conclusions:

VRI are frequent in NICU, most of them caused by rhinovirus and adenovirus. Abnormal breathing patterns and increased rate of desaturations are the main clinical features in the preterm infant. Infants with BPD are at particular risk of VRI.

Systematic Review Registration:

NA

ESPID19-0203
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Fluconazole prophylaxis for the prevention of invasive candidiasis among infants admitted to a neonatal intensive care unit

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Background and Aims:

Invasive candidiasis is a serious infection with high morbidity and mortality among neonates, especially those born prematurely. Prophylaxis with fluconazole is effective in preventing neonatal candidiasis in infants at high risk, and is generally safe and well tolerated. To standardize the use of fluconazole prophylaxis for high-risk neonates admitted to a level III/IV neonatal intensive care unit (NICU), we developed a protocol and prospectively audited its use.

Methods:

The new protocol (Figure 1) was developed through multidisciplinary collaboration between neonatal medicine, pediatric infectious diseases, and pediatric pharmacy providers based on review of the literature as well as expert consensus. Baseline rates of fluconazole prophylaxis use were retrospectively assessed by chart review of 100 consecutive neonates admitted to the NICU in 2017. The newly developed protocol was implemented in January 2018 and two three-month long cycles of prospective audit were conducted from January-March 2018 and April-June 2018, respectively, by chart review of all admitted infants.

Results:

Baseline fluconazole prophylaxis use in accordance with the new protocol (Figure 1) prior to implementation was 81% (n=81/100). Adherence increased to 94.5% (n=86/91) in the first audit cycle, and 98.7% (n=74/75) in the second audit cycle. Overall, adherence increased to 96.4% post-implementation (n=160/166 vs. 81/100 at baseline, $p<0.0001$). Sixteen (16%) infants in the baseline group and 47 (28%) in the post-implementation group received fluconazole prophylaxis. There were no cases of invasive candidiasis in the baseline or post-implementation

periods.

NICU Fluconazole Prophylaxis Protocol

The use of prophylaxis in some infants deemed at risk for invasive fungal infection (IFI) but not meeting the criteria outlined below still may be appropriate and prophylaxis may be prescribed at the discretion of the clinical team.

A. Does this patient require fluconazole prophylaxis?

Fluconazole prophylaxis should be initiated for infants in the NICU meeting the following criteria:

1. All infants with birth weight ≤1000 g
2. Infants with birth weight or current weight 1001 - 1500 g who have a CVC* and ≥1 of the following risk factors for IFI:
    a. Receiving antibiotic therapy for > 5 days
    b. Receiving total parenteral nutrition (TPN)
    c. Medical or surgical necrotizing enterocolitis (NEC)
    d. Abdominal surgery involving breach of bowel wall
3. Infants with birth weight or current weight > 1501g who have a CVC* and ≥2 of the following risk factors for IFI:
    a. Receiving antibiotic therapy for > 5 days
    b. Receiving total parenteral nutrition (TPN)
    c. Medical or surgical necrotizing enterocolitis (NEC)
    d. Abdominal surgery involving breach of bowel wall

If an infant meets any of the following criteria consider dose adjustment or use of an alternative agent (e.g. nystatin 100 000 units PO q 8H)

- Elevated liver enzymes (ALT > 100 U/L). See Section C below
- Receiving a medication which interacts with fluconazole (e.g. fosphenytoin, methadone, rifampin, sildenafil)
- Already receiving an antifungal for treatment of an IFI. Prophylaxis may be appropriate once the course of treatment is completed.

B. What dose should be prescribed and for how long?

- Fluconazole 3 mg/kg IV q 72H.
- First dose can be administered on day of NICU admission/birth
- Prophylaxis should be continued until the CVC is removed

C. What monitoring labs are required and if needed what alternative regimen can be used?

No routine lab monitoring required.

If ALT is 100 - 150 U/L, switch to once weekly fluconazole dosing until ALT is < 100 U/L.
If ALT is > 150 U/L consider using an alternative agent until ALT is < 150 U/L (e.g. nystatin 100 000 units PO q 8H)

* CVC includes UVCs, PICCs, cut-down CVCs, Broviacs, power PICCs

Conclusions:

A multidisciplinary approach to the development and implementation of a fluconazole prophylaxis guideline for the prevention of invasive candidiasis in a level III/IV NICU successfully increased adherence rates and standardized the use of prophylactic fluconazole. No cases of invasive candidiasis occurred.

Systematic Review Registration:

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ESPID19-0165
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Can we optimize antibiotic use in norwegian neonates? - a prospective comparison of antibiotic use in a univeristy hospital and a district hospital

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Background and Aims:

Increasing antibiotic resistance is a major health challenge, and neonates are particularly vulnerable to antibiotc exposure. The aim of this survey was to target potential for improved antibiotic use among neonates in two Norwegian hospitals with emphasis on choice of antibiotics, antibiotic exposure in none-confirmed infections (by blood culture or clinical criteria), and dosages of commonly used antibiotics.

Methods:

This is a prospective period incidence survey of antibiotic use in neonates in a university hospital (UH) and a district hospital (DH) in Norway, 2017. The registration period was one year at the DH and 15 weeks at the UH. Ninenty-five neonates at the DH and 89 neonates at the UH were treated with systemic antibiotics and included in the study. We defined term-infants (TI) as gestational age > 37 weeks, premature infants (PI) 28-37 weeks and extremely premature infants (EPI) < 28 weeks.

Results:

Ampicillin and aminoglycosides (mostly gentamicin at the UH and tobramycin at the DH) accounted for most antibiotic prescriptions in both hospitals (85% for TI and PI) and 57% for EPI). Median dosage for aminoglycoside was higher among TI at the UH (5.96, 95% CI 5.02-6.89) compared to the DH (4.98, 95% CI 4.82-5.14) ($p<0.001$). Among TI and PI, 82% (75% at the UH and 86% at the DH, $p= 0.128$) of the treatments for suspected early-onset sepsis were for none-confirmed infections with a mean treatment length of 3.02 days.

Table 3) Characteristic in treatment of early-onset sepsis (EOS) in two Norwegian neonatal units, gestational age (GA) > 28 weeks.

	All	University Hospital	District Hospital	P-value[1]
All				
EOS treatments, n	121	48	73	
Confirmed EOS[2], n (%, 95% CI)	21 (17, 10-24)	11 (23, 11-35)	10 (14, 6-22)	0.205
None confirmed EOS, n (%, 95% CI)	99 (82, 75-89)	36 (75, 63-87)	63 (86, 78-94)	0.128
Unknown (%)	1 (0.8)	1 (2)	0 (0)	n/a
GA >37 weeks				
EOS treatments, n	91	36	55	
Confirmed EOS				
Treatments, n (%, 95% CI)	21 (23, 14-32)	11 (31, 16-46)	10 (18, 8-28)	0.153
Treatment length, mean (95% CI)	5.95 (1.2)	6.1 (5.3-6.9)	5.8 (5.3-6.3)	0.586
Maximum CRP, mean (95% CI)	61.1 (20.3)	61.0 (48.4-73.6)	61.3 (49.5-73.1)	0.975
Bloodculture obtained, n (%)	21 (100)	11 (100)	10 (100)	n/a
Positive bloodculture, n (%)	2[3] (10)	1 (10)	1 (10)	n/a
Respiratory support, n (%)	5 (24)	4 (36)	1 (10)	0.172
None confirmed EOS				
Treatments, n (% 95% CI)	70 (77, 68-86)	25 (69, 54-84)	45 (82, 72-92)	0.153
Treatment length, mean (95% CI)	3.01 (1.40)	3.16 (2.39-3.93)	3.0 (2.72-3.28)	0.709
Maximum CRP, mean (95% CI)	17.3 (18.2)	18.2 (12.0-24.5)	16.8 (11.6-22.9)	0.751
Bloodculture obtained, n (%)	69 (99)	24 (96)	45 (100)	n/a
Respiratory support, n (%)	28 (40)	11 (44)	17 (38)	0.626
GA 28-37 weeks				
EOS treatments, n	30	12	18	
Confirmed EOS				
Treatments, n (%)	0 (0)	0 (0)	0 (0)	n/a
None confirmed EOS				
Treatments, n (%, 95% CI)	29 (97, 91-103)	11 (92, 77-107)	18 (100, 100)	n/a
Treatment length, mean (95% CI)	3.03 (1.19)	3.36 (2.52-4.21)	2.83 (2.39-3.28)	0.313
Maximum CRP, mean (95% CI)	8.6 (12.5)	5.9 (-0.65-12.45)	10.2 (3.42-17.02)	0.305
Bloodculture obtained, n (%)	28 (97)	11 (100)	17 (94)	n/a
Unknown				
EOSTreatments, n (%)	1 (3)	1 (8)	0 (0)	n/a

1) Chi square test was used for proportions and Student's t-test for means

2) Positive blood culture or CRP > 30 and minimum five days of treatment (or death before five days). Bloodcultures with Coagulase-negative staphylococci (CoNS) were considered positive if CRP > 10 and minimum five days of treatment (or death before five days)

3) One case of Streptococcus agalacticae (GBS) at the University hospital and one case of Staphylococcus epidermidis at the District hospital

Conclusions:

The study revealed that there is a potential for reduction in both antibiotic exposure and treatment length in these two neonatal units, and that a systematic risk/observational algorithm of sepsis should be considered in both hospitals. Variation in dosages and choice of aminoglycosides should be further studied

Systematic Review Registration:

No

ESPID19-0712
Science and Educational Track

E-Poster discussion session 03 - Neonatal infections - Station 05

Etiology and antimicrobial resistance patterns of neonatal sepsis at mulago national referral hospital, uganda

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Background and Aims:

Globally,approximately 2.6 million babies die in the first month of life. Nearly all (99%) of these neonatal deaths occur in low income countries. The aim of this study was to describe the bacterial etiology and the antimicrobial resistance patterns of the isolated bacteria among newborns clinically suspected of having sepsis

Methods:

A cross-sectional study was conducted at the Mulago national referral hospital in Kampala, Uganda. Venous blood for culture was collected from 305 newborns with clinical signs of sepsis. Validated questionnaires were used to obtain sociodemographic characteristics. An automated blood culture system was used (BD Bactec^{TM}). Kirby Bauer disk diffusion method was used for antimicrobial susceptibility testing. *mecA* PCR was conducted for confirmation of methicillin resistant Staphylococcus aureus (MRSA)

Results:

The proportion of patients with a bacterial pathogen known to cause sepsis was 14% (95% CI; 10%-19%). This included 27 *Staphylococcus aureus* isolates, *Escherichia coli* (6), *Klebsiella pneumoniae* (5), *Streptococcus pneumoniae* (1), *Neisseria* spp (1), *Enterobacter s*pp (1) and *Citrobacter freundii* (1). All the 5 *K.pneumoniae isolates*, 5/6 *E.coli* isolates and 26/27 *S.aureus* isolates were resistant to ampicillin. Resistance to the most commonly used aminoglycoside varied between species in that 6 (22%) of the *S. aureus*, one of the *E. coli* and two of the *K. pneumoniae* isolates were resistant to gentamicin. Among the *S.aureus* isolates, 20(74%) were MRSA and 8(30%) displayed erythromycin inducible clindamycin resistance but all were sensitive to vancomycin

Conclusions:

S. aureus was the most common bacterial isolate among newborns with clinical signs of sepsis at the national referral hospital. The high frequency of MRSA among these isolates is worrisome and questions the emperical management of neonatal sepsis. Erythromycin inducible clindamycin resistance further limits treatment options for MRSA infections

Systematic Review Registration:

NA

ESPID19-0347
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Blood culture sensitivity in neonates with suspected sepsis

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Background and Aims:

Although the gold standard diagnostic test for sepsis is a blood culture (BC), the yield of cultured organisms is relatively low and is affected by the blood volume inoculated, prenatal antibiotic use, level of bacteremia and laboratory capabilities. Physicians therefore rely on clinical signs and results of laboratory tests to confirm a diagnosis of sepsis. The primary aim of this study was to assess the sensitivity of BCs in neonates with suspected sepsis.

Methods:

All neonates admitted to the Neonatal and Paediatric Intensive Care Unit (NPICU) at Mater Dei hospital between 2012-2017 with suspected sepsis were included in this retrospective study. The BC results and the first and second CRP, after an initial BC, were analysed.

Results:

A total of 1,412 BCs were taken from 1,205 neonates. Organisms were isolated from 114 BCs(8.1%). However, only 67(4.7%) of these were significant and not contaminants. Of the significant BCs, a high CRP was observed in 56, giving a positive predictive value of 60.22% (95% CI: 50.40%-69.27%). Furthermore, 1,298(91.9%) BCs were negative, of which 335 were associated with a high CRP, giving a sensitivity rate of 14.32%(95% CI: 11.0- 18.19%). Of the 1,298 negative cultures, 958 were associated with a normal CRP, giving a specificity rate of 96.28%(95% CI: 94.91%-97.37%).

Conclusions:

The number of neonates with suspected sepsis that could not be confirmed microbiologically by blood cultures is high. Molecular diagnostics may be a useful tool to confirm the diagnosis and help in rationalising antibiotic regimes in these cases.

Systematic Review Registration:

ESPID19-0923
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

A novel method for identification of pathogen antigens within immune complexes by purification and metaproteomics

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Background

Immune complexes (ICs) comprising antibodies and antigens from pathogens are present in many infections. We postulated that antigens within ICs can be identified using IC isolation and peptide sequencing, offering a method to identify initiating agents of diseases of unknown cause. We demonstrate the approach using *in vitro* created ICs.

Methods

Serum samples from seven healthy adults known to have received influenza vaccine (Split Virion BP; SVBP) in the preceding 6 months were used for IC assay studies. The adult serum samples were spiked with SVBP to create ICs *in vitro*. Pooled samples were analysed by size exclusion chromatography followed by affinity chromatography on immunoglobulin-binding protein G columns.

In a second approach we used the established polyethylene-glycol (PEG) precipitation method to isolate influenza/antibody complexes from serum of 2 healthy adults previously immunised against influenza and spiked with SVBP or PBS as control.

Samples underwent mass spectrometry analysis in three laboratories. Database searches were performed using Mascot within Proteome Discoverer v1.4 and searched against SwissProt All Entries.

Results

High molecular weight fractions (corresponding to IgG and IgM peaks in molecular weight) recovered from size exclusion chromatography and further purified by affinity chromatography were found to contain influenza peptides. ICs precipitated from spiked serum using PEG precipitation were also shown to contain influenza proteins by western blotting, with no influenza proteins detected in the unspiked control.

Conclusions

The approach we have described enables recovery of *in vitro* formed ICs, and detection of the antigen within ICs. We suggest that the same approach may be useful for diseases (such as Kawasaki Disease) where the initiating agent has not been identified previously by standard culture based-diagnostic-methods.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0828
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Evaluation of matrix-assisted laser desorption ionisation time-of-flight mass spectrometry (maldi-tof ms) for the identification of group b streptococcus

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Background

Group B *Streptococcus* (GBS or *Streptococcus agalactiae*) is a gram-positive bacterium found colonising the genitourinary and gastrointestinal tracts of approximately 20% of pregnant women. Rapid and reliable tests are needed to accurately identify GBS from these women for timely intrapartum antibiotic administration to prevent neonatal disease.

Methods

We compared a direct plating method against a cell lysis method for MALDI-TOF analysis on 96 colonies that exhibit similar morphologies to GBS on CHROMagar from a sub-set of 33 clinically diverse swabs collected from mother-infant pairs. A further 842 presumptive GBS isolates were analysed using the direct plating method to show this method is applicable to be carried out in a hospital diagnostic setting as it is quicker than cell lysis.

Results

All 96 isolates were identified to the genus level (log score 1.70-1.99) using either of the two MALDI-TOF methods. Cell lysis was able to identify 91/96 isolates to the species-level (log score ≥2.00) and direct plating identified 88/96. Isolates were correctly identified by both methods as *Streptococcus agalactiae* (*n*=36), *Streptococcus salivarius* (*n*=1), *Weissella confusa* (*n*=2), *Lactococcus garvieae* (*n*=45), *Lactococcus lactis* (*n*=8) and *Aerococcus viridans* (*n*=4). A further 842 GBS isolates were analysed using the direct plating method and 100% were identified to the species-level. The sensitivity and specificity for direct plating compared to cell lysis were 0.97 and 1, respectively. Positive and negative predictive values for this method were 1 and 0.99, respectively.

Conclusions

In our study, we confirm that direct plating gives an accurate identification of GBS and species that resembled GBS on CHROMagar, without the requirement of a cell lysis extraction. These results are reassuring for laboratories worldwide who seek to identify GBS from swabs samples as quickly as possible.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0695
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Does monocyte human leukocyte antigen-dr expression predict nosocomial infection in critically ill children?

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Background

Human leukocyte antigen-DR expression (HLA-DR) on monocytes is proposed as marker to detect immunosuppression in critically ill children, but its relation to the occurrence of nosocomial infections is unclear. We aimed to assess the association of monocyte HLA-DR expression with nosocomial infections in critically ill children.

Methods

In this large prospective observational study, children <18 years with fever and/or suspected infection (community-acquired or hospital-acquired) were included at the pediatric intensive care unit (PICU) in 2017-2018. Healthy children were recruited as matched-controls. HLA-DR expression was determined by flow cytometry on day 1, day 2-3 and day 4-7 of the infectious episode. Acquisition of a secondary nosocomial infection in 28-days follow-up was defined using the guideline of European Centre for Disease Prevention and Control. The association between HLA-DR expression and secondary nosocomial infection was assessed by multivariate regression analysis, corrected for age and Pediatric Risk of Mortality Score.

Results

We included 84 patients at the PICU (median age 1.0 years (IQR 0.2-5.0), median PICU stay 11 days (IQR 4-27)) of whom seven patients (8.3%) developed a secondary nosocomial infection. Compared to 72 controls, monocyte HLA-DR expression of critically ill children was lower ($p<0.001$) at all time points. At day 1, HLA-DR expession was lower in patients with bacteremia (n=18) than those without bacteremia ($p<0.001$). HLA-DR expression was not associated with the development of nosocomial infection at day 1 (aOR 0.6 95%CI 0.1-3.9) and day 2-3 (aOR 0.3 95%CI 0.1-1.4).

Conclusions

Infectious critically ill children have lower monocyte HLA-DR expression. Monocyte HLA-DR expression was not related to the occurrence of nosocomial infection, although the incidence of nosocomial infection was low in this cohort.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0587
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Comparsion of fourier-transform infrared spectroscopy and maldi-tof mass spectrometry for characterisation of invasive bacterial isolates from critically ill children

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Background

Diagnosing invasive bacterial infection requires fast and reliable methods of detecting and identifying the pathogen. Novel technologies can identify the aetiological organism quickly and cheaply and we investigated the complementary bioanalytical methods of Fourier transform infrared (FT-IR) spectroscopy and matrix-assisted laser desorption ionisation time-of-flight mass spectrometry (MALDI-TOF-MS).

Methods

104 invasive isolates of *Streptococcus pneumoniae,* Group A streptococcus, *Staphylococcus aureus* and *Neisseria meningitidis* were cultured on blood agar plates in triplicate. 69 isolates were obtained from blood culture including 6 central line associated bacterial infections, 15 from joint aspirations, 9 from cerebrospinal fluid, 4 were surgical wounds and 7 from other sites.
Harvested biomass was analysed using FT-IR and MALDI-TOF-MS according to standardised protocols and spectral data were subjected to prinicpal component analysis (PCA).

Results

A total of 104 invasive disease isolates were studied using FT-IR and MALDI-TOF-MS. Median age was 2.34 years (IQR 0.77-7.3) Median length of stay was 10 days (6.5-19) and 34 patients required PICU admission with median length of stay 5 days (2-10.5) whilst 30 patients required a median of 4 ventilator days (2.5-7) and 12 patients required a median of 5 days of non invasive respiratory support (2-9).

Principal component analysis demonstrated clear discrimination of species. Overall prediction accuracy of the 4 species using discriminant analysis was 99.6% in FT-IR and 95.8% in MALDI-TOF. Furthermore, analysis of *N. meningitidis* serogroups was superior in FT-IR compared to MALDI-TOF.

Conclusions

Molecular fingerprinting of microbiology samples using spectroscopy techniques is highly accurate. As a rapid, low cost technique, FT-IR is a promising diagnostic tool to identify aetiology of invasive pathogens if it can be applied directly to clinical specimens.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0466
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Research to ensure blood culture positive rate with small specimen volume

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Background

The recommended sample volume required for blood culture in children is generally ≥1 ml. Thus, this study aimed to examine if the positive rate between blood sample volumes 0.5–<1.0 ml and ≥1 ml is different.

Methods

This study included 2857 pediatric blood culture bottles at a pediatric tertiary care center in Japan between March 2017 and July 2018. The specimen volume in *g* was calculated on the basis of bottle weight difference before and after obtaining a blood specimen sample. The blood culture positive rate was compared at sample volumes <0.5 ml, 0.5 ml–<1.0 ml, and ≥1.0 ml.

Results

The culture positive rate was 0% (0/129 bottles) in <0.5 ml of specimen, 2.1% (9/436 bottles) in samples 0.5 ml–<1.0 ml, and 3.1% (72/2290 bottles) in samples of ≥1.0 ml. The positive rate was higher when the blood sample volume was ≥0.5 ml compared to <0.5 ml (p = 0.04). There was no significant difference in the positive rate when blood sample volumes were 0.5 ml–<1.0 ml and ≥1 ml (P = 0.224).

Conclusions

We believe that the volume of blood sample required for pediatric culture bottles is ≥0.5 ml.

Clinical Trial Registration (Please input N/A if not registered)

N / A

ESPID19-0336
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

A prospective case control study regarding economic benefits of Biofire® Filmarray® meningitis/encephalitis (fa) panel in children with suspected central nervous system infection: preliminary results

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Background

Rapid detection of pathogens involved in Central Nervous System (CNS) infections could be important not only for the optimal patient management but also for the reduction of hospitalization cost. The aim of the study was to compare the possible economic benefits with the use Biofire® FilmArray® meningitis/encephalitis (FA) panel in children with possible CNS infections.

Methods

A prospective case-control study in children with clinical suspicion of meningitis or encephalitis with or without the diagnostic use of FA was performed. Cases were compared to age-matched controls regarding days of hospitalization and hospitalization cost, over the period of 1 year (2018) in a tertiary pediatric hospital. FA enables rapid automated cerebrospinal fluid testing for 14 common viral, bacterial and yeast pathogens that cause CNS infections. Conventional microbiological procedures were performed in all children. The cost was estimated according to ICD-10 diagnosis standard cost, adding additional daily hospitalization cost, FA or other molecular microbiological procedures costs.

Results

A total of 72 children were included in the study (36 cases). The median age of cases and controls was 13,5 months (IQR:1,5-105) and 12 months (IQR:1,3-105) respectively (*P*-value: 0,901). FA was positive in 18/36 (50%) children and detected: *Enterovirus* 14 (38,9 %), *Parechovirus* 2 (5,6%), *N.meningitidis* 1 (2,8 %), *Human herpes Virus* 6 (HHV-6) 1 (2,8%). The median hospitalization time in cases and controls were 5 days (IQR:4-6) and 7 days (IQR:5-10) respectively (*P*-value:0,009). The median cost of hospitalization was estimated in cases and controls 1042€ (IQR:822-1152) and 1412€ (IQR:1192-1742) respectively (*P*-value:0,0001).

Conclusions

The use of FA was able to reduce significantly the hospitalization days and the total cost comparing to the control group in children with suspected CNS infection.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0263
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

The relationship between positive drain tip cultures and the incidence of surgical site infection after pediatric cardiovascular surgery

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Background and Aims:

Surgical site infection (SSI) is a severe complication after pediatric cardiovascular surgery. Drain tip cultures (DTC) are sometimes performed postoperatively, however its diagnostic value of DTC for predicting SSI in pediatric cardiovascular surgery is undetermined. The aim of this study was to assess whether DTC is of diagnostic value after pediatric cardiovascular surgery.

Methods:

We conducted a retrospective, single-center cohort study of DTC and onset of SSI at a tertiary children's hospital in Japan. All samples of DTC between December 2014 and August 2018 were identified from our laboratory database. We examined demographic and clinical data of the patients and compared the incidence of SSI between positive and negative DTC.

Results:

A total of 555 samples from 254 patients was identified during the study period. 70 samples (12.6%) were positive and 27 patients (10.6%) were proved to have at least one positive DTC. Coagulase-negative Staphylococci (n=22) were the most frequently isolated organisms followed by *Candida* spp. (n=3), *Enterobacter cloacae* (n=1), and *Staphylococcus aureus* (n=1). There was no significant demographic difference in age, sex, rate of on-pump operation, and duration of drainage tube placement between patients with positive and negative DTC. In total, 19 (7.4%) patients developed SSI. The rate of SSI was not significantly higher in patients with positive DTC (14.8% [4/27 cases] vs. 6.6% [15/227 cases], p=.128). Only two patients developed SSI caused by the same organisms isolated from DTC (*Staphylococcus lugdunensis* and *Candida parapsilosis*).

Conclusions:

Positive DTC was not associated with the occurrence of SSI after pediatric cardiovascular surgery. Hence, routine culture of the tips of drainage tube should not be attempted unless there is any sign of infection.

Systematic Review Registration:

ESPID19-0122
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Need of invasive procedures to regulate intracerebral pressure in children with bacterial meningitis better predicted using our new predictive score meningisss

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Background and Aims:

Knowing the individual child's risk is highly useful when deciding treatment strategies. In this study, we aimed to develop and test a new predictive score for bacterial meningitis.

Methods:

We developed our Meningitis Swedish Survival Score (MeningiSSS) based on a previous systematic review of risk factors. Using data acquired from medical records of 101 children with bacterial meningitis, we tested the overall capabilities of the MeningiSSS compared to four existing predictive scores using a receiver operating characteristic curve (ROC) analysis. Finally, we tested all predictive scores at their cut-off levels using a chi-square test.

Results:

For predicting need of invasive procedures to manage intracerebral pressure, the MeningiSSS excelled in the ROC-analysis classifying it as excellent (AUC = 0.90) and also was the only predictive score able to identify all cases at its cut-off level (25 vs 0%, $p < 0.01$). For intensive care, only the MeningiSSS (AUC = 0.79) and the Simple Luanda Scale (AUC = 0.75) were classified as fair, whereas others performed poorly.

Whilst none of the scores did well at predicting complications, the MeningiSSS (AUC = 0.70), Niklasson Scale (AUC = 0.72) and the Herson-Todd Scale (AUC = 0.79) were classified as fair at predicting death.

Conclusions:

The MeningiSSS outperformed existing scores at predicting need of invasive procedures to regulate intracerebral pressure in children with bacterial meningitis and was able to predict death and need of intensive care with high certainty; making the MeningiSSS potentially very helpful when making difficult treatment decisions.

Systematic Review Registration:

ESPID19-0047
Science and Educational Track

E-Poster discussion session 04 - Diagnostics - Station 07

Accuracy of quantiferon-tb gold plus test for tuberculosis diagnosis in children.
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Background and Aims:

Diagnosis of childhood tuberculosis (TB) is challenging due to non-specific clinical and radiological signs and difficulty in obtaining microbiological confirmation.

The role of interferon gamma (IFN-g) release assays (IGRAs), in particular of QuantiFERON-TB Gold In-Tube (QFT-IT), for the diagnosis of TB infection in pediatric population has been evaluated and its efficacy demonstrated.

Recently, QFT-IT has been replaced by QuantiFERON-TB Gold Plus (QFT-Plus; Qiagen, Germantown, MD). The new generation QFT-Plus has two different antigen-coated tubes called TB1 (green tube), which contains peptides derived from ESAT-6 and CFP-10, and TB2 (yellow tube), which contains the same peptides with additional short peptides which potentially stimulate $CD8^+$ T cells.

In this retrospective cross-sectional study, we aimed to evaluate the accuracy of the QuantiFERON-TB Plus (QFT–Plus) among 196 young children aged 0 to 17 years old who were evaluated for LTBI screening, enrolled with suspected active TB or in therapy.

Methods:

Following clinical, microbiological and radiological assessment, children were tested by QFT-Plus assay and qualitative and quantitative responses to TB1 and TB2 stimuli are analyzed according to age, origin and diagnosis.

Results:

Among the 196 children enrolled in the study we identified 18 cases of LTBI and 10 cases of active disease. Sensitivity for active TB was 80% and specificity was 93.8%.

Among 5 (2,6%) children with indeterminate results, viral infections were diagnosed in 4 (80%) cases and 1 child was an oncologic subject (20%). Quantitative IFN-g response was not significantly different in children with active TB compared to those with LTBI.

Conclusions:

Our results indicate that QFT-Plus has specificity similar to QFT-GIT assay in pediatric population and quantitative QFT-Plus values (TB2-TB1 IFN-g UI/ml) do not provide additional prognostic information to discriminate active TB to LTBI.

Systematic Review Registration:

N/A

ESPID19-0847
Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Assessing the ongoing impact of rotavirus vaccination in the united kingdom

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Background and Aims:

The UK added rotavirus vaccine (Rotarix GlaxoSmithKline) to the national immunisation schedule in July 2013. We reported significantly reduced disease rates after one year of vaccination, with a smaller fall in the second year. Following ongoing active surveillance, we now report the epidemiological trends for five years since vaccine introduction.

Methods:

During the 2012-2018 rotavirus seasons, children attending our regional paediatric emergency department with gastroenteritis (>2 loose stools and/or >1 vomiting episode in preceding 24 hours) had stool virology analysis (real-time PCR), severity, and clinical outcome recorded.

Results:

Adjusting for overall rises in attendance; all cause gastroenteritis (AGE) attendances and admissions remained half of that in the pre-vaccine era. Median age of gastroenteritis cases rose from 18 to 31 months. In 2018 the proportion of rotavirus positive samples plateaued at 6% (95% CI 3-12%). There was no sustained shift towards non-vaccine genotypes or to disease in older unvaccinated children. Although a significant diagnostic gap remains, the predominant causes are now adenovirus (24%) and norovirus (16%).

Vaccine	Pre	Pre	Post	Post	Post	Post	Post
01 Jan - 31 Jun	2012	2013	2014	2015	2016	2017	2018
Total Attendances	16709	15816	16134	18305	20436	20112	21424
No. AGE attendances	1464(9%)	1207(8%)	689(4%)	865(5%)	820(4%)	1011(5%)	1050(5%)
No. AGE Admissions(%)	297(1.7%)	223(1.5%)	136(0.8%)	205(1.1%)	168(0.8%)	185(0.9%)	277(1.2%)
Attendance Percentage samples rotavirus positive	48	50	22	23	3	7	6

Conclusions:

Rotavirus vaccination introduction in the UK has drastically changed gastroenteritis epidemiology, with sustained reductions in hospital attendances and admissions consistent with high levels of vaccine coverage. We are seeing no biennial cycling as in the US, or evidence of genotype escape from the monovalent vaccine.

Systematic Review Registration:

n/a

ESPID19-0788
Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Persistence of the immune response after 4cmenb primary vaccination, and the response to a booster dose in infants, children, adolescents and young adults

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Background and Objective

Neisseria meningitidis serogroup B (MenB), the main cause of invasive meningococcal disease (IMD) in many countries, has incidence peaks in infancy and adolescence. The multicomponent 4CMenB vaccine has demonstrated real-life effectiveness. However, the need for/timing of booster doses is not yet established, and this remains a significant issue for start-up funding and future risk management for national programs. We studied the available data on antibody persistence and booster after 4CMenB priming across different age groups.

Methods

We analyzed the available data (8 studies – 9 cohorts) assessing antibody persistence after 4CMenB priming and the immunogenicity of a booster dose in infants, children, adolescents and young adults.

Learning Points Discussion

- Seroprotective hSBA (serum bactericidal assay using human complement) titres were demonstrated in ≥76% of infants for at least one 4CMenB vaccine antigen 2-3 years after 3 or 4 doses of 4CMenB.
- 7.5 years after two 4CMenB doses, ≥84% of adolescents showed seroprotective hSBA titres against at least 1 vaccine antigen.
- The precise level and combination of protective antibodies raised from the different antigens in 4CMenB that are responsible for real-life impact and effectiveness is not yet clear.
- The declining trend of vaccine-induced antibodies to 4CMenB antigens varies, with antibodies to NHBA (Neisserial heparin binding antigen) and NadA (*Neisseria* adhesin A) persisting longer than antibodies to PorA (porin A) and fHbp (factor H binding protein).
- A booster dose significantly and rapidly increased antibody levels to all 4 vaccine components, showing that primary 4CMenB vaccination induced robust immunologic priming irrespective of the schedule.
- Real-life data will further contribute to understanding correlations between immune patterns of 4CMenB-induced antibody persistence and long-term clinical protection against IMD, as well as the potential need for booster doses.

Funding: GlaxoSmithKline Biologicals SA

ESPID19-0295
Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Colonization with staphylococcus aureus in community-dwelling spanish children (cosaco). Preliminary data on a multicenter nationwide study

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Background

Prevalence of *Staphylococcus aureus* and MRSA colonization may be rising among European children. There is marked geographical variation in MRSA burden so nationwide paediatric data are warranted. Our aims are to assess current prevalence and epidemiology of nasal colonization by *S. aureus* and MRSA in children in Spain and risk factors associated in order to guide empirical treatment policies.

Methods

Observational, prospective, multicenter study in primary care centres all over Spain including patients <15 years with no other infectious diseases at time of enrolment. Clinical-epidemiological data were assessed and nasal aspirates collected (March to July 2018) for culture and characterization of antibiotic resistance of *S. aureus*. Molecular characterization of MRSA strains is currently being performed.

Results

A total of 1876 patients were enrolled (mean age 6.59 –SD: 4.36-; 50.4% female). Prevalence of colonization with *S. aureus* was 33% (95% CI, 30.8–35.1). Total MRSA prevalence was 1.44% (0.78–2.1) and 4.4% (2.72–6.08) among colonized children. Factors associated with increased risk of *S. aureus* colonization were age ≥ 5 years (OR 2.92; 95% CI, 2.33–3.67), male sex (OR 1.37; 1.13-1.67), urban setting (OR 1.37; 1.03-1.81), day-care or school attendance (OR 2.19; 1.65-2.92), previous cutaneous infection (OR 1.29; 1.01-1.63) and presence of chronic disease (OR 1.44; 1.18-1.76). The only factor associated with increased risk of MRSA colonization was rural setting (OR 3.49; 1.46-8.37). Logistic regression analysis showed significantly higher probability of colonization in older children, males, urban setting and chronic diseases. Percentage of susceptible, intermediate or resistant strains (Figure 1).

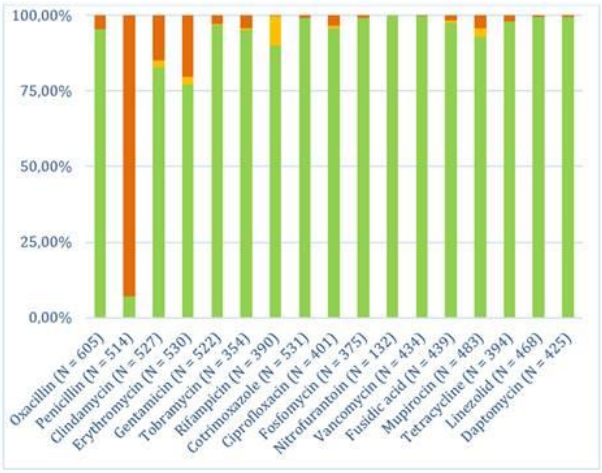

Figure 1. Antibiotic resistance of isolated *S. aureus* strains (Green - susceptible; Yellow - intermediate; Red - resistant). N means number of strains where antibiotic was evaluated.

Conclusions

Prevalence of colonization with *S. aureus* in Spanish children is higher than expected. MRSA colonization prevalence is low but higher than reported in adults.

Acknowledgement

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Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0515
Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Risk of cytomegalovirus transmission in women with igg avidity in the grey zone during first trimester prenatal testing

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Background and Aims:

Cytomegalovirus (CMV) is the most common congenital viral infection and regarded as the leading non-genetic cause of sensorineural hearing loss. Currently, international consensuses discourage prenatal screening of pregnant women. However, in few countries mainly in Southern Europe, screening of pregnant women for CMV infection is common practice. Management of women found with IgG+/IgM+ and IgG avidity titers in the grey zone during first trimester is difficult and causes significant stress to both parents and HCW.

Methods:

Pregnant women referred to our outpatient clinic because of diagnosis of acute CMV infection (IgM+/IgG+) during early pregnancy (gestational age ≤ 14 weeks) and IgG avidity in the grey zone were prospectively followed. The administration of CMV-HIG was discussed and follow-up included fetal U/S, amniocentesis for CMV-DNA detection and MRI when appropriate.

Results:

Eighty women (mean age 31) were retrospectively analyzed. Most (62 women) received CMV-HIG.Five women terminated pregnancy (3 for reasons unrelated to CMV and 2 because of CMV-positive amniotic fluid) and 77 babies were born asymptomatic. Two newborns were diagnosed with congenital CMV infection. The overall transmission rate was 5%. No adverse outcomes were detected during follow up (median 24 months). Maternal age, parity,IgG avidity levels, maternal CMV-viremia upon diagnosis, delay between diagnosis and consultation,gestational week of first consultation, administration of CMV-HIG and number of doses, were not associated with risk of vertical CMV transmission.

Conclusions:

Transmission of CMV infection to the fetus in pregnancies with acute CMV-infection and IgG avidity titers in the grey zone during first trimester was 5%, higher than that in infants born post non-primary infection during pregnancy. This information is of value when consulting pregnant women.

Systematic Review Registration:

N/A

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Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

The importance of developing a european network to study invasive group a streptococcal infection in children: results from a european multicenter survey

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Background and Aims:

Invasive Group A Streptococcal infection (iGASi) causes high morbidity in children**.** Aim: To evaluate the epidemiology and management of iGASi at different European Institutions and determine the feasibility of a European iGASi Network.

Methods:

Survey developed by the Spanish GAS Network (PeiSGA) following the ESPID2017 iGASi Research-Lunch.

Results:

Twenty-six institutions (9 European countries) participated (Spain: 62%). Median number of pediatric beds was 52 (28-145). Fifty-six percent of participants considered that the iGASi incidence is increasing: currently around 5 cases (2-11)/year. The estimated median rate of PICU admission and surgery for these children is 25% (10-55%) and 20% (3-22%), respectively, with community-acquired GAS-infection considered second in importance after pneumococcal disease. Mortality rate is low (<1%). Most frequent clinical syndromes are skin/soft tissue infections, followed by pneumonia, ENT infections, toxic shock syndrome (TSS) and osteoarticular infections. Pneumonia, TSS and necrotizing fasciitis (NF) are considered most severe. Ninety-two percent of centers perform GAS antigen, whereas only 32% (47% in centers with PICU vs 10%; p=0.08) and 16% determine GAS-PCR and serotypes, respectively. The estimated rate of Macrolide/Clindamycin-resistance is 13% (5-20%) and 5% (2-10%), respectively.

Penicillin/Ampicillin is the preferred therapy for iGASi (96%), adding Clindamycin in severe cases, especially TTS/NF (100%), sepsis (69%), complicated pneumonia (58%) and osteoarticular infections (54%). IVIG is administered in TSS (65%) and NF (38%). Participants considered it important to further study iGASi in European children (rated 9; 0-10 scale) and 92% would join a European/International iGASi Network; 96% of institutions could collect blood samples, 48% serotype/genotype strains and 56% study toxins.

Conclusions:

Pediatricians within Europe consider it important to further study iGASi. To determine serotypes and toxins of circulating strains, as well as developing a management consensus may be of great interest.

Systematic Review Registration:

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Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Whole genome analysis of longitudinal pharyngeal samples shows persistence of carriage with the same meningococcal strain

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Background

Prevalence and duration of meningococcal carriage are likely to vary according to host, organism and environmental factors. Genome analysis of meningococcal carriage strains within an individual over time should show dynamic changes in the bacteria and the persistence of specific strains.

Methods

Longitudinal pharyngeal samples were collected from students in Bristol, UK at five monthly visits. After culture, meningococci were whole genome sequenced using Illumina. The genetic diversity of ten paired longitudinal samples were compared based on MLST allelic distance metrics.

Results

The ten paired samples were from students in six different schools, the interval between samples in each pair varying from one to five months. Paired samples in nine individuals were closely related (three ST53_complex, two ST198_complex, one (ST_213_complex, ST_1167_complex, ST_3551_complex, ST_22_complex)). Of these nine, three ST53_complex pairs were cnl, strain designation (cnl: P1.7,30: F1-2: ST-53 (cc53), *Fhbp* variants B, *fhbP* peptide 2. Two of these three subjects attended the same school, both males in the same school year. The third subject with the same stain came from a different school. Social connection between these students is not known. Samples from one pair (one of two pairs with a five-month interval) had different capsular genogroups, STs, *fHbp* variants and strain designations.

Conclusions

The persistence of carriage with same strain in the same individual over several months confirms that meningococcal carriage sometimes persists for several months. Whole genome sequencing is a valuable tool in such longitudinal studies to assess the dynamics of meningococcal carriage.

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Clinical Trial Registration (Please input N/A if not registered)

N/A

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Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Modelling the potential impact of 4cmenb infant vaccination against invasive meningococcal disease (imd) caused by neisseria meningococcal (nm) serogroups w and y in england

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Background

Recently, *Nm* serogroup W and Y IMD cases (MenWY) have risen across Europe with MenWY causing 38% of IMD cases in England in 2017/2018 alone. 4CMenB-induced killing of non-MenB strains with human serum bactericidal assay (hSBA) suggests potential cross-protection of 4CMenB vaccination against MenWY. We assessed the potential impact of the cross-protection of hypothetical 4CMenB infant with quadrivalent meningococcal conjugate ('4CMenB/MCV4') toddler and adolescent vaccination against MenWY in children aged 0-4 years in England.

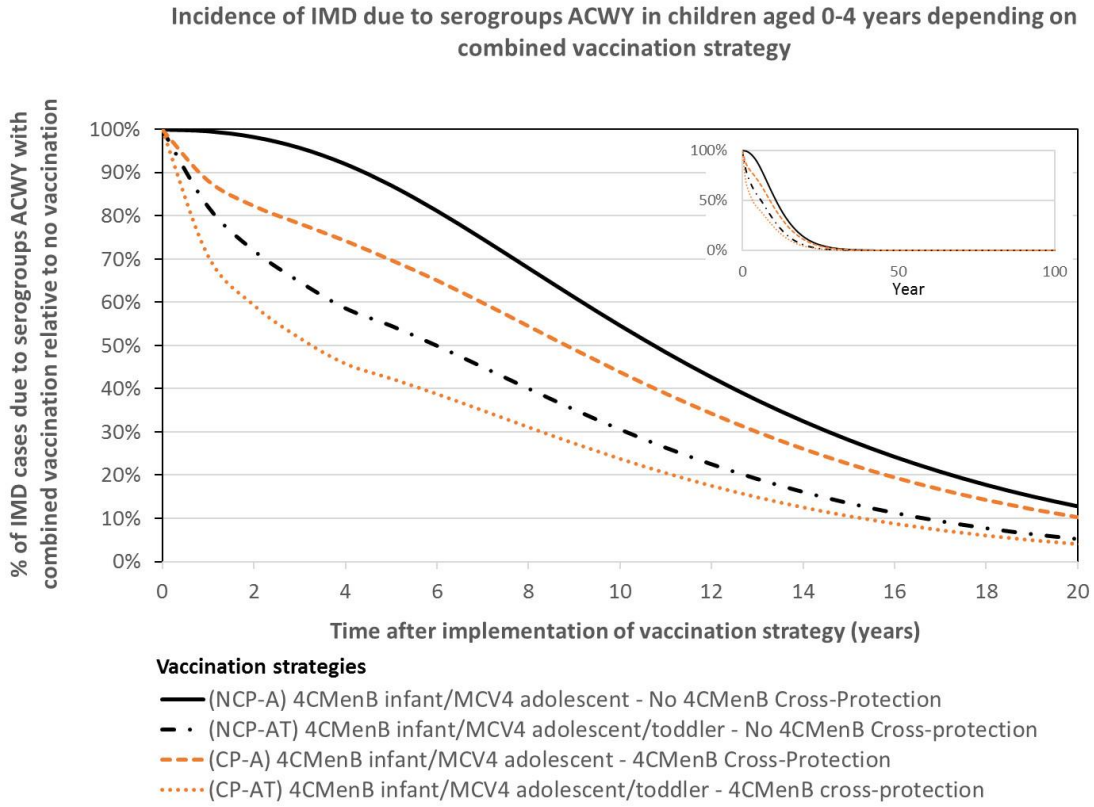
Methods

A dynamic disease transmission model was developed to study the impact of '4CMenB/MCV4' vaccination in comparison to no '4CMenB/MCV4' vaccination on transmission of meningococcal carriage and IMD of MenB, MenACWY and 'other' serogroups. 4CMenB was assumed to protect against MenWY conditional on protection against MenB and hSBA killing rate was used to estimate vaccine effectiveness against MenWY. Impact of 4CMenB infant vaccination on MenWY in ages 0-4 years was studied assessing 4CMenB infant with either MCV4 adolescent(A) or MCV4 adolescent/toddler(AT) vaccination with and without 4CMenB cross-protection (CP/NCP).

Results

Short term, cross-protection of 4CMenB-vaccinated infants results in a steeper decline in MenACWY incidence in 0-4 year olds (Figure:CP-A;CP-AT) when compared with '4CMenB/MCV4' vaccination without 4CMenB cross-protection (NCP-A;NCP-AT). Steepest decline occurs in infants. At 5y post vaccination implementation, (CP-A) '4CMenB/MCV4' adolescent with cross-protection and (NCP-AT) '4CMenB/MCV4' adolescents/toddler without cross-protection result in 30.2% and 45.4% reduction in MenACWY incidence. Long-term, differences diminish due to herd-effects of MCV4 adolescent

vaccination [Figure].



Conclusions

Short term, 4CMenB infant vaccination may confer cross-protection, more rapidly reducing MenWY incidence in ages 0-4 years than '4CMenB/MCV4' vaccination without 4CMenB cross-protection. Results suggest that policy decisions regarding MCV4 toddler vaccination should incorporate 4CMenB infant vaccination, potential cross-protection and combined cost-effectiveness.

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Clinical Trial Registration (Please input N/A if not registered)

N/A

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Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Prevalence of non-susceptible bloodstream isolates is higher among hospitalized older children and patients from non-neonatal units: a multicentre spanish study

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Background and Aims:

Increase in antibiotic resistance is becoming a threat. Although data about isolates from adults are broad, they are scarce for children. We aimed to describe and compare antibiotic resistance prevalence in bloodstream isolates from high-complexity paediatric units in Madrid according to unit and age.

Methods:

From January 2013 to December 2017, Enterobacterales, *Staphylococcus aureus*, *Enterococcus* spp. and *Pseudomonas aeruginosa* isolated from bloodstream in <18-year-old patients admitted to Paediatric Intensive Care (PICU), Neonatology or Oncology-Haematology ward at three tertiary hospitals in Madrid (Spain) were evaluated. The same isolate within 14 days of a previous one was excluded. Non-susceptibility prevalence was compared according to unit and age groups (<6 and ≥6 months). Isolates with resistance or intermediate susceptibility were classified as non-susceptible according to EUCAST breakpoints.

Results:

A total of 770 isolates were included (436 Enterobacterales, 198 *Enterococcus* spp., 78 *S. aureus*, and 58 *P. aeruginosa*). There were 472 isolates from Neonatology, 198 from PICU and 100 from Oncology-Haematology ward. A great majority of isolates were from children <6 months (566, 74%). Enterobacterales isolated from Oncology-Hematology had the highest prevalence of non-susceptible isolates (table 1), whereas *P. aeruginosa* from PICU had a trend to higher non-susceptibility compared to other units. MRSA prevalence was low in all units, without differences among them. Children ≥6 months had a higher odds (adjusted to hospital and unit) for non-susceptible Enterobacterales and *Enterococcus* spp., a non-significant trend to higher resistance in *P. aeruginosa*, but no differences in *S. aureus*

susceptibility.

	Total (N=770)	Neonatology (N=472)	PICU (N=198)	Oncology-Haematology (N=100)	p-value
Enterobacterales (n=436)					
ESCs	59/433 (13.6%)	23/ 268 (8.6%)	20/10 (19%)	16/60 (26.7%)	**<0.001**
Fluoroquinolones	45/433 (10.4%)	19/268 (7.1%)	10/105 (9.5%)	16/60 (26.7%)	**<0.001**
Carbapenems	16/433 (3.7%)	3/268 (1.1%)	8/105 (7.6%)	5/60 (8.3%)	**0.001**
Aminoglycosides	133/433 (30.7%)	69/268 (25.7%)	45/105 (42.9%)	19/69 (31.7%)	**0.005**
MDR	30/433 (6.9%)	8/268 (3%)	13/105 (12.4%)	9/60 (15%)	**<0.001**
S. aureus (n=78)					
Methicillin	4/78 (5.1%)	2/51 (3.9%)	0/9 (0%)	2/18 (11.1%)	0.375
P. aeruginosa (n=58)					
Antipseudomonal ESCs	13/58 (22.4%)	3/16 (18.8%)	8/29 (27.6%)	2/13 (15.4%)	0.625
Fluoroquinolones	18/58 (31%)	2/16 (12.5%)	12/19 (41.4%)	4/13 (22.2%)	0.134
Carbapenems	18/58 (31%)	4/16 (25%)	10/29 (34.5%)	4/13 (30.8%)	0.805
Aminoglycosides	16/58 (27.6%)	2/16 (12.5%)	11/29 (37.9%)	3/13 (23.1%)	0.173
MDR	13 /58 (25.9%)	3/16 (18.8%)	8/29 (27.6%)	2/13 (15.4%)	0.625
Enterococcus spp (n=198)					
Ampicillin	29/198 (14.6%)	7/136 (5.1%)	20/53 (37.7%)	2/9 (22.2%)	**<0.001**
Vancomycin	5/198 (2.5%)	0/136 (0%)	3/53 (5.7%)	2/9 (22.2%)	**<0.001**

Table 1. Number and percentage of non-susceptible bloodstream isolates from the different units. P-value calculated using χ^2 test. PICU, Paediatric Intensive Care Unit; ESCs, extended-spectrum cephalosporins; MDR, Multidrug-resistant.

Conclusions:

Older children and patients from non-neonatal units had the highest risk for non-susceptible isolates, but, overall, Neonatology accounted for the highest burden of bloodstream isolates. The existence of antibiotic resistance surveillance seems important in these units.

Systematic Review Registration:

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Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Safety data for menb-fhbp in healthy individuals 10 years of age and older: a review of clinical trials

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Background

The vaccine MenB-FHbp (Trumenba®; bivalent rLP2086; Pfizer Inc, Philadelphia, PA) is licensed to prevent meningococcal serogroup B disease in those aged ≥10 years in Europe and 10–25 years in the United States. The MenB-FHbp clinical development program in this age group included 11 completed trials in which a primary vaccination series was given. However, individual randomized clinical trials usually do not enroll enough subjects to detect rare events. Therefore, the current analysis assessed pooled safety data from all 11 clinical trials, allowing evaluation of MenB-FHbp safety in a large population and increasing the likelihood of detecting rare events or safety signals not identified during individual clinical trials.

Methods

The safety dataset included pooled adverse event (AE) data from all 11 trials involving individuals aged 10–65 years. AEs were categorized as immediate AEs (IAEs), medically attended AEs (MAEs), serious AEs (SAEs), newly diagnosed chronic medical conditions (NDCMCs), and autoimmune or neuroinflammatory conditions. Reactogenicity data were pooled for 7 of the 8 controlled trials.

Results

15,294 and 5509 subjects were included in the MenB-FHbp and control groups, respectively. Local and systemic reactogenicity events were reported more frequently in the MenB-FHbp groups compared with controls, consistent with individual trial observations. The frequencies of grouped IAEs, SAEs, MAEs, NDCMCs, and autoimmune or neuroinflammatory conditions were similar between MenB-FHbp and control groups.

Table

	MenB-FHbp n=15,294*		Control n=5509*	
	n (%)	95% CI	n (%)	95% CI
During vaccination phase				
AE	6454 (42.2)	41.42, 42.99	2296 (41.7)	40.37, 42.99
Related AE	1627 (10.6)	10.15, 11.14	336 (6.1)	5.48, 6.76
Severe AE	489 (3.2)	2.92, 3.49	159 (2.9)	2.46, 3.36
Immediate AE (within 30 minutes after any dose)†	227 (1.5)	1.34, 1.75	69 (1.3)	1.00, 1.62
Serious AE	191 (1.3)	1.08, 1.44	74 (1.3)	1.06, 1.68
Medically attended AE‡	2090 (23.3)	22.45, 24.22	864 (23.8)	22.44, 25.24
Newly diagnosed chronic medical conditions	88 (0.6)	0.46, 0.71	41 (0.7)	0.53, 1.01
Throughout study				
Serious AE	269 (1.8)	1.56, 1.98	106 (1.9)	1.58, 2.32
Related serious AE	8 (0.1)	0.02, 0.10	2 (0.04)	0, 0.13
Medically attended AE‡	2514 (28.1)	27.13, 29.00	1047 (28.9)	27.40, 30.37
Newly diagnosed chronic medical conditions	119 (0.8)	0.64, 0.93	57 (1.0)	0.78, 1.34
Neuroinflammatory conditions	8 (0.1)	0.02, 0.10	4 (0.1)	0.02, 0.19
Autoimmune conditions	25 (0.2)	0.11, 0.24	6 (0.1)	0.04, 0.24
AE leading to discontinuation	163 (1.1)	0.91, 1.24	28 (0.5)	0.34, 0.73
Deaths	5 (0.03)	0.01, 0.08	0 (0.0)	0, 0.07

AE=adverse event; MenB-FHbp=meningococcal serogroup B – factor H binding protein vaccine (Trumenba®).
*Unless otherwise specified.
†Excluding subjects from NCT00879814, NCT00808028, and NCT00780806 for the MenB-FHbp group and NCT00879814 and NCT00808028 for the control group because AE start times were not recorded; MenB-FHbp, n=14,783; control, n=5376.
‡Including only subjects from NCT01830855, NCT01352845, and NCT01352793; MenB-FHbp, n=8960; control, n=3627

Conclusions

Pooled analysis of >15,000 vaccine recipients provided the opportunity to review rigorously collected clinical trial data to identify potential rare or very rare adverse events. No safety signals were identified in this pooled analysis that had not been identified in review of the individual studies; safety and tolerability findings from individual studies were confirmed.

Clinical Trial Registration (Please input N/A if not registered)

NCT00879814/NCT00808028/NCT01830855/NCT01323270/NCT01461993/NCT01352793/NCT01461980/NCT01352845/NCT00780806/NCT01299480/NCT01768117. Funded by Pfizer.

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Science and Educational Track

E-Poster discussion session 05 - Public health and epidemiology - Station 09

Rsv: 19 years of active surveillance in a children´s hospital

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Background and Aims:

Respiratory Syncytial Virus (RSV) is the leading cause of acute lower respiratory infection (ALRI) in children. We aimed to describe the clinical-epidemiological pattern and risk factors for mortality associated with RSV infection.

Methods:

A prospective, cross-sectional study of ALRI in children admitted to a Children's Hospital among 2000-2018. Viral diagnosis was made by fluorescent antibody techniques or real time-PCR. We compared clinical-epidemiological characteristics of RSV infection in non-fatal versus fatal cases. Multiple logistic regression was used to identify independent predictors of mortality.

Results:

From a total 16,018 patients with ALRI, 13,545(84.6%) were tested for respiratory viruses, 6047(45%) were positive: RSV 81.1%(4907), influenza 7.5%(456), parainfluenza 6.9%(419) and adenovirus 4.4%(265). RSV had a seasonal epidemic pattern coinciding with months of lowest average temperature. RSV mortality rate: 1.7%(83/4855). Fatal cases had a higher proportion of: prematurity($p<0.01$), perinatal respiratory history($p<0.01$), malnourishment($p<0.01$), congenital heart disease($p<0.01$), chronic neurological disease($p<0.01$) and pneumonia as clinical presentation (<0.01). No significant difference between gender was observed. The annual mortality rate distribution was not stable over the study period with the highest mortality in the year 2002. Most deaths occurred among children who had complications: respiratory distress (80.7%), sepsis (31.3%) and atelectasis (13.2%). Independent predictors of RSV mortality were: moderate to severe malnourishment OR 3.46 (95% CI 1.86-6.43) $p< 0.01$, chronic neurological disease OR 3.96 (95% CI 2.03-8.07) $p< 0.01$, congenital heart disease OR 3.93 (95% CI 2.25-6.87) $p<0.01$, age under 6 months OR 2.25 (95% CI 1.39-3.64) $p<0.01$ and pneumonia as clinical presentation OR 1.80 (95% CI 1.13-2.85) $p=0.01$.

Conclusions:

RSV showed an epidemic pattern affecting mostly young children. Malnourishment, chronic neurological disease, congenital heart disease, age under 6 months and pneumonia were the independent risk factors for RSV mortality.

Systematic Review Registration:

N/A

ESPID19-0948
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Emergence of mycobacterium lentiflavum as the main cause of cervical nontuberculous lymphadenitis in madrid, spain

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Background and Aims:

Nontuberculous mycobacteria (NTM) are a common cause of cervical lymphadenitis in otherwise healthy children. Prompted by the increasing number of *M. lentiflavum* isolates identified at our health area, we investigated the current prevalence and clinical characteristics of NTM lymphadenitis in children.

Methods:

Retrospective single-center study including patients below 18 years with culture-confirmed cervical NTM lymphadenitis in the 1996-2018 period.

Results:

Fifty-four patients (50% males; median[IQR] age, 2[1.6-2.8] years) were included. Most patients had unilateral (94%), single-site (69%) lymphadenitis (68% submandibular, 32% cervical, 22% preauricular). Clinical stages at diagnosis were 1 (painless and firm), 2 (fluctuant), 3 (skin changes) and 4 (fistula) in 54%, 9%, 35% and 2%, respectively. *Mycobacterium lentiflavum* (27 cases, 50%) and *M.avium*, (19 cases, 35%) were the most common causative species. TST induration was ≥5mm in 54%. IGRAs were performed in 20 cases (37%), 17 were negative and 3 positive (2 *M.lentiflavum*, 1 *M.avium*) which became negative when repeated. Initial treatment was clinical observation (7%), antibiotics (28%), surgery (17%) and antibiotics plus surgery (48%). Complications included fistula formation (30%), hypertrophic/keloid scars (17%), facial nerve palsy (15%) and recurrence (14%).

Infections caused by *M.lentiflavum* were more frequent in the 2008-18 period (85% vs 15%,p<0.001). Compared to other NTM, there were no differences regarding age, location, stage at diagnosis or complications. However, *M.lentiflavum* lymphadenitis were more frequently treated initially with antibiotics plus surgery (67% vs 30%,p=0.01), needed longer treatment (16[11-24] vs 7.5[4-16] weeks, p=0.007) and surgical excision (78% vs 37%,p=0.006).

Conclusions:

Mycobacterium lentiflavum is an emerging pathogen in NTM cervical lymphadenitis in children in Madrid. It is clinically similar to other NTM adenitis, but requires more often long-term antibiotic therapy and complete surgical excision.

Systematic Review Registration:

ESPID19-0929
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Evaluation of quantiferon-tb gold test in mycobacterium lentiflavum lymphadenitis

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Background and Aims:

Most nontuberculous mycobacteria (NTM) lack the TB-specific antigenic proteins used by QuantiFERON-TB Gold test (QFR-G) with the exception of *M.szulgai, M.marinum, M.kansasii* and *M.flavescens,* which are very infrequent in pediatric lymphadenitis. *M. lentiflavum* has recently emerged as the most common cause of NTM lymphadenitis in our area. Our aim was to assess the performance of QFR-G in children with *M. lentiflavum* lymphadenitis.

Methods:

In the 1996-2018 period, 54 patients with culture-confirmed NTM lymphadenitis were diagnosed at our hospital: 27 (50%) caused by *M.lentiflavum* and 27 caused by other NTM (19 *M. avium*, 2 *M.intracellulare*, 2 *M.simiae*, 2 *M.fortuitum*, 1 *M.chelonae*, 1 *M.scrofulaceum)*.

Results:

Infections caused by *M. lentiflavum* were more frequent in the 2008-18 period (15% vs 85%, $p<0.001$). Median [IQR] age at diagnosis was 22.9 [19.5-32.3] months. Only two patients were immigrants and had been BCG-vaccinated. Tuberculin skin test (TST) was performed in 24 cases, with 14 (58.3%) positive results (median [IQR] induration 9 [7-11]mm). QFR-G was performed in 14 patients, 5 with negative and 9 with positive TST. Two were positive (14%) at baseline, but negative when repeated. Both patients had positive TST.

We examined the data from patients diagnosed with NTM lymphadenitis in 1996-2018 included in the national NTM lymphadenitis registry, excluding those from our institution. Out of 139 NTM, there were 50 *M.lentiflavum* (35.9%), mostly in the Madrid area (78%). QTF-G was performed in 28 (56%), 2 were indeterminate and one positive, which became indeterminate when repeated.

Conclusions:

Most children with *M.lentiflavum* lymphadenitis have negative QFR-G results, but positive or indeterminate results may occur. In patients with positive QFR-G, repeated testing is recommended to distinguish between tuberculosis infection and a false-positive test result.

Systematic Review Registration:

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ESPID19-0320
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Performance evaluation of clinical criteria and antibodies in lymphocyte supernatant in diagnosing tuberculosis in severely malnourished children

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Background

The diagnosis of childhood tuberculosis (TB) can be difficult in severely malnourished children as the clinical signs of TB are often subtle in these children. Data on the diagnostics of TB in such population are also very limited. Our aim was to evaluate the performance of composite clinical criteria and a technique that measures antibodies in lymphocyte supernatant (ALS) for the diagnosis of TB in such children.

Methods

Severely malnourished Bangladeshi children under five hospitalized for cough or respiratory distress and radiological pneumonia were enrolled consecutively following informed consent. We collected venous blood for ALS, gastric lavage fluid and induced sputum for microscopy, mycobacterial culture, and real-time PCR by Xpert MTB/RIF. We compared the sensitivity, specificity, positive and negative predictive values, and accuracy of modified Kenneth Jones criteria (MKJC) score, World Health Organization (WHO) criteria, and ALS in diagnosing TB in severely malnourished children with pneumonia for “Confirmed TB” and “All TB” (“Confirmed TB” plus “Probable TB”) versus “Not TB”.

Results

Compared to culture confirmed TB, the sensitivity and specificity (95% CI) for MKJC were 60 (27-86)% and 84 (79-87)% and for WHO criteria were 40 (14-73)% and 84 (80-87)% respectively. Compared to culture and/or Xpert MTB/RIF positive TB, the sensitivity and specificity (95% CI) for the criteria were 37 (20-58)% and 84 (79-87)%; and 22 (9-43)% and 83 (79-87)% respectively. For both these comparisons, the sensitivity and specificity of ALS were 50 (14-86)% and 60 (53-67)% respectively.

Conclusions

The results underscore the importance of using clinical criteria for the diagnosis of TB in severely malnourished children that may help to minimize the chance of over treatment with anti-TB in such population, especially in resource limited settings.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0908
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

The changing trends of paediatric tuberculosis 2010-2018 – a uk single-centre experience

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Background and Aims:

The epidemiology of Tuberculosis (TB) in the United Kingdom (UK) is changing; the overall incidence of TB is decreasing. Recommendations for screening and management of paediatric TB contacts were revised in the National Institute for Health and Care Excellence (NICE) 2016 guidelines. We describe the incidence of paediatric TB in Bristol and assess the impact of the NICE guidelines changes to our patient cohort.

Methods:

We conducted a retrospective cohort review of the electronic patient records of children ≤17 years old referred to the paediatric TB service at Bristol Royal Hospital for Children for TB screening between the period 2010 and 2018. Descriptive analyses were carried out on demographic, clinical and microbiological data.

Results:

In total,1162 children were referred for screening. 196 (17%) children were diagnosed with latent TB infection (LTBI) and 64 (5.5%) with active TB (ATB). Since 2016, the number of referrals decreased by 38% however, the proportion of LTBI and ATB cases increased by 37% and 43% retrospectively. The majority of children were contacts of pulmonary TB. There were 3 LTBI and 2 ATB cases in contacts of extra-pulmonary TB. Microbiological confirmation was achieved in 15 (24%) children diagnosed with ATB. Mortality was low (0.1%) and all children otherwise completed treatment.

Conclusions:

The landscape of paediatric TB in our centre has changed over time with a decreasing annual number of children requiring TB screening and rising incidence rates in LTBI and ATB cases. This is likely to reflect the impact of the recommendation changes in the NICE 2016 guidelines. The data suggests that children exposed to both pulmonary and extra-pulmonary TB should be screened. Diagnosis of childhood TB remains problematic.

Systematic Review Registration:

not applicable

ESPID19-0755
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

The diagnostic challenge of nontuberculous mycobacteria lymphadenitis in children: possible role of mycobacterium avium lysate inf-γ, il-17 and il-2 elispot assays

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Background

Nontuberculous mycobacteria are the most frequent cause of chronic cervical lymphadenitis in childhood. The aim of the study was to evaluate the performance of IL-2, IL-17 and INF-γ in-house enzyme-linked immunospot assays using a *Mycobacterium avium* lysate, in order to identify a noninvasive diagnostic method of nontuberculous mycobacteria infection.

Methods

Children with subacute and chronic lymphadenopathies or with a previous diagnosis of nontuberculous mycobacteria lymphadenitis were prospectively enrolled in the study. For each child enrolled an additional sample of blood (3 mL) was obtained in occasion of venipuncture for the study test.

Results

Sixty children with lymphadenitis were included in our study: 16 with confirmed infection (Group 1), 30 probable infected (Group 2) and 14 uninfected (Group 3). Significantly higher median cytokine values were found in Group 1 *vs* Group 2, in Group 1 *vs* Group 3 and in Group 2 *vs* Group 3 considering IL-2 based enzyme-linked immunospot assay ($p=0.015$, $p<0.001$, $p=0.004$, respectively). INF-γ based enzyme-linked immunospotassay results were significantly higher in Group 2 vs Group 3 ($p=0.010$), while no differences were observed between Group 1 and Group 3. Differences between infected and uninfected children were not significant considering IL-17 assays ($p=0.431$). Comparing children included in Group 1 and Group 2 *vs* Group 3, significantly higher IL-2 and IFN-γ results were found in NMT infected children ($p<0.001$, $p=0.010$, respectively). *M. avium* lysate IL-2 based enzyme-linked immunospot assay showed sensitivity of 87.5% and specificity of 85.7% in discriminating between Group 1 and Group 3. Poorer performance was observed for IL-17 and INF-γ.

Conclusions

Mycobacterium avium lysate IL-2 and INF-γ based enzyme-linked immunospot assays are promising noninvasive diagnostic techniques for discriminating children with nontuberculous mycobacteria lymphadenitis and non-infected subjects.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0617
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Infections caused by rapidly growing mycobacteria

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Background and Aims:

Rapidly growing mycobacteria (RGM) are opportunistic pathogens, seldom affecting children. The aim of our study was to describe RGM infections in paediatric patients.

Methods:

Retrospective review of patients below 18 years with RGM infections in a tertiary hospital in Spain (2010 to 2018).

Results:

We identified 20 RGM isolates in 16 patients, median (IQR) age 7.5 (2-14.5) years, 62% female. Twelve had comorbidities (8 cystic fibrosis –CF-, 2 bronchiectasis, 1 liver transplant, 1 *complex* heart disease). Microbiological samples included respiratory tract (14), skin (2), adenitis (2), blood (1), urine (1). One was considered as environmental contamination (*M.mucogenicum* in urine in a healthy patient) and three as colonization in patients with chronic respiratory disease (2 *M.mucogenicum, 1 M.chelonae*). Final diagnoses of the remaining 12 patients were: 7 respiratory infections in patients with chronic respiratory disease (6 *M.abscessus* in CF, 1 *M.phocaicum* in a patient with bronchiectasis), 2 cervical adenitis (*M.fortuitum*), 1 skin infection (*M.chelonae*), 1 surgical wound infection (*M.senegalense*), 1 catheter-related bacteremia (*M.chelonae*). Eighteen percent of isolates were resistant to clarithromycin, 37% to amikacin, 66% to linezolid and imipenem and 82% to ciprofloxacin. Three of the six CF patients with *M.abscessus* infection did not receive initial antimicrobial therapy, and two had persistent positive cultures and worsening x-ray and lung function. The other three received prompt treatment with good outcome, although one suffered recurrences. The remaining infections resolved with antimicrobial therapy, but 3 required surgery (2 skin infections, 1 adenitis).

Conclusions:

RGM affect children with chronic respiratory disease, but they can also cause skin infections and adenitis. The most frequent species is *M.abscessus*, mainly in CF patients, requiring prompt aggressive treatment. As antimicrobial resistance is highly prevalent, combined prolonged therapy is recommended.

Systematic Review Registration:

N/A

ESPID19-0592
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Nontuberculous mycobacterial lymphadenitis in children: a 13-year retrospective study in a tertiary hospital.

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Background and Aims:

Nontuberculous mycobacterial (NTM) infection is an increasingly common cause of subacute lymphadenitis in children and sometimes presents a diagnostic challenge. Fine-Needle Aspiration Cytology (FNAC) can be a valuable diagnostic tool in this situation. This study describes clinical features, diagnostic and management strategies of NTM lymphadenitis in a tertiary hospital in Spain.

Methods:

FNAC of subacute lymphadenitis performed in patients <17 year-old from 2003 to 2016 were reviewed. Cases classified as “granulomatous inflammation” on cytopathological examination were selected. Within this group, cases that fulfilled criteria for NTM lymphadenitis were reviewed. Epidemiological, clinical and therapeutic features were registered.

Results:

367 FNAC were performed, of whom 58 (15,8%) were considered “granulomatous inflammation”. Within this group, 41 NTM lymphadenitis patients were identified. In children 1-5 year-old with subacute lymphadenitis, this diagnosis represented 33,3% of the FNAC performed.
Median age was 2,1 years (IQR=1,7-2,7). All affected nodes were cervical, mainly submandibular (28/41; 68,3%) and unilateral (37/41; 90,2%). Tuberculin skin test was > 10 mm in 10,7% of patients (3/28). Mycobacterial cultures were positive in 36,8% of cases (14/38). The most frequently isolated mycobacteria was *Mycobacterium lentiflavum* (9/14; 64,3%). Complete excision was performed in 75,6% of cases. An increasing trend of NTM lymphadenitis was observed in our cohort over the study period with 4 cases (9,8% of all FNAC) in 2003-2008 and 37 cases (90,2%) during 2009-2016.

Demographic characteristics	
Female gender, n (%)	25/41 (61.0%)
Age (years), median (IQR)	2,1 (1.7-2.7)
Clinical characteristics	
Time of evolution (weeks), median (IQR)	4 (2-8)
Location of lymphadenopathy, n (%)	
Submandibular	28/41 (68.3%)
Laterocervical	7/41 (17.1%)
Preauricular/Parotid	6/41 (14.6%)
Node size (cm), median (IQR)	2,8 (2-3,6)
Additional skin changes or fistula formation, n (%)	16/28 (57.1%)
Fever, n (%)	6/27 (22.2%)
Diagnostic tests	
TST induration, n (%)	
≥ 5 mm	4/28 (14.3%)
>10 mm	3/28 (10.7%)
Mycobacterial culture, obtained from FNAC or lymph node excision, n (%)	
Positive	14/38 (36.8%)
Mycobacterium lentiflavum	9/14 (64.3%)
Mycobaterium Avium Complex	4/14 (28.6%)
Mycobacterium Malmoense	1/14(7.1%)
Treatment options, n (%)	
Surgery alone	31/41 (75.6%)
Surgery and medical treatment	3/41 (7.3%)
Medical treatment alone	1/41 (2.4%)
Expectant management	6/41 (14.6%)
Abbreviations used: n=number; IQR=interquartile range; TST=tuberculin skin test; FNAC=fine needle aspiration cytology.	

Conclusions:

This study shows the usefulness of FNAC in the approach of subacute lymphadenopathies in children, particularly in the case of suspected NTM infections, where samples for cytopathology and microbiology

are valuable for diagnosis. In our setting, an increasing proportion of NTM lymphadenitis, as well as of the number of *Mycobacterium lentiflavum* cases over the last years are described.

Systematic Review Registration:

N/A

ESPID19-0541
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Tuberculin skin test, interferon-gamma release assays and bcg vaccination: correlation, discordance or misunderstanding?

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Background and Aims:

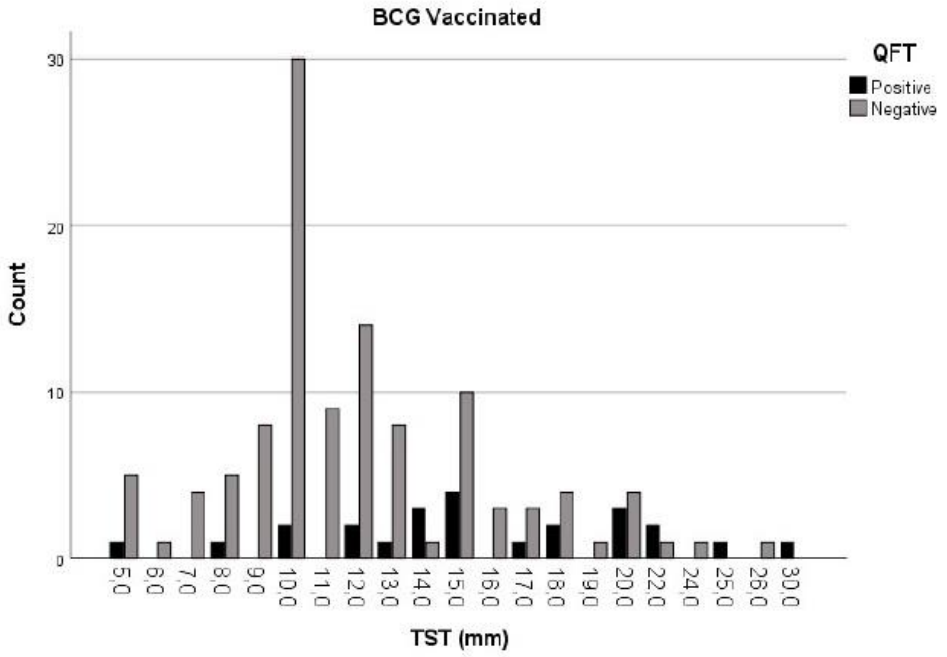
Childhood tuberculosis (TB) is still a major health problem worldwide. Migrants are a risk population for TB in low burden countries. TB contact tracing or latent tuberculosis infection (LTBI) screening, even with available tuberculin skin test (TST) and IGRA, is a challenge. Aim: to determine the correlation between TST and QuantiFERON®-TB Gold (QFT) test regarding BCG-vaccination and to evaluate the association to demographic factors.

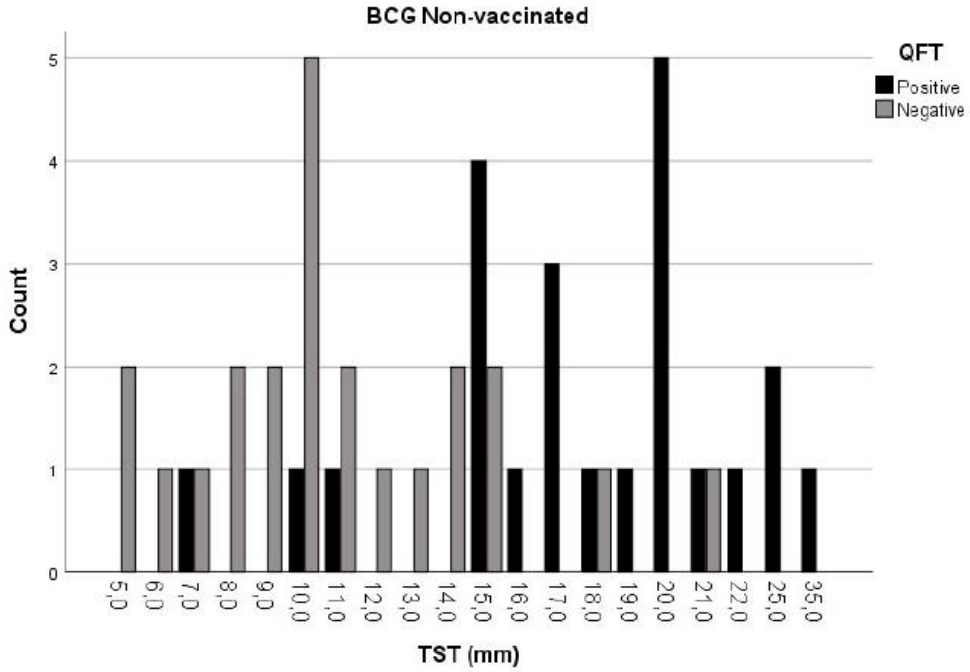
Methods:

Observational retrospective study of patients <18 years attended for the first time at a referral TB Unit for TB or LTBI assessment (January 2015-December 2017). Data were registered from clinical records and included epidemiological, demographic and clinical information, reason of consultation, TST/QFT results and final diagnosis. Children with positive TST and/or TB were studied in detail.

Results:

A total of 475 patients were included (52% female): 77.1% were uninfected, 16.6% were classified as LTBI and 6.3% as TB disease. Screening identified LTBI cases and contact tracing TB cases. Most of LTBI were immigrants, and travelers visiting friends and relatives were associated with TB. TST was positive in 210 children, 72.4% (152/210) vaccinated with BCG. Concordance TST+/QFT+ was good in non-vaccinated children with TST>15mm (88.9%, p<0.001). The discordance TST+/QFT- was high in non-vaccinated with TST 10-15mm (68.4%) and in vaccinated with TST 10-15mm (85.7%) and >15mm (64.3%) (p=0.019).





Conclusions:

Routine and sequential use of TST and QFT in a referral TB Unit that attends to immigrant and traveler population with a history of BCG vaccination seems reasonable for LTBI screening. The discordance TST/QFT in non-vaccinated children is a reason of concern and needs further evaluation. New definitions adapted to actual migration movements that permit a proper classification of traveler children are needed for adequate risk assessment and pre-travel counseling.

Systematic Review Registration:

ESPID19-0486
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Candidaemia in paediatric patients: what other investigations should we do?

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Background and Aims:

Current international guidelines for the management of candidiasis recommend that treatment 'depends on evidence of involvement of the CNS, cardiac valves, and/or visceral organs'. However there are no recommendations about which imaging should be performed in these patients. This retrospective project aimed to review the imaging that our patients undergo after diagnosis with candidaemia.

Methods:

Local laboratory records were accessed to obtain data about all positive blood cultures for Candida species between January 2010 and December 2018. A retrospective analysis of available electronic medical records was completed to identify the timing of any imaging of the abdomen and heart. Data was analysed using Microsoft Excel.

Results:

There were 119 patients with candidaemia during this period; median age 2.5 years (range 5 days- 17.5 years)

A total of 84 patients (71%) had an abdominal ultrasound. These ultrasounds occurred 0-28 days after the blood culture (median 4 days). Seven (8%) children had evidence of disseminated candida (kidney n=3, liver 2, spleen 1, bladder 1).

69 patients (58%) had an echocardiogram. The proportion screened improved significantly from 2015 onwards (38% vs 88%; $P<0.05$) Echocardiograms occurred between 1-12 days of the blood culture (median 7 days). Six (7%) children had endocarditis, 4 of whom had underlying congenital heart disease.

A single positive blood culture for candida occurred in 3 children with disseminated disease and one with endocarditis.

Conclusions:

This 9-year study of candidaemia in a tertiary paediatric hospital shows that screening children with candidaemia by abdominal ultrasound and echocardiogram is worthwhile, even in those with a single positive blood culture for candida.

Systematic Review Registration:

N/A.

ESPID19-0310
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Efficacy and safety of low dose liposomal amphotericin b prophylaxis in paediatric allogenic hematopoietic stem cell transplantation (the ambilow project)

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Background and Aims:

Paediatric allogenic hematopoietic stem cell transplant (HSCT) recipients are at risk of invasive fungal infection (IFI) even when receiving antifungal prophylaxis (7-12% in published series). Low dose liposomal amphotericin B (L-AmB 1 mg/kg/day) is an attractive alternative due to intravenous route of administration and the low risk of drug interactions. To date, no published data is available to validate low L-AMB prophylaxis in children. Our aim was to evaluate the efficacy and safety of this approach.

Methods:

Restrospective, observational study including all consecutive paediatric (<18 years) patients that underwent HSCT and received antifungal prophylaxis with intravenous L-AmB, from January 2012 to December 2016. Patients were classified as high (HR) or low risk (LR) for IFI following previously published recommendations. IFI and clinical outcome were stratified according to EORTC classification. L-AmB-related toxicity was graded following Common Terminology Criteria for Adverse Events.

Results:

We included 121 patients (129 HSCT), 61.2% male, median age 7.14y (IQR 4.24-11.5). Haematological malignancies were main underlying condition (52%). 113 (93%) were considered as HR for IFI. Eleven (9%) –all HR- developed a breakthrough IFI (4 *Candida* spp. 7 invasive mould infections) and tend to have higher mortality. Significant risk factors were CMV infection and prolonged neutropenia. Thirty-five (29%) presented L-AmB-related toxicity: 18 infusion-related events, 14 renal (grade I), 3 liver (grade I) toxicity. 90-days mortality was 8.2% (10 patients), one due to IFI.

Conclusions:

Breakthrough IFI in our study was comparable to previous reports. Thus, this is the first study that demonstrates that prophylactic L-AmB is an efficacious and safe option for antifungal prophylaxis in children receiving HSCT, even in high-risk patients, and could be considered in future pediatric guidelines. Risk factors for IFI coincided with those previously described.

Systematic Review Registration:

NA

ESPID19-0022
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Quantiferon-tb gold in-tube test performance in a large pediatric population investigated for suspected tuberculosis infection

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Background and Aims:

The performance of QuantiFERON-TBGold In-Tube (QTF-IT) in children is under debate, especially under 5 years of age and for the interpretation of discordant results between QFT-IT and Tuberculin-Skin-Test (TST).

Methods:

Children consecutively referred to our Center between 2010-2017 for suspected tuberculosis infection (TB) were enrolled. All children underwent clinical evaluation, TST and QFT-IT. Finally, the sensitivity of QFT-IT and TST in active TB cases and the risk factors associated with discordant TST+/QFT-IT- results were assessed.

Results:

In this study 4631 children (median age 5.67; confidence interval [CI]95%:5.58-5.83; 2099 [57.1%] males) were enrolled. Overall, 205 active TB cases were reported (83 microbiologically confirmed). Considering microbiologically confirmed active TB children, a high sensitivity of QFT-IT was observed (95.0%; 95%CI:85,4-100; n=19) among children between 2-4 years of age and in those between 5-18 years (89.1%; 95%CI:79.2-99.2; n=33) while sensitivity was suboptimal in children younger than 2 years (84.6%; 95%CI:65.0-100; n=11). Indipendent risk factorsassociated withdiscordant TST+/QFT-IT- results, in LTBI children investigated with both tests, were: previous BCG vaccination (aOR:2.18; 95%IC:1.33-3.58; p=0.002), age <2 years *vs*. 5-18 years (aOR:7.54; 95%IC:2.52-22.59; p<0.0001), and age 2-4 years *vs*. 5-18 years (aOR:4.63; 95%IC:2.66-8.06; p<0.0001) and investigation for screening rather than for contact with a suspected or confirmed case (aOR:3.58; 95%IC:2.30-5.59; p<0.0001).

Conclusions:

Our data suggest that QFT-IT might be used as unique assay in children over two years of age investigated for screening or suggestive symptomatology and this approach could considerably reduce the number of childrenundergoing pharmacological treatment, but further studies are needed at this regard.

Systematic Review Registration:

N/A

ESPID19-0020
Science and Educational Track

E-Poster discussion session 06 - Fungal and mycobacterial infections - Station 11

Clinical profile of children with mediastinal tuberculosis

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Background and Aims:

To study clinical profile of children with mediastinal tuberculosis (TB).

Methods:

Children diagnosed with mediastinal TB were included. Prevalence of mediastinal TB was calculated. Factors associated with mediastinal TB and outcome were analysed.

Results:

Out of total 1407 patients with TB, 58(4.12%) had mediastinal involvement. Fever was seen in 49(84.5%) patients, positive MT in 32(68.1%), cough in 28(48.3%), loss of appetite in 24(41.4%) and weight loss in 17(29.3%). Associated PTB was present in 22(37.9%) patients. Associated EPTB was observed in 12(20.7%) patients. Fifty-one(87.9%) had an abnormal X-ray. Baseline CT chest was done in 54(93.1%) patients and all of them showed necrotic caseous mediastinal nodes. Total 42 patients were tested with the geneXpert out of which 13(31%) showed presence of MTB of which 19% were mediastinal lymphnode biopsy, 9.5% were gastric lavage (GL) and 2.4% were sputum samples. TB MGIT culture was done in 39 patients out of which 13(33.3%) grew MTB. of which 25.6% were mediastinal node biopsy 7.7% were GL samples. Five(8.6%) had MDR-TB, 5(8.6%) were Pre-XDR TB, 2(3.45%) were in contact with an MDR patient, 1(1.72%) was polyresistant TB and 3(5.2%) were RR-TB. Resolution occurred after a mean treatment duration of 11.67 months in patients with drug sensitive TB.

Conclusions:

Mediastinal TB is common in children with EPTB. Associated PTB is seen in only about one-third of the patients. X-ray chest can be normal in a few patients, hence CT chest may be required to make a diagnosis. Bacteriological confirmation is necessary due to high incidence of DR-TB in these patients. Most of the patients require treatment for a longer duration as resolution takes a longer time.

Systematic Review Registration:

N/A

ESPID19-1041
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Adherence to antimicrobial stewardship advice in a tertiary children's hospital

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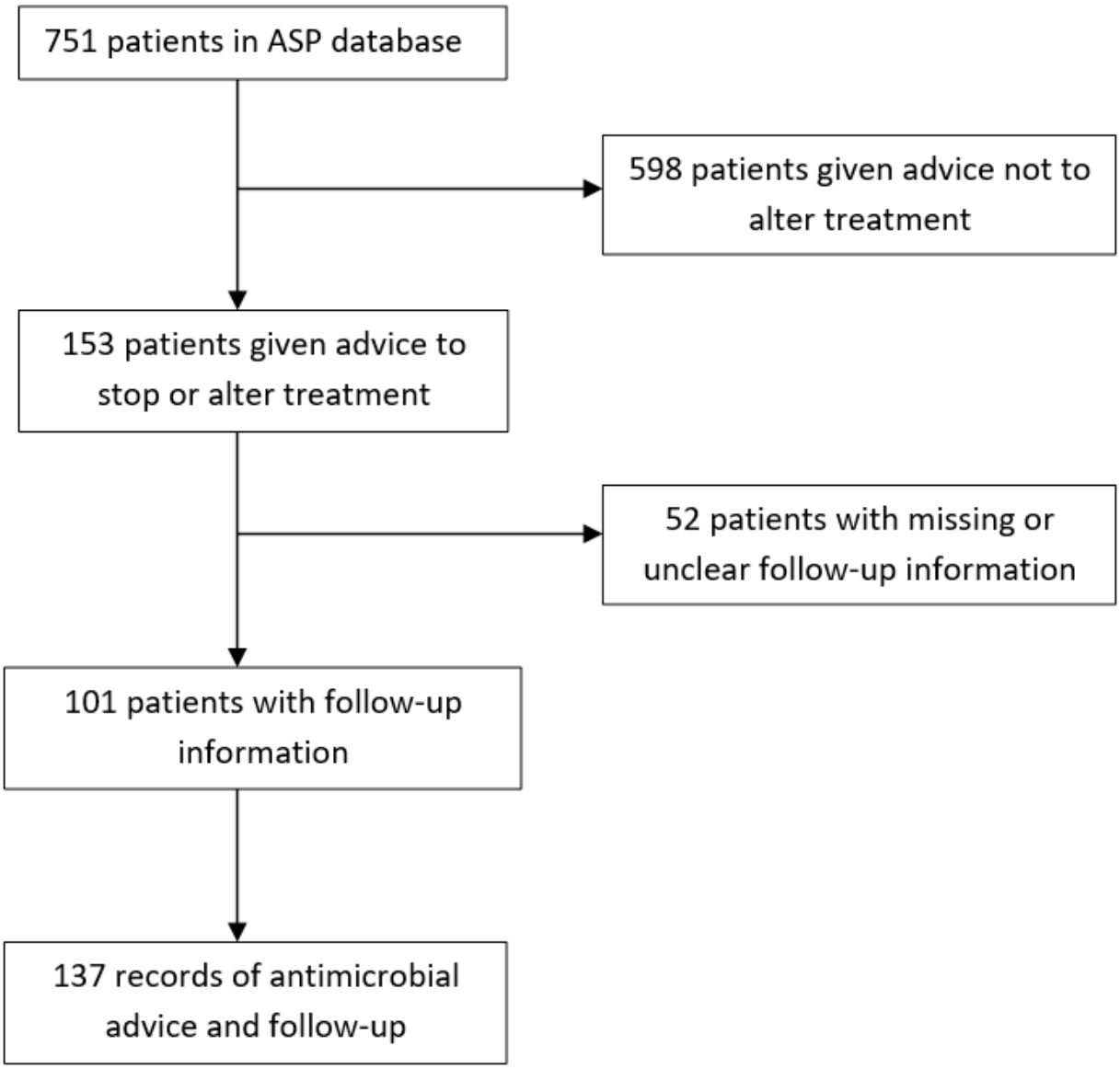
Background and Aims:

A significant proportion of children admitted to paediatric wards receive antibiotics. Antimicrobial Stewardship Programmes (ASP) aim to rationalise antimicrobial use and are effective in reducing and improving prescribing of antimicrobials without a negative impact on morbidity and mortality. We present an audit conducted in a tertiary paediatric hospital to assess the adherence to the local ASP.

Methods:

Records from April 2017 to April 2018 were extracted from our ASP database and analysed to establish whether the advice provided by the ASP team was adhered to.

Results:



Among the 101 patients identified with follow up information, there were 137 antimicrobial prescriptions. 52% (n= 71) of the cases were receiving multiple antimicrobials. The most frequently used antimicrobial was amoxicillin and clavulanic acid, (28%, n= 39). In 75% (n= 103) of instances ASP advice was to stop the antimicrobial. Clinicians were more likely to adhere to the advice given for patients with co-morbidities (73%, n= 69/94) and for those on parenteral antibiotic therapy (83%, n= 77/93). ASP advice was followed in 100% (n= 18/18) entries for sepsis and in 65% (n= 20/31) of cases with proven or probable lower respiratory tract infections (LRTI).

Conclusions:

Advice from the ASP team was usually followed by the medical or surgical teams, in particular for more complex patients with co-morbidities and on parenteral therapy. Clinicians were less likely to adhere to advice for previously well patients with LRTI.

Systematic Review Registration:

ESPID19-0608
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Use or abuse of macrolides in spanish children?

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Background and Aims:

Indications for the use of macrolides in children are limited, however they are commonly prescribed due to the short courses which facilitate treatment adherence. The objective of the study is to describe the prescription of macrolides as first intention of treatment in mild respiratory tract infections in primary care in Valencia, Spain.

Methods:

Retrospective cohort of children 2 months to 5 years of age, born between 2008 and 2013 in Valencia. Data was obtained from the Valencian health electronic databases (covering over 95% of the population). All databases were linked through a unique personal identification number. Diagnoses: Acute Otitis Media (AOM) (CIE-9 381 and 382), Nasopharyngitis (460), Pharyngitis (462), Tonsillitis (463), Bronchitis and bronchiolitis (466), Fever (780.6). Antibiotic prescriptions were retrieved from the primary care databases.

Results:

From a cohort of 480.558 children, there where 3,722,466 diagnoses of mild respiratory tract infections in a 5-year period, with a ratio of 7.8 diagnoses per children. 1,249,862 antibiotics were prescribed (ratio 2.6 antibiotic prescriptions per children), from which 187,099 were macrolides (ratio 0.39 macrolide prescription per children).

	Non-suppurative AOM	Suppurative AOM	Naspharyngitis	Pharyngitis	Tonsillitis	Bronchitis & Bronchiolitis	Fever
Total cases (N)	155,057	270,115	1,693,351	406,613	505,727	405,578	286,025
Antibiotic prescription (%)	65.6	76.9	13.7	38.6	67.0	34.8	25.0
% Macrolides from total antibiotic	8.8	7.7	21.0	21.8	12.3	19.0	15.0

Conclusions:

There is an excessive antibiotic prescription for mild respiratory infections. Macrolide prescriptions for this pathology may be disproportionate.

Systematic Review Registration:

N/A

ESPID19-1179
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Emergence of carbapenem-resistant enterobacteriaceae colonization in a portuguese neonatal intensive care unit

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Background and Aims:

Carbapenem-resistant Enterobacteriaceae (CRE) are an emerging global public health burden, with significant morbimortality, mostly affecting intensive care units and immunosuppressed patients. Few therapeutic options are available, making this approach in Neonatal Intensive Care Units (NICU) a major challenge.
The aim of our study is to characterize risk factors for newborn CRE colonization.

Methods:

A matched case control study, from June to December 2018, was conducted in a Portuguese NICU. Cases were defined as CRE colonized patients, detected by molecular methods, and were individually matched to 3 CRE-negative controls by admission period. Risk factors for colonization were evaluated using bivariable logistic regression.

Results:

Nine cases of CRE colonization (7 VIM, 1 KPC and 1 OXA-48) in 8 patients were enrolled, and matched to 27 controls. Very low birth weight (OR. 7.1; 95%CI 1.2-40.8, p=0,003), treatment with domperidone (OR, 11.7; 95%CI 1.9-71.8, p=0.008), mechanical ventilation (OR, 10.2; 95%CI 1.1-91.4, p=0.04), indwelling catheter (OR, 13.6; 95%CI 1.5-125.3, p=0.02) and parenteral nutrition (OR, 10.2; 95%CI 1.1-91.4, p=0.04) were identified as risk factors for colonization with CRE. All colonized patients were extremely preterm and previously treated with antibiotics. No cases of CRE infection were reported. Spontaneous decolonization occurred within the first 15 days, 1, 2 and 3 months in 33%, 56%, 77% and 100% of cases, respectively.

Conclusions:

Our study showed increased risk for CRE-colonization associated with interventionism in NICUs. Antibiotic therapy plays a major role in bowel colonization, probably in relation with commensal gastrointestinal flora disruption. Minimal intervention, antibiotic stewardship and isolation measures are essential to prevent the widespread emergence of CRE in NICUs.

Systematic Review Registration:

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ESPID19-1173
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Combined strategies to reduce healthcare associated infections in a pediatric intensive care unit

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Background

To evaluate the effectiveness of two combined strategies to reduce the incidence of heathcare associated infections (HCAI) in a pediatric intensive care unit (PICU): 2% chlorhexidine gluconate (2%CHG) daily bathing and ESBL-producing germs (ESBL-PG) colonization screening.

Methods

An exploratory study including children with risk factors for ESBL-PG colonization admitted to PICU, between July 1st-December 31st 2018, was performed. A chromogenic agar method for ESBL-PG colonization screening and 2%CHG daily bathing were applied to at-risk children. The results were compared with an equal period before institution of this procedures (July 1st-December 31st 2016). IBM SPSS *Statistics* version 24 was performed.

Results

A total of 174 children were admitted, 75 of whom (43.1%) had risk factors for ESBL-PG colonization. Screening was performed in 44 (58.7%): 39/44 with central venous catheter *in situ*, 27/44 had previous admission and 17/44 were submitted to surgery. Nine of the 44 children (20.5%) tested positive (5 carbapenemase-producing *Enterobacteriaceae*). Forty-seven children (62.7%) fulfilled criteria for 2%CHG daily bathing. There were 9 HCAI (5.2%): 5 bloodstream infections (2.9%) and 4 respiratory infections (2.3%). Incidence rate of HCAI decreased after the introduction of those two methods (10.6% *versus* 5.2%, p=0.082), mostly due to the decrease in the incidence of surgical site infections and urinary tract infections, that were absent during the study period. There were no infections caused by ESBL-PG (50% of gram negative strains in previous period).

Conclusions

This study suggests the effectiveness of those combined two methods in order to reduce the incidence of HCAI. It also highlights the need of systematic search for at-risk patients at admission, considering the high number of missed screenings (41.3%), in order to improve the quality of care.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESPID19-1016
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Risk factors for extended- spectrum betalactamase enterobacteriaceaes in children with community acquired urinary tract infections

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Background

Community acquired urinary tract infections (CA- UTI) due to extended- spectrum betalactamase uropathogens (ESBL) have been described throughout the world. The aim of this study was to investigate the risk factors (RF) for CA-UTI caused by ESBL in pediatric population.

Methods

Retrospective multicentre cross- sectional study about CA- UTI due to ESBL in patients younger than 14 years old diagnosed in Spain during 2016. CA-UTI was defined as every patient with a positive urine culture and clinical symptoms of UTI, excluding patients with RF for nosocomial UTI: children with chronic diseases, bladder catheter carriers, having had a surgery the two previous weeks or having developed an UTI after 48 hours of admission.

Results

Thirteen hospitals participated in the study including 1,200 CA-UTI. From the sample, those urine cultures positive to the most frequents enterobacteriaceaes were analysed (n=1,119). 86.6% were *Escherichia coli*, 7.7% *Proteus*spp and 5.7% were *Klebsiella*spp. ESBL positive strains were found in 37 (3.3%). A logistic regression analysis was made to determine the RF to develop a CA-UTI caused by ESBL. Patients with antibiotic prophylaxis ($p<0.001$) and those with a lower age ($p=0.007$), were associated with ESBL CA-UTI. Recurrent UTI, the presence of urologic pathology, previous antibiotic the month before the UTI and a hospital admission during the previous month, were factors not related with ESBL CA- UTI ($p>0.05$). The development of complications (sepsis, renal abscess, renal failure) during the infection was not associated with ESBL.

Conclusions

- In our study, a low rate of ESBL CA- UTI was found (3.3%).

- Prophylactic antibiotic treatment and low age were associated with ESBL CA-UTI.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0951
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Impact of an antimicrobial stewardship program on antibiotic use in children with complicated or uncomplicated appendicitis

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Background

Appendicitis is the commonest cause of admission in paediatric surgical wards and one of the conditions that may benefit the most from antimicrobial stewardship programs (ASP).

Methods

Quasi-experimental study in a tertiary-care paediatric (0-18 years) university hospital with approximately 300 admissions/year due to complicated or uncomplicated appendicitis. An ASP consisting of postprescription review with feedback (PPRF) as core strategy was implemented in January 2017. Comparison of antibiotic use (AU) calculated in days-of-therapy/100 patient-days (DOT/100PD) and in length-of-therapy (LOT) in days, median length-of-stay (LOS) in days and readmission rates (RR) due to postoperative complications in appendicular complicated and uncomplicated intraabdominal infections from 2012 until 2017 were analysed. During 2017 the quality of antibiotic prescriptions was also evaluated quarterly.

Results

The evolution of AU, LOS and RR are shown in the Table. DOT/100PD reflected changes in treatment protocols over the years, i.e. an increase was observed in 2017 due to the inclusion of 2 drugs of narrower spectrum for peritonitis instead of one broad-spectrum antimicrobial. However, LOT decreased as did LOS, with no changes in RR. The use of meropenem, not the standard of care according to local protocols, decreased by 2.68 DOT/100PD in 2017 as compared with the average use in the pre-ASP period. During 2017, 299 antibiotic prescriptions corresponding to 239 patients diagnosed with intraabdominal infections (184, 61.5% phlegmonous or gangrenous appendicitis and 115, 38.5% secondary peritonitis) were evaluated. The percentage of optimal antibiotic prescriptions increased from 65.6% in the 1st quarter to 80.8% in the 4th quarter (p=0.046).

		2012 (n=296)	2013 (n=303)	2014 (n=315)	2015 (n=309)	2016 (n=299)	2017 (n=377)	*P*
TOTAL (n=1899)	AU	211,5	201,9	135,4	117,4	119,5	130,3	0.261
	LOT	5.4	5.4	4.9	4.8	5.1	4.2	**0.035**
	LOS	5.9	5,7	5.2	5,3	5.6	4,7	**0.046**
	RR	5,1	6,0	2,6	3,3	6,1	4,6	0.427

Antimicrobial use (AU) is expressed in days-of-therapy (DOT)/100 patient-days (PD). Length-of-therapy (LOT) is expressed in days receiving any antimicrobial/n of admissions. Length-of-stay (LOS) is expressed in days of admission/n of admissions. Readmission rate (RR) is expressed in % of readmitted patients.

Conclusions

ASPs can improve the quality of antibiotic prescriptions, reduce LOT and broad-spectrum antimicrobial use and avoid unnecessary prolonged hospital stays in children with appendicular intraabdominal infections safely.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0835
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Successful control of a carbapenem resistant klebsiella pneumoniae outbreak in a neonatal intensive care unit

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Background and Aims:

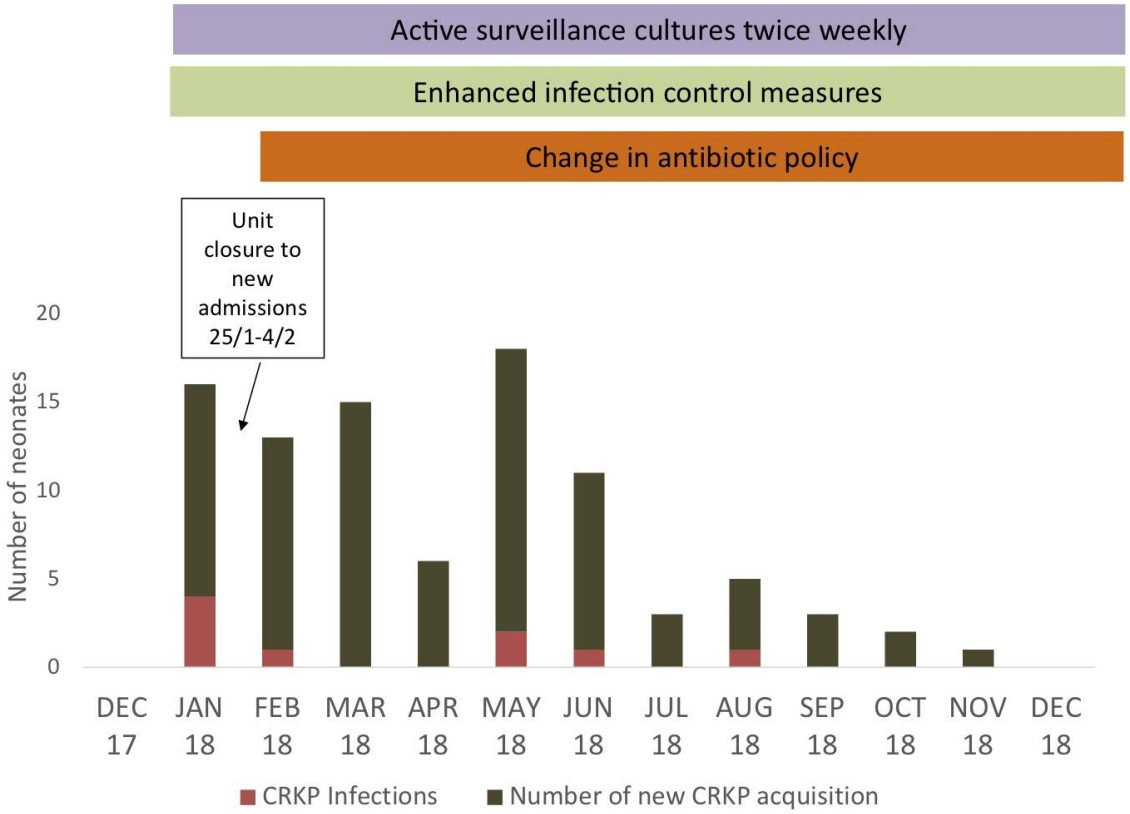
Emergence of carbapenem-resistant*Klebsiella pneumoniae* (CRKP) is a major public threat especially for critically ill patients including neonates. The aim of this study was to describe a multifaceted intervention applied to control an outbreak of CRKP in a neonatal intensive care unit (NICU).

Methods:

In January 2018, two cases of CRKP bloodstream infection (BSI) occurred for the first time in our 40-bed NICU (15 intensive care beds) located in a tertiary general hospital. After the outbreak identification, the following interventions were implemented with a combined “bottom-up” and “top-down” approach: a) active surveillance cultures for CRKP (pharyngeal and stool swabs taken twice weekly), cohorting of neonates with CRKP colonization/infection and alert codes, b) enhanced infection control measures such as compliance to universal/contact precautions, hand hygiene and environmental cleaning, continuous education and feedback, temporarily stop of new admissions for 2 weeks, and c) change in antibiotic policy by restricting carbapenem use.

Results:

Figure 1: Timeline of new carbapenem-resistant *Klebsiella pneumoniae* (CRKP) acquisitions/infections in Neonatal Intensive Care Unit



The outbreak was successfully contained within 12 months (Figure 1). During this period, a total of 538 neonates were hospitalized (511 new admissions) 84 of which acquired CRKP (15.6%). Among colonized neonates 9 (10.7%) developed bloodstream infection due to CRKP. The last case of CRKP acquisition occurred early in November 2018. All CRKP isolates were susceptible to ceftazidime/avibactam and most of them to colistin.

Conclusions:

Implementation of an active surveillance program for the early detection of CRKP colonization among neonates together with enhanced infection control measures and cohorting of neonates successfully prevented CRKP transmission. A multifaceted approach should be considered for the control of the CRKP outbreaks in the NICU setting.

Systematic Review Registration:

N/A

ESPID19-0510
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Optimal dosing of meropenem in a small cohort of critically ill young children receiving continuous renal replacement therapy

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Background

Meropenem dosing in critically ill children with septic shock and continuous renal replacement therapy (CRRT) is complex. The CRRT circuit can alter meropenem pharmacokinetics (PK) and optimal dosing in this population is largely unknown. This study objective is to determine the PK and optimal dosing of meropenem for the treatment of sepsis in critically ill children on CRRT

Methods

A prospective single-center pharmacokinetic study was performed in critically ill children receiving meropenem while on CRRT. Blood and effluent fluid samples were collected from each patient at scheduled time points. A population PK model was developed using nonlinear mixed effects modeling software (NONMEM®). Monte Carlo simulations were performed for several dosing regimens. The pharmacokinetic/pharmacodynamic (PK/PD) target was set to achieve meropenem plasma concentrations above minimum inhibitory concentration (MIC) of 4 mg/L for 100% of dosing interval (100%fT>MIC).

Results

Nine patients contributed 53 plasma and 38 dialysate samples. A two-compartment model best characterized meropenem PK. Mean (range) clearance and elimination half-life was 0.091 L/hr/kg(0.04-0.157) and 3.9 hr(2.1-7.5) respectively. The fraction of CRRT clearance (CLCRRT) to total CL and the sieving/saturation coefficient values were 0.816 and 0.958. Standard meropenem CRRT dose of 40mg/kg/dose q12h over 30-mins infusion achieved PK/PD target in 32% of simulated patients. Dosing of 20mg/kg q8h over 4-hour infusion or 40mg/kg q8h over 2-hour infusion achieved 100%fT>MIC target for at least 90% of the patients.

Conclusions

Based on a small cohort of critically ill children receiving CRRT, meropenem 20 to 40mg/kg/dose q8h over extended infusion provided therapeutic exposures for common microorganisms.

Clinical Trial Registration (Please input N/A if not registered)

CIRB Ref No: 2011/538/E

ESPID19-0315
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Surveillance of antibiotic use in pediatric patients in 9 selected hospitals in china

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Background and Aims:

Due to antibiotic overuse and misuse, the growing trend of antimicrobial resistance (AMR) has been a significant threat to public health. Tracking the antibiotic use is one of the core lists for antibiotics stewardship program. So far, the surveillance network of antibiotics usage hasn't been well established yet for pediatric patients in China. This retrospective prescription investigation aimed to survey the current status of antibiotic use for outpatients in different level of pediatric hospitals in China, in order to guide the intervention measures to improve rational antibiotic use.

Methods:

The prescription monitoring was implemented in April, May and June in 2017. Nine public hospitals from primary to tertiary levels in three main cities of China participated in this study. Consecutive 7-day prescriptions per month were sampled. The pediatric patients of the sampled prescriptions were restricted to those <12 years old attending outpatient and emergency departments.

Results:

Among a total of 232386 outpatient encounters, 74239 received antibiotics. The proportion of children receiving intravenous antibiotics was 31.7% (95%CI, 31.4%-32.0%). Broad-spectrum antibiotics constituted the majority of prescribed antibiotics. Third-generation cephalosporins was most frequently prescribed (40.9%, 95%CI, 40.6%-41.2%), followed by macrolides, second-generation cephalosporins, β-lactam antibiotics with β-lactamase inhibitors and penicillins with β-lactamase inhibitors.Thirty-seven percent antibiotic prescriptions were related with respiratory tract infections. Forty-four percent of pediatric patients diagnosed as upper respiratory infections, bronchitis or bronchiolitis were prescribed with antibiotics and third-generation cephalosporins were the most prescribed antibiotics (50.0%, 95%CI, 49.3%-50.7%).

Conclusions:

Antibiotic prescribing rate is significantly high in Chinese pediatric outpatients. The over-prescribing of broad-spectrum antibiotics, especially for respiratory tract infections is a big concern. Strengthening the antibiotic surveillance and implementing pediatric antimicrobial stewardship are urgent in China.

Systematic Review Registration:

N/A.

ESPID19-0081
Science and Educational Track

E-Poster discussion session 07 - Use of antibiotics - Station 13

Survey of antibiotic prescribing behavior toward children in a japanese primary care center

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Background and Aims:

Japanese government adopted a national action plan on antimicrobial resistance in April 2016; reducing antimicrobial use in 2020 to two-thirds of the level in 2013. Himeji-city has a population of half a million. Himeji-city Emergency Medical Center for Nights and Holidays(HEMCNH) is the hub medical institution ran mainly by private physicians every night; therefore, the information about antibiotic prescribing behavior in this center provides useful hints to promote antimicrobial stewardship at the community level. We aimed to analyze antibiotic prescribing behavior toward children in HEMCNH.

Methods:

Primary care data of children <15-year-old recorded from September 2014 to March 2018 in Himeji Emergency Medical Service Association database was analyzed. Records about patients age, specialty of clinicians, diagnoses, and antibiotics prescribed were extracted. We assessed which antibiotic classes were prescribed and which conditions resulted in the greatest share of prescribing. We used Days of therapy per 1,000 patients-visits (DOTs) for evaluation.

Results:

Antibiotics were prescribed toward 13% of patients (10,136/77,180). 54% of patients (41,752/77,180) were diagnosed as acute respiratory infections, and 17% of them were prescribed any kind of antibiotics (7,217/41,752). Oral 3rd-generation cephalosporins were frequently prescribed regardless of ages (DOTs 44.2~132.6), and clinical conditions (respiratory infections; 122, gastroenteritis; 28.2, otitis media; 442, Streptococcal infections; 191). Antibiotics were prescribed for 62% of patients seen by otolaryngologists, and most of them were 3rd-generation cephalosporins.

Conclusions:

This study has identified substantial overprescribing of antibiotics in pediatric acute primary care in our area particularly in acute respiratory tract conditions. We have started interventions such as feedback to the primary care physicians, distributing a manual to standardize the utilization of oral antibiotics, which have led to changes in antibiotic prescribing behavior.

Systematic Review Registration:

Not applicable.

ESPID19-0867
Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

Hemophagocytic lymphohistiocytosis (hlh) 2nd to visceral leishmaniasis (vl): diagnosis and management of 23 children in sevilla between 2004-2018

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Background

Visceral leishmaniasis (VL) is associated with hemophagocytic lymphohistiocytosis (HLH). We describe and compare the epidemiologic and clinical characteristics of paediatric VL with and without HLH. Medical records of all children (<14y) admitted (2004-2018) with VL to our tertiary care center in Seville were retrospectively reviewed. For inclusion, the diagnosis of VL had to be based on clinical features, unequivocal serology, PCR or bone marrow findings. HLH-diagnosis was established according to the HLH-2004 criteria.

Case Presentation Summary

Summary of clinical and laboratory parameters of patients with VL

Visceral Leishmaniasis (n=23)				
	>5 HLH criteria			
	Yes (n=8)	**No (n=6)**	**Not checked (n=9)**	**p value***
Age (months)	6.5 (3-84)	9.5 (4-20)	5 (10-36)	0.903
Gender	62.5%F, 37.5%M	83.3%F, 16.7%M	55.5%F, 44.4%M	0.729**
Fever (days)	20.5 (7-60)	12 (4-50)	30 (1-120)	0.603
Days of fever after initiation of treatment (L-amB)	3.5 (1-20)	0.5 (0-1)	2 (0-48)	0.010
Hospitalization (days)	16 (7-28)	8.5 (4-12)	10 (4-15)	0.107
Treatment duration (days)	7 (6-33)	6.5 (5-8)	7 (5-7)	
Hb (g/dl)***	7.85 (6.1-9.3)	8.25 (6-11.1)	8 (5.5-9.5)	0.849
Leukocytes (cells/mm^3)***	5135 (1250-7000)	8235 (4640-15470)	4600 (2150-13800)	0.061
Neutrophils (cells/mm^3)***	880 (700-1100)	900 (600-4200)	595 (230-2140)	0.412
Lymphocytes (cells/mm^3)***	2880 (900-4200)	7100 (3600-10300)	2700 (1700-7300)	0.055
Platelets (cells/mm^3)***	63500 (46000-150000)	108500 (65000-172000)	79000 (42000-127000)	0.0615
CRP (mg/L)***	99.25 (37.3-195.9)	68.8 (13.1-170)	82.55 (27.8-156.6)	0.522
GOT (UI/l)***	21.5 (9-38)	48 (36-188)	53.5 (27-99)	0.928
Ferritin (mcg/l)***	1742.5 (428-6810)	601.5 (289-1877)	193 (69-4239)	0.171
CD25s (ng/ml)	30.25 (11.08-426)	18.125 (16.07-20.18)	NA	NA
Blood transfusion	100%	50%	50%	NA
Relapse	12.5% (1/8)	16.7% (1/6)	11% (1/9)	NA

* comparison between HLH vs no HLH groups (U-Mann Whitney)
** chi square
***at hospital admission or first available value

23 cases were identified. Median age was 9 months (3mo-7y). All patients presented with fever and splenomegaly. Neutropenia (86.9%) and thrombocytopenia (86.9%) were the most common hematologic alterations followed by transfusion dependent anemia (15.7%) and lymphopenia (21.7%). Pancytopenia was observed in 19/23, bicytopenia in 2/23, 1/23 showed no cytopenia. CRP levels were raised (median 85.8mg/l, range 16.5-332).

21/23 patients received intravenous liposomal amphotericin B, L-amB (3 mg/kg/d,5+2 days) and 3/23 had a VL relapse responding to a 2nd course of L-amB.

HLH criteria were checked in 14 patients; 8/23 (57%) fulfilled 5 or more criteria (table). 3 patients received adjuvant corticosteroid therapy (2 mg/kg/d) due to raised inflammatory markers and profound cytopenias; no relapses were observed. None of the patients with HLH received cyclosporinA nor etoposide (HLH-2004 protocol). Overall survival was 100%.

Learning Points/Discussion

Fulfillment of HLH criteria was common.
Careful monitoring and elimination of the infectious trigger (L-amB) is crucial.
Further studies are needed to predict those patients prone to relapse or to develop HLH.
Whilst none of the patients relapsed after receiving corticosteroid treatment, the role of immunomodulation in VL driven HLH remains to be determined.

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Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

Accuracy of a sequential approach including observation in a short stay unit to identify infants < 29 days at low risk for severe bacterial infection

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Background and Aims:

The development of step by step strategies has improved the identification of infants <90 days old at low risk of severe bacterial infection (SBI) in pediatric emergencies. However, the youngest, those <29 days old, are often excluded from these strategies.

Objectives: To assess the value of a step by step approach including observation in a short stay unit to febrile neonates in order to identify patients at a low risk for SBI who are suitable for early discharge without antibiotic therapy.**Methods:**

A descriptive retrospective study (September 2013 to August 2015) that included all infants aged younger than 29 days who presented with fever (≥ 38°) to our pediatric emergency department. The management included CRP levels, urine dipstick, lumbar puncture, 12 hours observation in short stay unit, and control of the CRP level at H12. Neonates with a history of surgery or treated with antibiotics were not included. Classification in low risk according to our strategy required to fulfill the following criteria in this order: 1) well appearing, 2) negative leukocyturia and a normal cerebrospinal fluid profile 3) CRP level < 20 mg/L 4) well appearing during the observation period without antibiotic therapy and a control CRP < 20 mg/L.

Results:

226 patients met the inclusion criteria, of whom 49 were diagnosed as SBI: 42 pyelonephritis, 3 bacteremias, 2 meningitis, 1 arthritis, 1 skin infection. Overall 96 (42%) neonates were classified as low risk and were discharged home without antibiotic therapy; no SBI was diagnosed among them.

Conclusions:

An observation period in a short stay unit seems a promising element to improve identification strategies for febrile young infants at low risk of SBI.

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N/A

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Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

Bloodstream infections and antibiotic resistance in febrile neutropenic children with hematologic malignancies: epidemiology of two italian centers

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Background and Aims:

Bloodstream infections (BSI) are a major cause of morbidity and mortality in children with cancer. Neutropenia (granulocyte count <1000/mm^3) is the most important risk factor. Guidelines recommend antibiotic monotherapy for initial empirical therapy of febrile neutropenia, but local epidemiological and antibiotic susceptibility data are pivotal to design a correct management strategy.

Methods:

We conducted a retrospective analysis of bacterial BSI diagnosed form January 1st 2012 to December 31st 2017 in neutropenic patients with hematologic malignancies followed at Pausilipon Hospital Oncohematology (PHO) of Naples and Istituto Giannina Gaslini (IGG) of Genoa. Proportions of strains resistant to selected antibiotics were calculated. Resistance was defined according to EUCAST rules. At IGG antibiotic prophylaxis (amoxicillin-clavulanate) for febrile neutropenia is administered only in pre-engraftment periods in stem cell transplant, at PHO prophylaxis (ciprofloxacin) is administered also during chemotherapy-induced neutropenia. At PHO empirical therapy consists in ceztazidime + amikacin, at IGG piperacillin-tazobactam + amikacin.

Results:

89 [5 (6%) polimicrobial] and 96 [7 (7%) polimicrobial] BSI were diagnosed during febrile neutropenia at PHO and IGG, respectively. A total of 95 strains at PHO (Gram positive, G+ 51: S. aureus 4%, Coagulase Negative Staphylococcus, CoNS 49%; Gram negative, G- 44: Enterobacteriaceae 70%, P. aeruginosa 25%) and 103 at IGG (G+ 38: S. aureus 29%, CoNS 26%; G- 65: Enterobacteriaceae 72%, P. aeruginosa 21%) were isolated. The Gram pattern between the centers was statistically different (chi square p=0.018). The table reports the proportions of resistant strains by center. No statistically significant

difference between centers was found.

	PHO	IGG	F-Fisher
Enterococcus	**4**	**6**	
Ampicillin	0 (0%)	3 (50%)	P=0,167
Vancomycin	0 (0%)	1 (17%)	P=1
Staphylococcus aureus	**2**	**11**	
Oxacillin	0 (0%)	1 (9%)	P=1
CoNS	**25**	**10**	
Oxacillin	23 (92%)	10 (100%)	P=1
Enterobacteriaceae + Pseudomonas aeruginosa	**42**	**61**	
Amikacin	1 (2%)	3 (5%)	P=0,644
Ceftazidime	6 (14%)	17 (28%)	P=0,148
Ciprofloxacin	21 (50%)	19 (31%)	P=0,066
Meropenem	0 (0%)	1 (2%)	P=1
Piperacillin-tazobactam	11 (26%)	17 (28%)	P=1

Table: proportion (%) of resistant strains over the total number of tested strains for any given antibiotic CoNS: Coagulase Negative Staphylococcus

Conclusions:

Recommended monotherapy could be not appropriate for initial empirical therapy, especially in high resistance setting. Local survey on etiology and antibiotic susceptibility is mandatory for an effective management of this complication in cancer patients.

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Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

Blood stream infections in children with cancer: a 7-year experience at a single center

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Background and Aims:

Children with cancer are at increased risk of life-threatening infections due to their underlying disease, intensive treatment and the presence of central venous catheters (CVC).

Methods:

Patients' characteristics & clinical/laboratory findings of children with cancer who developed a blood stream infection (BSI) (1/2/2011-28/2/2018) were recorded retrospectively and correlated with the cancer type; Patients with haematologic malignancy were assigned to group A and those with solid tumors to group B.

Results:

259 BSI episodes were recorded in 107 patients of group A (180 episodes) and in 55 of group B (79). Sixty-three children (group-A:46, group-B:17, ***p=0.026***) experienced more than one episodes. Gram-/Gram+ ratio was 1.2/1 and 0.6/1 in groups A and B respectively (***p=0.024***) (Table 1a). Table 1b shows the most common organisms isolated. In 174 episodes (67%), patients were neutropenic (group-A:81.1%, group-B:32.4%, ***p=0.000***) whereas in 235 (91%) episodes, children had a CVC in place (no difference between the two groups); neutropenia & CVC at the same time in 68% of episodes. Mucositis was observed more frequently in group-A patients (***p=0.025***) who also had significantly lower platelet count (PLT) (***p=0.000)***. Thrombocytopenia, neutropenia and previous BSI episodes were associated with the cancer type also in multivariate analysis. Complications occurred in 50/259 (19.3%) episodes; 15.7% and 28.4% in group A and B respectively, ***p=0.024***. Two patients -both in group A- died due to the infection.

Table 1a	Number of BSI episodes (monomicrobial)	No of BSIs (%)	
		Hematologic	Solid
Gram -	110 (*E. coli* in 30%)	88 (54.7%)	22 (32.4%)
Gram +	114 (*Staphylococcus coagulase negative* in 58%)	70 (43.5%)	44 (64.7%)
Fungi	5 (*Candida sp.*: 3, *Trichosporon sp.*: 1, *Aspergillus sp.*: 1)	3 (1.8%)	2 (2.9%)

Table 1b: Most common pathogens	Cases (N)	%	Hematologic	Solid
Staphylococcus coagulase negative	66	28.8%	36 (21.7%)	31 (45.6%)
Esherichia coli	33	14.4%	27 (16.8%)	6 (8.8%)
Pseudomonas sp.	31	13.5%	26 (16.1%)	5 (7.4%)
Klebsiella sp.	20	8.7%	15 (9.3%)	5 (7.4%)
Staphylococcus aureus	17	7.4%	13 (8.1%)	4 (5.9%)

Conclusions:

1.Three out of 4 cancer patients with BSI suffer from haematologic malignancy. 2.BSIs are not rare in non-neutropenic patients. 3. BSIs among children with haematologic malignancy are more frequently associated with lower PLT count and neutropenia. 4. Children with solid tumors are at a decreased risk for multiple episodes of BSIs but also at a higher risk for complications.

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Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

Catheter-associated bloodstream infection in very low birthweight infants. Do the number of catheter days or daily manipulation frequency play a role?

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Background and Aims:

Invasive central venous catheters (CVC) are essential for clinical management in very low birth weight (VLBW) infants. CVC are the major risk for catheter-associated blood stream infections (CABSI) which are related to significant morbidity and mortality. The aim of this study is to evaluate the influence of catheter days and daily manipulation frequency on CABSI in VLBW.

Methods:

Prospective evaluation of CVC management in VLBW in a 10-bed tertiary care pediatric intensive care unit in Switzerland. During 2010 three prevention bundles were implemented. Interventions (e.g. CVC insertion), manipulation frequency or laboratory results were directly entered by the correspondent clinician, nurse, or laboratory technician to a central electronic database. All VLBW infants age ≤90 days with placement of a CVC between January 2011 and December 2017 were included. CABSI was defined as presence of any pathogen in blood cultures more than two days after CVC insertion.

Results:

During 7 years, 552 CVCs were placed in 427 VLBW. Blood culture was positive in 32 cases whereof in 11 cases the result was interpreted as contamination and in 21 cases (4.9%) CABSI was diagnosed with an overall CABSI rate of 6.6 / 1000 catheter days. The most frequent pathogen was coagulase negative staphylococci (62%). CVC manipulation frequency in infants with CABSI was 1.58 ±0.26 and 1.64 ±0.0.5 without CABSI. The number of catheter days in VLBW with CABSI was significantly higher compared to infants without CABSI (10.1±2.1 versus 6.4±0.5, $p < 0.001$).

Conclusions:

Although the CABSI rate has varied strongly over time, the CABSI risk correlated with longer catheter placement. However, association with manipulation frequency was not detected. Daily questioning of the indication could help to shorten catheter days and thus may reduce the CABSI rate.

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N/A

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E-Poster discussion session 08 - Severe infections - Station 01

Risk factors for development of more severe osteoarticular infections in infants: spanish multicenter study (rioped network).

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Background and Aims:

Osteoarticular infections (OAI) in young infants are not very well described.

Methods:

Prospective study evaluating risk factors associated with worse clinical outcome in infants with OAI (Spanish cohort from 66 hospitals; RIOPed Network); 2015-2018. Specific comparison was performed between Group 1 (<4 months) and Group 2 (4-12 months).

Results:

Ninety-three infants (26 hospitals) were enrolled (32 in Group 1; 63 in Group 2). Median age: 29 and 286 days, respectively. Significant differences between Group 1 and Group 2 were: fever (50 vs 76%; p=0.02), septic arthritis (29 vs 54%; p=0.028), IV antibiotics (Group 1 cloxacillin+cefotaxime; Group 2 cefuroxime; p=0.01), days of admission (16 vs 9; p=0.047) and duration of IV antibiotics (14 vs 7; p=0.047). Rate of isolation was similar (64 vs 50%) with *S. aureus* (44 vs 29%) and *K. kingae* (11 vs 33%) being the most common pathogens. Analyzing the whole cohort, 22 and 11% of infants developed complications and sequelae, respectively. Main risk factors associated with complications were higher neutrophil count (7400 vs 5500; P=0.026), positive blood culture (59 vs 14%; p<0.001) and surgery (55 vs 22%; 0.01), especially if surgery was delayed (0.5 vs 3 days; p=0.001). Risk factors associated with sequelae were performing joint drainage (87 vs 40%; p=0.02), surgery (67 vs 28%; p=0.05) and development of complications (63 vs 17%; p=0.009). Multivariate analysis: positive blood culture (OR:14.6[2.3-91.8]) was associated with complications and development of complications (OR:9.1[1.4-55.5] with sequelae. Age was not related to complications/sequelae.

Conclusions:

Increased inflammatory parameters, positive blood cultures or surgery may be related to worse outcome in infants with OAI. Young infants received longer IV therapy but did not develop more complications/sequelae. These results may be useful for the management of these young infants.

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Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

Defining the standard of care for neonatal and paediatric sepsis caused by carbapenem resistant organisms

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Background

The optimal standard of care (SOC) for carbapenem-resistant organisms (CRO) infections in children is currently unknown. The aim of this study was to systematically review the published evidence on the effectiveness of the antibiotic regimens commonly used for CRO bloodstream infections (BSIs) in children to establish the best available SOC and inform the design of future paediatric/neonatal clinical trials (CTs).

Methods

A systematic review was conducted on Medline and Embase for studies published until September 2017 reporting data on 1) single-patient level outcome related to 2) a specific antibiotic treatment 3) for BSIs 4) caused by carbapenem-resistant Gram-negatives 5) in children.

Results

15 papers fulfilled the inclusion criteria. Outcome data were available for 49 patients, of whom 29 were <3 months and 26 were neonates. All were admitted to Intensive Care Units and had comorbidities. 24/49 isolates belonged to *Klebsiella pneumoniae*, 22 to *Acinetobacter baumannii*, 2 were *Enterobacter cloacae* and 1 was an *Escherichia coli*. The genetic carbapenemase was available only for 25 isolates. 18 out of 49 children received a monotherapy whereas 31 were treated with a combination of two or more antibiotics. 25 different regimens were reported, 7 including one and 18 including multiple antibiotics. The most frequently used regimen included carbapenems plus polymyxins (12/25). Among the cohort, the case-fatality rate was 41% (20/49), 10 of which were neonates. The mortality was higher in patients receiving monotherapy (10/18) compared with children treated with combinations (10/31).

Conclusions

This systematic review reveals the paucity of data available on the treatment of children with CRO BSIs. Paediatric and neonatal CTs using simple and standardised trial designs are now a global priority in order to inform the optimal management of these life-threatening infections.

Systematic Review Registration (Please input N/A if not registered)

N/A

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Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

A 5-year retrospective, epidemiological study of blood stream infections (bsi) in immunocompromised children – a single centre study

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Background and Aims:

Bacteraemia is a major cause of hospital admission in immunocompromised patients. These patients have an increased risk of infection due to their underlying illnesses, treatment and other factors such as gut translocation and central venous catheters. The aim of this retrospective study was to describe the microbiological results and clinical outcomes of blood stream infections in immunocompromised children.

Methods:

Retrospective cohort study of all patients admitted under paediatric haematology, oncology and immunology between 01/08/2013 and 01/08/2018 at a tertiary London hospital. Clinical and microbiological data were collected for each episode and main characteristics are shown in Table1.

Results:

There were 371 BSI episodes from 102 patients. Of the 366 BSI: 66.3% were Gram positive (GP), 21.9% Gram negative (GN), 7.6% fungi. The most prevalent GP organisms: Coagulase-negative staphylococci(n=151), *S.aureus*(n=18), *E.faecium* (n=16); GN: *K.pneumoniae* (n=12), *P.aeruginosa* (n=11), *P.agglomerans* (n=8), *E.coli* (n=8); 53 episodes(15%) were considered contaminants.

Local febrile neutropenia guidelines recommend piperacillin/tazobactam and gentamycin: 1/366 GN-BSI with *Klebsiella.variicola* (ESBL) was resistant to both. There were 7 vancomycin-resistant *E.faecium*, no multi-resistant *P.aeruginosa* and no MRSA. 3 ALL patients had 5 GN-BSI episodes with ciprofloxacin-resistant organisms, *E.coli* and *K.variicola*.

Conclusions:

In our series, most patients were non-neutropenic, had relapsed malignancy and were on steroid treatment. An incidence of 3.8% of GN BSI were resistant to piperacillin/tazobactam, where the additional gentamicin given in our setting proved beneficial. Low (6.25%) fluoroquinolone resistant BSI was identified among haemato-oncology patients and BMT patients.

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E-Poster discussion session 08 - Severe infections - Station 01

Low-level rotavirus activity in children despite high vaccine coverage in finland

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Background

Rotavirus (RV) vaccine (Rotateq®) was added into National Immunization Program in Finland in September 2009 with a coverage of ≥90 %, and the number of hospitalizations and outpatient visits due to rotavirus have both decreased by 90 %. We studied the remaining RV disease burden in 5 seasons from 2013-2018.

Methods

Since 2013, all stool samples from laboratory diagnosed RV cases in Finland have been referred for typing. RV VP7 and VP4 were studied by reverse transcription-polymerase chain reaction (RT-PCR). Positive amplicons were further sequenced and compared to reference strains.

Results

A total of 1155 clinically confirmed RV samples were received and 826 (87.8 %) were RT-PCR positive for RV and occurred in children (under 16 years of age). During the whole follow-up period, G12P[8] (190 cases) was the predominant genotype followed by G9P[8] (149 cases), G1P[8] (126 cases) and G3P[8] (124 cases). We detected a distinct season by season change in the genotypes during the follow-up as G1P[8], G2P[4], G3P[8] were replaced by G12P[8], G9P[8] and G9P[4]. Vaccination status was known in 281 children of whom 109 (38.9 %) had received at least one dose of vaccine. In vaccinated children, G12P[8] (38 cases, 34.9 %) was the most predominant genotype whereas in unvaccinated children no clear predominance was seen. The difference of genotype distribution between vaccinated and unvaccinated was statistically significant (p=0.02).

Conclusions

RV activity in children remains constant at low-level despite long-term high coverage vaccination indicating that RV disease may be controlled but not eradicated with the current live RV vaccines. Replacement of G1P[8] by G12P[8] as predominant genotype is similar to other countries using RotaTeq® vaccine.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0404
Science and Educational Track

E-Poster discussion session 08 - Severe infections - Station 01

A single institutional review of pediatric bacillus spp. Bacteremia

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Background

Although nonanthrax Bacillus species have been increasingly recognized as pathogens in immunosuppressed patients with indwelling devices, reports in pediatric patients are still scarce. The purpose of this study was to investigate the characteristics of Bacillus spp. bacteremia in children.

Case Presentation Summary

We retrospectively identified 39 cases of Bacillus bacteremia in 34 patients between March 2010 and April 2018 at Tokyo metropolitan children's medical center. Number of cases with B cereus and non-B cereus were 14 and 25, respectively. Median age was 4.0 years (IQR 1.5 – 6.0). Boys were 64.7% (22/34). Among 34 patients, 26 patients (76.5%) were hematology/oncology, 5 patients (14.7%) had gastrointestinal diseases, and 2 patients (5.9%) were newborn. In all cases, central venous catheter (CVC) was placed. The median duration of CVC placement at the onset of bacteremia was 95.5 days (IQR 33.3 – 146.3). Most of patients were febrile (94.5%) except 2 newborn cases. Gastrointestinal symptoms were observed in 8 patients (20.5%). Vancomycin was used in 32 cases (82.1%) for the median 14 days (IQR 12 – 15). Recurrence rate in total, B careus and non-B cereus was 11.7% (4/34), 8.3% (1/12) and 13.6% (3/22), respectively. Management of CVC which was kept, exchanged and withdrawn were 25 (64.1%), 9 (23.1%) and 5 (12.8%), respectively. Two mortality cases were newborns with Bacillus cereus bacteremia. They were both premature infants with extremely low birth weight.

Learning Points/Discussion

Bacillus bacteremia in children were exclusively observed in patients placed with CVC. One third of patients were eventually managed with CVC removal or exchange. Two cases (14.2%) of B careus bacteremia resulted in mortality that they were premature infants.

ESPID19-0630
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Vitamin d receptor, vitamin d binding protein and cyp27b1 single nucleotide polymorphisms and susceptibility to infections in infants

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Background

The role of Vitamin D in innate and adaptive immunity has been recently demonstrated. The purpose of this project is to study the potential role of genetic variances in vitamin D pathway and infections in infancy.

Methods

This is a prospective case-control study; the population includes infants 0-24 months with infection and age-matched controls. The single nucleotide polymorphisms (SNPs) of Vitamin D Receptor (VDR) gene (BsmI, FokI, ApaI, and TaqI), vitamin D binding protein (VDBP) (Gc gene) and CYP27B1-1260 were genotyped by polymerase chain reaction-restriction fragment length polymorphism. Statistical analysis was conducted with two-tailed Fisher exact test.

Results

115 infants, 35 with bacterial and 47 with viral infection, and 33 healthy controls were enrolled. TaqI polymorphism, was more frequent in infants with viral infection compared to controls (OR 2.14, 95% CI 1.11 to 4.13). Moreover, *t* allele was more frequent in infants with RSV bronchiolitis compared to controls (OR 3.06, 95% CI 1.29 to 7.21). Haplotype Gc1F of VDBP, wild type for both SNPs, was significantly more frequent in the control group compared to infants with viral infection (OR 3.5, 95% CI 1.3 to 9.7). No significant difference was observed regarding allele frequencies of BsmI, ApaI, FokI and CYP27B1 polymorphisms between the two groups.

Conclusions

Genotypic differences between infants with infection and controls suggest that vitamin D pathway could be associated with the host defense against viral infections during infancy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0418
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Kawasaki disease in younger than 6 months of age: results from multicentre spanish study (kawa-race)

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Background and Aims:

A retrospective cohort study was performed within the KAWA-RACE study group of children diagnosed of KD between 2011-2016 in Spain. The clinical medical records collected on an online database (REDcap) were reviewed and children divided into to 2 cohorts according to age: group 1 (<6 months) and group 2 (≥6 months). Differences in epidemiology, clinical and laboratory data, response to treatment and outcomes were compared.

Methods:

A retrospective cohort study was performed within the KAWA-RACE study group of children diagnosed of KD between 2011-2016 in Spain. The clinical medical records collected on an online database (REDcap) were reviewed and children divided into to 2 cohorts according to age: group 1 (<6 months) and group 2 (≥6 months). Differences in epidemiology, clinical and laboratory data, response to treatment and outcomes were compared.

Results:

Out of the 598 patients, 42 (7%) were <6 months and incomplete/atypical KD presentation was greater in this group (52%vs28%;*p=0.001*). Moreover, 52% in group 1 had an abnormal echocardiogram result vs 30% in group 2 with a significantly higher incidence of CAA (19%vs8.6%;p<0.001). The median time between the onset of fever and IVIG treatment was 7 days in patients <6 months vs 6 days in ≥6 months (*p=0.505*), and IVIG resistance, 14.3%vs15.6% respectively.

Conclusions:

Children <6 months of age in our cohort presented more frequently with incomplete KD and cardiac abnormalities, which is consistent with other studies. No significant increased delay in diagnosis nor resistance to first line treatment was found in infants <6 months suggesting that these factors may be

independent for higher risk of CAA. The clinical course observed in infants <6 months of age could respond to a more severe inflammatory disease in this age group.

Systematic Review Registration:

N/A

ESPID19-0258
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Functional maturation and self-reactivity of the human b-cell system assessed by b-cell receptor repertoire sequencing

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Background

B cells play a central role in adaptive immune processes, mainly through the production of antibodies. Children are born without having had much contact with foreign antigens and are initially protected by maternal antibodies. Through continuous antigen exposure, the human immune system builds a repository of cells bearing diverse antigen-specific adaptive immune receptors that enable a targeted, rapid and extensive secondary immune response.
Little is known about the speed and magnitude or the detailed characteristics of this antigen-driven maturation of the B-cell system throughout childhood.

Methods

We investigated the naïve and antigen-experienced B-cell receptor (BCR) repertoire in 46 healthy individuals aged 6m to 50y. Heavy chain BCR transcripts were amplified and sequenced and data analysis was performed with an in-house bioinformatic pipeline to assess repertoire characteristics and the self-reactive and structural nature of BCR transcripts.

Results

The final dataset consisted of ~7M unique sequences (~150K sequences/individual). In the first 10 years of life, frequencies of highly mutated transcripts greatly increased through positive selection. These changes were accompanied by an increased usage of more downstream constant region genes (IgG2, IgA2) and a decrease in the frequency of transcripts with self-reactive properties indicating that somatic hypermutation has driven specificity of these sequences away from self. Structural analysis showed a higher frequency of antibodies, whose shapes differed from germline, with increasing age.

Conclusions

This study demonstrates an extensive maturation of the B-cell system in the first 10 years of life as a consequence of environmental antigen exposure. Further antibody repertoire alterations continue to be made thereafter, although at a lower rate. This study also provides a reference data set of BCR repertoires and stresses the importance of using well-selected, age-appropriate controls in future studies.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0060
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

The role of 15-lipoxygenase pathway in pathogenesis of pediatric acute respiratory infection

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Background

Acute respiratory infection (ARI) accounts as a leading cause of respiratory difficulties which imposes devastating burden of morbidity in children less than 5 years of ages worldwide. Amongst multiple environmental and pathogenic factors, the relevance of inflammatory mediators in ARI pathogenesis is well documented. 15-Lipoxygense enzyme and derived products have received attention as possible mediators of inflammatory responses. The involvement of 15-Lipoxygense pathway in pathogenesis of acute respiratory infection has yet to be illustrated which is perused in the current study.

Methods

The total number of 80 cases including, 50 patients aged less than 5 years who were diagnosed for acute respiratory infection and hospitalized due to their signs and 30 healthy age-matched controls with no history of diseases was enrolled in this study. The expression level of 15-Lipoxygense isoforms was assessed via Real-Time PCR in nasopharyngeal swab from patients and healthy subjects. The level of 15-Lipoxygense products (15(S) HETE, 13(S) HODE) were evaluated using enzyme immunoassay kits in serum samples.

Results

15-Lipoxygense-1 and 2 expression level was increased in patients suffering from acute respiratory infection comparing to healthy subjects which was more obvious in patients with severe lower respiratory tract infection. The elevated level of 15-Lipoxygense isoforms was accompanied with 15(S) HETE, 13(S) HODE enhancement in serum of patients was consistent with higher expression of 15-Lipoxygense in patients group. The diagnostic value of 15-Lipoxygense isoforms and products were considerable between patients and healthy groups.

Conclusions

The possible effect of 15-Lipoxygense pathway in the regulation of inflammatory responses due to the remarkable role of lipoxygenses in lipid signaling, cytokine secretion, cell development and virus proliferation may light up new therapeutic approaches to relief acute respiratory infection symptoms in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0054
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

The role of cannabinoid receptor 1(cbr1) in the immunopathology of respiratory syncytial virus in mice model

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Background

Endocannabinoid system plays an important role in pathophysiologic processes such as immune functions and impacts on disease severity. Given the potential effects of cannabinoid-mediated regulation of immune function and the complicated RSV associated immunopathology, is tempting to speculate two hypotheses: (i) the endocannabinoid signaling might participate in the RSV infection outcome and (ii) targeting of cannabinoid receptors may be a novel approach for alleviation of RSV immunopathogenesis. In this study, we investigated the role of cannabinoid receptor 1 (CBR1) in RSV immunopathology and its therapeutic potential in mice model.

Methods

To study the role of CBR1 in the immunopathology of RSV, CBR1 was blocked daily with AM281 as a selective antagonist in Balb/c mice and were infected by intranasal inoculation of RSV-A2 24 h following the first dose of antagonist administration. The potential pharmacological therapeutic effects of cannabinoid receptor activation during RSV infection were studied using JZL184 as a selective indirect agonist, 24 h after infection. Mice were sacrificed on day 5 after infection and experimental analyses were performed to study the CBR1 expression, airway immune cell influx, cytokine/chemokine secretion, lung histopathology, and viral load.

Results

RSV infection of airways significantly induced the expression of CBR1 in lung cells of mice. Blockade of CBR1 using AM281 enhanced immune cell influx and cytokine/chemokine production, and aggravated lung pathology. Activation of cannabinoid receptors using JZL184 decreased immune cell influx and cytokine/ chemokine production, and alleviated lung pathology.

Conclusions

This study and our previous finding indicated that endocannabinoid signaling regulates the inflammatory response to RSV infection, and is a potential therapeutic candidate for alleviation of RSV-associated immunopathology.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1047
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Measles immunity in children after oncological treatment

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Background

Immunity against vaccine-preventable diseases is usually impaired by oncological treatment in children with malignancies. They require additional doses of vaccines after the completion of chemotherapy. The aim of the study was to evaluate the immunity against measles in children after oncological treatment with regard to the number of previous measles vaccine doses (one/two) acquired before cancer diagnosis.

Methods

34 children with hematological malignancies after completing chemotherapy were recruited in the study – 19 vaccinated with 1 dose(CHT1) and 15 with 2 doses (CHT2) of measles vaccine before the malignancy diagnosis. The control group included 97 healthy children vaccinated with 1 dose (CONTROL 1) and 102 children vaccinated with 2 doses (CONTROL 2) of measles vaccine. All children were evaluated for the concentration of specific anti-measles antibodies.

Results

GMCs (among the children who presented protective antibodies levels >150 IU/ml) were: CHT1 - 280,0 IU/ml (n=15); CHT2 - 615,9 IU/ml (n=13); CONTROL 1 - 910,2 IU/ml (n=72); CONTROL 2 - 1347,1 IU/ml (n=86) [CHT1 vs CHT2 --> $p<0,05$; CHT1 vs CONTROL 1, CHT2 vs CONTROL 2, CONTROL 1 vs CONTROL 2 -->$p<0,01$]

Conclusions

Chemotherapy impairs the humoral immunity against measles. Two doses of measles vaccine before cancer diagnosis assure higher concentration of antibodies after chemotherapy than only one dose. The number of vaccine doses before cancer diagnosis should obligatorily be taken into consideration while making a decision concerningfurthervaccinations. Measles vaccination should be particularlyimportant in children vaccinated with only one dose of vaccine before cancer diagnosis.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-1082
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Local and systemic cytokine response during respiratory viral infections in children with cancer, fever and neutropenia

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Background

Respiratory viral infections (RVI) in fever and neutropenia (FN) episodes in children with cancer have been poorly characterized. Our aim was to describe local and systemic cytokines profiles during RVI in two groups of children with cancer and FN.

Methods

Prospective, multicenter study in children with cancer and FN from six hospitals in Santiago, Chile (Nov 2013-Nov 2018). One group of children ("Day 1") was enrolled at admission and nasal wash samples were studied. Other group was enrolled at day 4 of fever and a serum sample was obtained ("Day 4"). Detection of RVI was performed by multiplex-PCR for 17 viruses and cytokines were assessed by a panel for 38 cytokines. Description for Day 1 and Day 4 groups was completed, comparing "unknown etiologic agent (UEA)" and "RVI" cases.

Results

A total of 164 episodes of FN were enrolled, of whom 52% were male, 64% had leukemia. Median age was 79.7 months. RVI cases were 71% (117/164), with similar clinical characteristics from UEA group. Most detected viruses were rhinovirus, RSV and parainfluenza. All cytokines levels were significantly lower in Day 1 group ($p<0.001$), with no differences between RVI and UEA cases. For Day 4 group, increased plasmatic cytokines levels were detected in the RVI group: G-CSF;GM-CSF; FLT-3L, IFN-gamma; IL-10; MCP-3; IL-15; IL-17A; IL-1alpha; IL-9; MIP-1alpha; IL-2; IL-5; IL-6; IL-7; IL-8; IP-10; MCP-1 and VEGF.

Conclusions

RVI at day 1 or 4 was not associated with poor clinical outcome. Cytokines at admission in respiratory samples did not increase in RVI cases. At day 4, children with RVI showed a significant increase in systemic cytokines. To our knowledge this is the first report about dynamic cytokine response in FN episodes in children with cancer.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0216
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Prevalence, risk factors, and outcome of viral hemorrhagic cystitis following unmanipulated haploidentical hematopoietic stem cell transplantation in pediatric patients

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Background and Aims:

Viral hemorrhagic cystitis (VHC) can be a severe complication after hematopoietic stem cell transplantation (HSCT), especially haploidentical-HSCT (haplo-HSCT). Although the epidemiology and outcomes in adult haplo-HSCT have been frequently reported, data in pediatric population are still scarce.

Methods:

A retrospective study of 104 pediatric patients underwent haplo-HSCT at Ramathibodi Hospital between November 2013 and October 2018 was performed. Patients diagnosed with BK virus (BK-VHC) and/or adenovirus (Ad-VHC) hemorrhagic cystitis were identified. Severity of VHC was defined as grade I-IV (I=microscopic hematuria, II=macroscopic hematuria, III=presence of blood clot, IV=urinary tract obstruction). Prevalence, clinical characteristics and outcome were described. Possible risk factors associated with VHC were determined using logistic regression model.

Results:

Thirty-seven patients (35.6%) developed VHC in a median time of 36 days (IQR 24.5-43). The mean age was 11.2 (4.8) years and 73% of them were male. Among cases, 17 (45.9%), 9 (24.3%) and 11 (29.7%) were BK-VHC, Ad-VHC, and mixed-viruses, respectively. Majority of cases were defined as grade II and III (45.9% and 35.1%). The median duration between onset of VHC and clinical response was 20 days (IQR 10-39). Intravenous cidofovir were used in 24 (64.9%) patients who failed conservative treatment with hyperhydration. Eight (21.6%) patients died due to non-VHC related causes. Male gender was associated with VHC [OR 3.0 (95%CI 1.17-7.69)]. The mean age at transplantation in patients with VHC was significant higher than those without VHC (11.2 vs 7.3 years; p=0.001). Each increasing year of age at transplantation increased the OR of VHC by 1.2 folds.

Conclusions:

The prevalence of VHC in pediatric haplo-HSCT recipients is considerably high. Therefore, frequent viral monitoring and prompt treatment is required for better outcome.

Systematic Review Registration:

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ESPID19-0158
Science and Educational Track

E-Poster discussion session 09 - Immunology and the host pathogen interaction - Station 03

Ancestry patterns inferred from massive rnaseq data highlights the importance of controlling infectomic studies for the potential confounding effect of ancestral genetic background

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Background

There is a growing body of evidence suggesting that patterns of gene expression vary within and between human populations. However, the impact of this variation in human diseases has been poorly explored, in part owing to the lack of a standardized protocol to estimate biogeographical ancestry from gene expression studies.

Methods

Here we examine several studies that provide new solid evidence indicating that the ancestral background of individuals affects the host gene expression patterns in response to infectious diseases. Next, we test a procedure to infer genetic ancestry from RNAseq data in 25 datasets where information on ethnicity was reported. Genome data of reference continental populations retrieved from The 1000 Genomes Project were used for comparisons

Results

We demonstrate the ancestral background of donors could be inferred very efficiently, even in datasets including samples with complex patterns of admixture (e.g. American-admixed populations). For most of the gene expression datasets of questionable quality, ancestral inference yielded odd patterns.

Figure legend:

MDS plots and ancestry analysis for each of the eight datasets that overcome all the quality filters; their GEO ID numbers are indicated on top of each MDS analyses together with the number of SNPs involved in each analysis. In the admixture barplots (right) the label of the test population is bolded and their ancestral memberships barplots slightly separated from the barplots of the reference continental populations (from 1000G)

Conclusions

The present study thus brings a cautionary note for future biomarker research and infectomic studies highlighting the importance to control for the potential confounding effect of ancestral genetic background

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1187
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Virologic failure among children and adolescents in Kenyatta National Hospital, Kenya

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Background and Aims:

Children and adolescents on ART are more likely to fail treatment due to their lifelong treatment and reliance on caregivers. We sought to determine incidence rates, time to virologic failure and factors associated with virologic failure among children and adolescents on follow up at the Kenyatta National Hospital (KNH) Comprehensive Care Centre (CCC)

Methods:

A retrospective review of electronic records of HIV infected children and adolescents aged less than 20 years on follow up for longer than 6 months at the KNH CCC between January and December 2017,excluding those with missing data. We estimated incidence rates of virologic failure, defined as viral load above 1000 copies/ml. Chi-square test of association and multivariate analysis were used to explore factors associated with virologic failure while Cox proportional hazard (CoxPH) regression with time-dependent covariates determined time to virologic failure with its co-variates.

Results:

Of the 819 children and adolescents included in the analysis, 52% were males, 60% were children (0-14 years). Average age at enrolment was 5.5 years and median duration on ART was 98 months. Overall incidence of virologic failure was 13.1%. Predictors of virologic failure were 2nd line or 3rd line ART regimen, aOR 4.6 (95% C.I: 1.8-12, p=0.002) and non-adherence to treatment, aOR 3.5 (95% C.I: 2.1-5.6, p<0.001). The mean time to virologic failure was 114 months (95% CI 107-121) and median time to virologic failure was 125 months (IQR 111-138). Duration in months on ART (aHR =0.965, 95% CI=0.952-.978), BMI (aHR= 1.168, 95% CI 1.012-1.349) and age at last visit (aHR =0.826, 95% CI=0.702-.971) significantly predicted time to virologic failure.

Conclusions:

Interventions addressing adherence are required so as to maintain patients on first line regimens for longer.

Systematic Review Registration:

None

ESPID19-0984
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

High rates of measles seronegative status among adolescentes and adults living with hiv despite previous vaccination

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Background and Aims:

People living with HIV (PLHIV) may be more susceptible to infections due to their poor response to immunisation. At the global concerning scenario of measles re-emergence, assessing measles immunological status of PLHIV might be of interest.

Methods:

This study was approved by the local ethics committee (CAAE: 97464718.4.0000.5505) and was conducted from July to December 2018. PLHIV were divided into 2 groups: vertical and horizontal HIV transmission. Clinical data and measles vaccination status were recorded, and a blood sample was taken to measure measles IgG titres. We used the ELISA kit from Euroimmun®. As designated by manufacturer, titres above 275 UI/L were considered positive.

Results:

We studied 81 patients, 48 females (59%) and 33 males (41%). Age ranged from 10 to 43 years (median, 22 years). Vertical group had 58 patients and Horizontal group, 23. All patients were receiving cARV, except 1 from Vertical group. In Vertical group, 53 (91%) had at least 1 registered dose of MMR and in Horizontal group, 9 (39%). A total of 54 patients from Vertical group and 16 from Horizontal had negative measles IgG antibodies (93.1% vs 69.6%). In Vertical group, median CD4+ T cells was 619 in the negative and 1164 in the positive; in Horizontal group, these values were 606 and 498, respectively (ANOVA, p= 0.214). In Vertical group, 37 individuals (64%) had viral load levels below 40 copies/mL and in Horizontal group, 21 (91%). All patients with measles positive results had levels below 40 copies/mL.

Conclusions:

With the present increased risk of acquiring measles, we should consider measuring measles antibodies routinely and revaccinating PLHIV with low titres, especially patients who acquired the infection vertically and were immunocompromised at the time of routine vaccination.

Systematic Review Registration:

N/A

ESPID19-0644
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Vertical transmission, genotyping and virological outcome in children under 18 months old living with hiv-1 in brazil

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Background

HIV-1 mother-to-child transmission is still a public health issue in Brazil, despite free access to antiretroviral therapy (ART) and easily available diagnostic tests. Recent studies have shown vertical transmission rates between 1.9% and 6.6%.

Methods

Our study evaluated perinatal prophylaxis, genotyping and virological outcome of 21 infected children, among 546 patients assessed for vertical transmission (VT) in our lab, between 2013 and 2017.

Results

We found a VT of 3.85% (95% CI 2,46%-5,72%) in the metropolitan area of São Paulo. Little over half of the infected children received perinatal ART and less than half of the mothers took ART during pregnancy. No evidence of transmitted resistance was found in these infants. At the end of 2017, 18 children were under ART but only a third of these had an undetectable viral load.

Conclusions

Many of the infected mothers are presumed to be homeless and drug addicts. This marginalized and hard-to-reach population contributes to the maintenance of the HIV epidemics, in contrast to other populations in which we are close to achieving the WHO's 90-90-90 goal. It is essential to create strategies to involve these women in the public health system in order to prevent HIV-1 VT, as well as to control the epidemics.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-1168
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

10 years status of the national cohort of hiv positive children in Denmark

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Background and Aims:

Considerable progress has been achieved in the prevention and management of HIV in children globally and particularly in the European perspective. However, we may still improve. We report the characteristics of the Danish national paediatric HIV cohort over the last 10 years.

In Denmark, the HIV incidence is stable, and 5400 people are living with HIV. Since 2010, screening has been included in antenatal care. Paediatric HIV care is centralized in 4 hospitals and managed according to the guidelines of The Paediatric European Network for Treatment of AIDS.

Methods:

All children, < 18 years of age diagnosed with HIV in Denmark in the study period from January 2008 to December 2017, were included from the patient lists in the 4 hospitals responsible for paediatric HIV management in Denmark. No exclusion criteria were applied. Data was obtained retrospectively from the electronic patient files.

Results:

54 children were included. Approximately half were girls, most of foreign origin (94%), born abroad (72%) and >1 year of age at diagnosis in Denmark (85%). We evaluated possible suboptimal prevention or delayed diagnosis in Denmark in several of the children born here, and in none born abroad. Care prior to immigration was not evaluated.

Management was uncomplicated in the vast majority with CD4 count >25 %, HIV RNA< 200, no comorbidity and no side-effects to antiviral treatment. However, a third required psycho-social support and comprehensive support was needed in half of those.

Conclusions:

In this 10 years status of our national paediatric HIV cohort of 54 children, the majority was of foreign origin and born abroad. Delayed diagnosis or suboptimal prevention was identified in several children born here leaving a potential for improvement. Treatment management was uncomplicated in most children.

Systematic Review Registration:

not-relevant

ESPID19-1143
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Mother-to-child transmission of hiv infecton: a 11-year experience of a portuguese pediatric hospital unit

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Background and Aims:

Pediatric Human Immunodeficiency Virus (HIV) infection is almost exclusively acquired by vertical transmission. Interventions to prevent mother-to-child transmission (MTCT) can decrease transmission rate below 2%. National implementation of these measures has resulted in a decline in HIV MTCT in Portugal.

Methods:

We conducted a retrospective observational study, from January 2008 to December 2018, and analyzed pregnancy, delivery and pediatric follow-up data collected from HIV-infected mothers and their newborns.

Results:

460 children were born to HIV-mothers and 7 were infected (transmission rate of 1.52%). 94.4% of the mothers were infected through sexual transmission. 87.2% HIV-1, 9.8% HIV-2 and 3.0% HIV 1 and 2. 15% had other coinfections. 72.0% were African immigrants. HIV diagnosis was known prior to pregnancy in 58%, during pregnancy in 36.3%, and intrapartum in 3.7% of mothers. 84,5% had prenatal care. 85% received Antiretroviral (ARV) therapy during pregnancy. 82.0% received intrapartum zidovudine. The duration of membrane rupture was less than 4 hours in 67.4%, and greater than 4 hours in 26.5%. 55.7% of mothers had vaginal delivery, and 13.3% had elective C-section.
None of the infants were breastfed. 99.6% completed ARV-prophylaxis (87.8 % zidovudine, 11.7% triple).
Seven infants were diagnosed with HIV-1 infection. Five were born to African mothers. Three out of the seven women received prenatal care and of these, two started ARV during pregnancy. Three did not receive intrapartum zidovudine. All infants completed ARV-prophylaxis (3 zidovudine monotherapy, 4 triple ARV).

Conclusions:

The transmission rate reported is in line with Portuguese data. The HIV-diagnosed children described above come from a MTCT high-risk population (African immigrants, no prenatal care, late diagnosis) in which the success of MTCT protocol application is limited.

Systematic Review Registration:

N/A

ESPID19-1057
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Growth determinants in hiv-exposed and uninfected infants in a tertiary care hospital in spain

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Background and Aims:

HIV-exposed and -uninfected (HEU) infants may be at increased risk of poor growth outcomes, as long term effects of intra-utero ART exposure are unknown. Most studies addressing growth in these populations come from resource limited settings in which malnutrition is frequent and ART regimens are limited. We aim to characterize birth outcome and infant growth during first months of life in a cohort of HEU infants, to identify factors associated with healthy growth.

Methods:

HIV-positive women and their babies born 2000 to 2017 participating in the Madrid Cohort of HIV-infected mother-infant pairs were included. Infant anthropometrics were regularly collected up to two years.

Results:

A total of 325 mother-infant pairs were included, 73% caucasian. The mean age of HIV-infected mothers was 33.3 years (±5.6). A 69% were on treatment before pregnancy, and 31% started ART during pregnancy; 25.2% on a regimen containing tenofovir. The rate of viral suppression at partum was 96.7%. Median gestational age was 38 weeks [37-38]; intrapartum AZT was administered in 70%, caesarian section in 11.3%, 89% newborn started prophylaxis within 48h and only one was breastfed. Mean weight at birth was 2.814 gr (±533), 53% were female, 22% preterm babies and 1% delayed intrauterine growth. Rates of children below 2SD for weight at birth, 12 months and 24 months were 5.2%, 5.2% and 3.1% respectively, and for length 10.9%, %, and 8.5%. No association was found between tenofovir exposure and weight or length at birth, 12 or 24 months follow-up.

Conclusions:

In our cohort of HIV-infected mother and their offspring, preterm births were frequent. Growth patterns among HEU children were comparable to general population. Exposure to tenofovir did not seem to have any effect on growth in this cohort.

Systematic Review Registration:

ESPID19-0970
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Simplification to EVG or DTG single-tablet regimens in adolescents in Spain (corispe)

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Background and Aims:

There are important issues and challenges in the treatment of HIV-infected adolescents. The aim of the study was to describe the characteristics of adolescents who were switched to a single-tablet regimen containing an integrase inhibitor (II) as a simplification strategy.

Methods:

A multicentre, retrospective study of adolescents with HIV infection from the Spanish Paediatric HIV Cohort (CoRISpe). All patients older than 12 years who had received treatment with TAF/FTC/EVGc and ABC/3TC/DTG in a single tablet (STR) until December 2017 were included. Before switching, patients should have been with HIV-1 RNA <50 copies /ml for at least 6 months. The characteristics of the patients at baseline and at 6 months were analyzed.

Results:

Fifty patients were included (27 women, 54%), with a median age of 14.5 years (IQR 16.9-19.7). According to CDC, fifteen patients (30%) were in category C/3. Baseline ART regimens included PI (19, 38%), NNRTI (26, 52%) and II (5, 10%). Seventeen patients (34%) were in twice daily regimens and fifteen patients (30%) with a STR. Twenty-three patients (46%) were simplified to TAF/FTC/EVGc. Four patients who had previously selected the M184V mutation were switched to ABC/3TC/DTG. Forty-six patients (92%) had HIV-1 RNA <50 copies/ml at 6 months. There was no case of discontinuations due to adverse effects. A non-significant increase in GFR (+5,45 ml/min/1.73m2) was observed at six months in 18 patients (36%) who were receiving TDF before switching. There were no significant differences in lipid profile.

Conclusions:

This study showed that simplification to a STR (TAF/ FTC/EVGc or ABC/3TC/DTG) in adolescents with HIV-infection has durable maintenance of virologic suppression. Further studies are needed to assess if this strategy may lead to greater adherence and improved quality of life.

Systematic Review Registration:

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ESPID19-0253
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Safety and immunogenicity of measles vaccination in hiv-infected and HIV-exposed uninfected children: a systematic review and meta-analysis

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Background

HIV-infected and HIV-exposed uninfected (HEU) children have an increased risk of measles that may be due to altered immune responses or suboptimal timing of measles vaccination. We aimed to evaluate the safety and immunogenicity of measles vaccination in HIV-infected and HEU children.

Methods

Health Library and IndMED on May 9, 2018. Studies were included if they reported on safety or seroresponse (either seroprotection/seropositivity/seroconversion) after measles vaccination in HIV-infected or HEU children. We calculated pooled estimates to compare immunogenicity outcomes between HIV infected, HEU and HIV-unexposed children, using risk ratios [RRs] (with 95%CIs).

Results

Seventy-one studies met the inclusion criteria (15,363 children). Twenty-eight studies reported on safety; vaccine-associated adverse events and deaths were uncommon. Sixty-two studies reported on immunogenicity, 27 were included in the meta-analysis. HIV-infected children had lower seroresponse rates after primary vaccination compared with HIV-unexposed (RR 0.74; 95%CI: 0.61–0.90, I2= 85.9%) and HEU children (0.78; 0.69–0.88, I2=77.1%), which was mitigated by antiretroviral therapy and time interval between vaccination and serology. HEU and HIV-unexposed children had similar seroresponses. Vaccination at 6-months resulted in similar proportions of HIV-infected children having seroresponse compared with HIV-unexposed (0.96; 0.77–1.19) and HEU children (1.00; 0.73–1.37, I2=63.7%).

Conclusions

Primary measles vaccination at 6-months of age may provide protection against measles during early infancy in settings with high prevalence of maternal HIV-infection, however, further studies are needed to evaluate this strategy in HEU children and HIV-infected children receiving antiretroviral therapy.

Systematic Review Registration (Please input N/A if not registered)

PROSPERO registration number: CRD42017057411

ESPID19-0117
Science and Educational Track

E-Poster discussion session 10 - HIV in children - Station 05

Clinical scores for non-alcoholic fatty liver disease in vertically HIV-infected children and adolescents: do they work?

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Background and Aims:

In western countries, the prevalence of non-alcoholic fatty liver disease (NAFLD) has increased during the last years, associated to obesity and the metabolic syndrome. Data suggest that inflammation secondary to HIV-infection could contribute to progression to steatohepatitis. Different clinical scores have been suggested for screening of NAFLD in adult population, but data in pediatric and vertically HIV-infected youths are scarce.

Methods:

A retrospective multicenter study was performed within the Spanish Cohort of HIV-infected children and adolescents, including vertically HIV-infected youths with at least two blood test during 2017. Co-infected patients (HCV and/or HBV) were excluded. Clinical, immunovirological and analytical parameters were reviewed. Analytical parameters were considered altered when above the following thresholds in at least two determinations: glucose >100 mg/dl, ALT >35 IU/L, AST >40 IU/L, total cholesterol >200 mg/dl, triglycerides >150 mg/dl. HSI, APRI, TyG and FIB-4 liver steatosis and fibrosis scores were calculated, cut-off pints [HSI>30; TyG>8.38; APRI>0.7; FIB-4>1.3].

Results:

109 patients included, 56% women, median of 16 years age (IQR 11.0-20.0). All patients were on antiretroviral treatment (35.8% PIs), 85.8% virologically-suppressed, median CD4 T-cell counts of 770 cel/ml (IQR 543.5-1060.5). Unexplained alteration of ALT 4.6% and 2.3% AST. Regarding scores, 22.1% had HSI altered and 16.1% had APRI altered in at least two independent measurements. TyG and FIB-4 scores were not altered in any patient.

Patients with higher HIS scores were more frequently immunosuppressed (CD4<500 cel/ul: 36%; vs 15.7%, p=0.046) and displayed lower CD4/CD8 ratio (CD4/CD8ratio<1: 40% vs 10%, p=0.004).

Conclusions:

In this cohort of vertically HIV-infected youths concordance among the different scores for stratification of liver damage was very low, suggesting that new imaging techniques might be needed to establish the prevalence of NAFLD in this unique population.

Systematic Review Registration:

No

ESPID19-1097
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Distribution of serotypes causing pediatric invasive pneumococcal disease (ipd) in canada according to the current and next-generation higher-valency pneumococcal conjugate vaccines (pcv) coverage

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Background and Aims:

13-valent pneumococcal conjugate vaccine (PCV13) has been routinely used in Canada since 2010/2011, replacing PCV7/PCV10. Two higher-valency pneumococcal conjugate vaccines, PCV15 and PCV20, are currently under development. The objective of this retrospective study is to assess serotype distribution among Canadian pediatric IPD isolates collected from 2010 to 2016 according to coverage by PCV10, PCV13, PCV15, and PCV20 formulations.

Methods:

The National Microbiology Laboratory (NML) has been conducting laboratory-based national surveillance of IPD since 2010, and publicly reporting yearly case counts for pediatric and adult populations. We calculated the proportion of IPD caused by serotypes covered by higher-valence vaccines for children <5 years of age by using currently available NML's annual reports (2010- 2016 surveillance years). Only vaccine-type isolates were included in coverage calculations (vaccine-related serotypes were not considered). Since NML did not consistently distinguish between serotype 15B and 15C isolates, 15B/C counts were included as proxy for 15B-type disease.

Results:

In 2010, the year when Canadian provinces began replacing the existing PCV7/PCV10 programs with PCV13, 17% of IPD in children under 5 years of age was due to PCV10 and 67% was due to PCV13 serotypes (total n=332). By 2016, 4% of all IPD was due to PCV10 and 19% to PCV13 serotypes (total n=260). In 2016, PCV15- and PCV20-type IPD represented 35% and 60% of the disease.

Conclusions:

Proportion of IPD due to PCV13 serotypes has decreased considerably among children <5 years of age since the introduction of routine pediatric PCV13 programs in Canada. Majority of remaining vaccine-preventable disease is represented by PCV13/non-PCV10 serotypes. Higher-valent PCV formulations could provide progressively larger coverage against *S. pneumoniae*, with PCV20 potentially addressing considerable proportion of the remaining invasive pediatric disease in Canada.

Systematic Review Registration:

n/a

ESPID19-1039
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Does bcg vaccination improve protection against pertussis infection?

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Background and Aims:

BCG could have enhancing effect on the immune response to unrelated vaccines. It has been suggested that the recent increase in whooping cough cases could be higher in countries that use DTaP (diphtheria-tetanus-acellular pertussis) than those using DTwP (whole-cell pertussis), suggesting the importance that the Th1 immune response might be implicated in protection against *Bordetella pertussis*. As BCG is a strong inducer of Th1 response, we intrigued if it could improve protection against *B. pertussis*. In addition, preliminar results in mice (unpublished) have shown that BCG is able to improve cellular and humoral immune response of DTaP. Consequently we aimed to assess wether pertussis incidence worldwide varies according to the use of BCG.

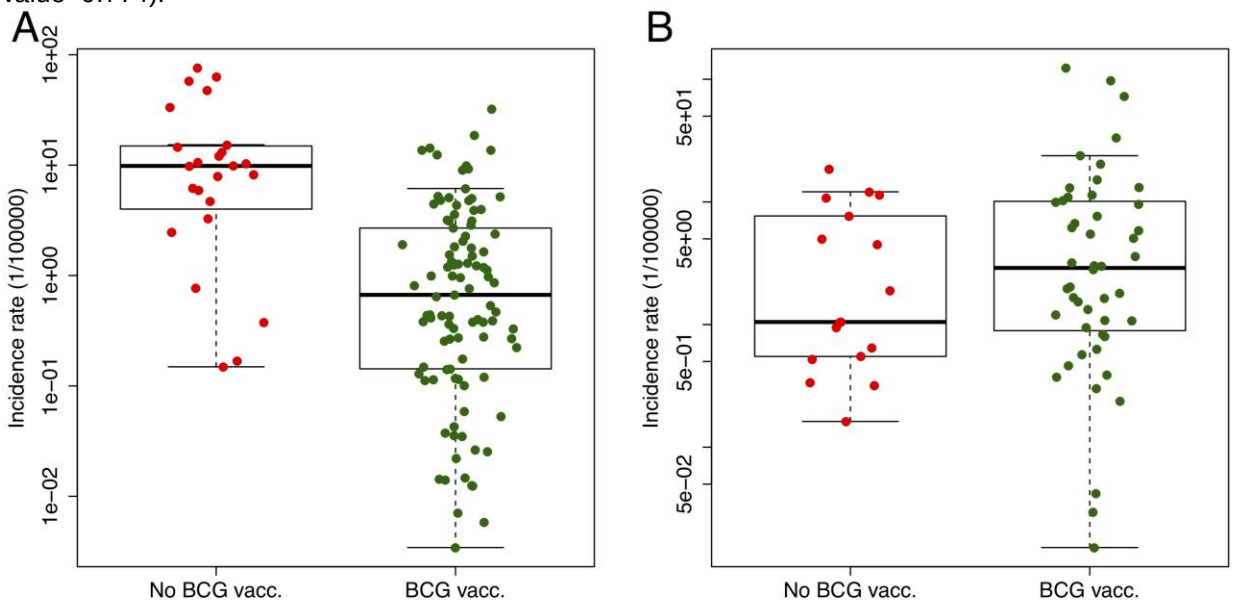
Methods:

We conducted a retrospective epidemiological study using pertussis data from *World Heatlh organisation* (WHO), population data from *World Development Indicators* webpage and BCG vaccination policies from BCG atlas website. Yearly incidence rates of pertussis, maeasles and mumps were computed for each of the 161 included countries and Wicoxon test was considered to assess if there were significant differences between countries with and without BCG vaccination. The same analysis was performed only for Europe and comparing DTwP and DTaP using countries.

Results:

Pertussis incidence was higher in countries without BCG vaccine program (Figure 1A; *P*-value=3.8×10^{-8}), while no differences were found for mumps (Figure 1B; *P*-value=0.345). This was similar in Europe (*P*-value=5.2×10^{-6}), where the use of either DTaP or DTwP had no differential effect over that of BCG (P-

value=0.774).



Conclusions:

Our data, despite the limitations inherent to ecological studies, strongly suggest that the use of BCG may be benefitial in terms of pertussis prevention, irrespective of the use of wP or aP component. This finding warrants further analysis.

Systematic Review Registration:

N/A

ESPID19-0947
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Factors associated with trends in hospitalization and mortality rates due to invasive pneumococcal disease in the southeast region of brazil from 2005 to 2015

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Background and Aims:

The aim of this study was to evaluate the trends and the effects of socioeconomic factors, access to health services, vaccination coverage and vaccination schedule in the hospitalization and mortality rates due to invasive pneumococcal disease (IPD) in children under one year of age in municipalities of the southeastern region of Brazil (2005-2015), before and after the incorporation of the IPD vaccination in the Brazilian national immunization program.

Methods:

In this ecological study we used the joinpoint regression to describe changes in rate trends and the Poisson multilevel regression model to analyze the effects of the independent variables on rates.

Results:

Both hospitalization and mortality rates showed a decreasing trend along the period of the study. The introduction of the vaccine was associated with a reduction of 14% in the hospitalization rate and of 6% in the mortality. In the post-vaccination period, after 2010, the municipal human development index was associated with lower rates of hospitalization and mortality. Higher vaccine coverage was associated with lower hospitalization rates, while access to health services was directly related to hospitalization. The vaccination schedule with doses at 3-5-7 months compared to the schedule at 2-4-6 months was associated with higher mortality, while access to health services was associated with lower mortality. Mortality rates did not show a trend pattern like that of hospitalization, with a decrease observed in the pre-vaccination period, which can be related to other socioeconomic aspects.

Conclusions:

The results highlight the importance and difficulties of performing research with data from health information systems and point to the need for new studies seeking to understand the phenomenon through different approaches, contributing to the improvement of surveillance systems and the consolidation of public health policies.

Systematic Review Registration:

N/A

ESPID19-0936
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Molecular epidemiology and virulence gene content of bordetella parapertussis producing whooping cough in barcelona

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Background and Aims:

Bordetella pertussis and *Bordetella parapertussis* (Bpp) are the main etiologic agents of whooping cough. There is little information about the molecular epidemiology and the virulence traits of Bpp. The aim of the present study was to describe the molecular epidemiology and the virulence traits of Bpp isolates from Barcelona.

Methods:

Whole genome sequencing of 23 Bpp isolates collected between 1993 and 2018 from patients diagnosed with pertussis at the Hospital Vall d'Hebron (Barcelona, Spain) was performed. Phylogenetic relationship was established by SNP analysis. Identification and genotyping of virulence-related genes were performed by the CLC Genomics Workbench and the BIGSdb.

Results:

290 variable positions were identified in the SNP analysis. The phylogenetic tree showed: I) a major cluster (cluster#1) including 15 (65.2%) isolates collected from 2007 to 2018, all of them presenting the ΔG1895 mutation in the pertactin gene, and II) a small cluster (cluster #2) containing 3 (13%) isolates obtainedin 2007 presenting the ΔA988 mutation in the pertactin gene. Both mutations are associated with lack of pertactin production. Five isolates were in single divergent branches associated with other three pertactin genotypes. No relationship was found between phylogeny and genes encoding other virulence traits of the microorganism. Virulence-related genes were identical in all isolates except for genes encoding pertactin, filamentous hemagglutinin and dermonecrotic toxin. According to MLST scheme, all isolates belonged to ST19.

Conclusions:

In our geographical area, one cluster of Bpp has been circulating predominantly since 2007. The results suggest that the presence of ΔG1895 mutation in the pertactin gene may confer an advantage for the cluster dissemination. Unlike other virulence traits, pertactin loss could have conditioned the Bpp phylogeny.

Systematic Review Registration:

N/A

ESPID19-0719
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Similarities in the distribution of s. Pneumoniae serotypes of invasive disease and nasopharyngeal colonization over the seven years of introduction of pcv10 in brazil

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Background and Aims:

PCV10 was introduced into the Brazilian Childhood Routine Immunization Program in 2010. We sought to evaluate the distribution of invasive and nasopharyngeal pneumococcal serotypes along the seven years of the PCV10 introduction.

Methods:

Isolates of *S. pneumoniae* nasopharynx were obtained from three surveys, 2010 (n= 501; baseline), 2013 (n=400), and 2017 (n=531), for children aged 12-<24 months living in São Paulo. Invasive pneumococcal isolates were obtained from the national laboratory-based surveillance from January-2008 to December-2017 for 931 children <5 years of age living in São Paulo state. Serotyping was performed by Quellung. MLST was performed to all 19A serotypes. Analysis of the invasive isolates was performed biannually from 2008-2017. Comparison of the distribution of serotypes amongst invasive and carriage considered the respective study periods.

Results:

In the pre-PCV10 period the common serotypes for carriage were 6B, 19F, 6A and 14 and for invasive isolates 14 and 6B. Carriage vaccine-types sharply decreased in 2013 and 2017 surveys, while increase in proportion of non-PCV10-types was observed, mainly due to the sharp increase in 19A serotype. A reduction in the proportion of serotype 6A was observed among carriage. The same was observed for invasive isolates as serotype 19A sharply increased from 2012-2013 to 2016-2017 and serotype 6A markedly decreased from 2014-2017 (although not among the most prevalent in pre-PCV10). For serotype 19A clonal complex 320 was the most prevalent either for invasive or carriage isolates.

Conclusions:

A consistently similar pattern was observed for the most prevalent serotypes over 7 years after PCV10 introduction in Brazil with a clear tendency to increase of serotype 19A and decline of serotype 6A for invasive and carriage isolates.

Funding: The 2017 carriage survey was supported by Pfizer, Inc., USA.

Systematic Review Registration:

N/A

ESPID19-0663
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Screening of hepatitis b in immigrant pregnant women and mother to child transmission in a low-prevalence latin american country

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Background and Aims:

Migration is a worldwide phenomenon with high impact on public health. Hepatitis B (HBV) prevalence in Asian, Sub-saharan, Latin-American and Caribbean countries (LAC) are considered intermediate-high. Chile is a very low-prevalence country, with an overall rate <1%, were universal screening for HBV during pregnancy is not established. Nowadays, the greatest migratory flow to Chile comes from LAC. Newborns of mothers with HBsAg(+) should receive HBV immunoprophylaxis (IP) (hepatitis B immunoglobulin+vaccine) during first day of life to reduce the risk of vertical transmission by more than 90%.

The aim of this study was to determine HBsAg prevalence in pregnant women and to assess the IP administration timing in the newborn.

Methods:

Prospective study in immigrants and Chilean pregnant women, with high risk factors (HR)(illicit drug users, positive sexual partner, other sexual transmitted infections(STIs)). Serum HBsAg screening was performed between July 1, 2017 and June 30, 2018 in one tertiary health-care center. All newborns from an HBsAg(+) mother should receive IP within <12 hrs of life. The study was approved by the IRB.

Results:

During the study period,there were 4193 deliveries in the obstetric department. 30% of them from immigrant's mothers**.** HBsAg samples were collected from 1415 mothers: 1265 immigrants and 150 chileans with HR. HBsAg was positive in 35 cases, reaching a prevalence 2.7%(34/1265) in immigrants and 0.66%(1/150) in chileans with HR($p<0.05$). All newborns(33) received IP with a median timing of 3 hrs (4 pregnancies still in progress).

Conclusions:

HBV prevalence in pregnant women was four times higher in immigrants than in Chilean mothers with HR. Efforts to increase case identification during pregnancy must be implemented to avoid vertical transmission. Tailored or universal screening in pregnancy against HBV should be considered in our country.

Systematic Review Registration:

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ESPID19-0641
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Evaluation of the investigation, treatment and clinical outcomes of paediatric patients with whooping cough (bordatella pertussis) at leicester university hospital trust from 2012-2017

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Background and Aims:

This retrospective study investigates the adherence to local guidelines and clinical outcomes of paediatric patients with *Bordatella pertussis*at University Hospital of Leicester (UHL) NHS Trust between 1st January 2012 and 31st December 2017. Performance was measured against the internal guidelines for investigation, treatment and reporting of cases to Public Health England (PHE). It formed part of an audit into care for paediatric pertussis patients.

Methods:

Forty-four pertussis patients were identified through clinical coding or microbiological confirmation. Five patients were excluded due to insufficient clinical data, duplication or community treatment. The remaining thirty-nine patients were evaluated by systematically reviewing their clinical notes; recording whether the patients were correctly investigated, treated and notified to PHE, as well as the patient's clinical outcome. This information was corroborated against PHE records.

Results:

31 (84%, n=37) patients were correctly investigated and 17 (46%, n=37) patients were correctly treated. 8 (21%, n=39) patients had notification to PHE recorded in their clinical notes, well below the 23 (53%, n=43) cases in the PHE records. 11 (28%, n=39) patients were admitted to Paediatric Intensive Care Unit (PICU), 5 (13%, n=39) patients received Extracorporeal Membrane Oxygenation (ECMO) and 6 (15%, n=39) patients died. There was a statistically significant increased average length of time between admission and diagnosis for those that died compared to those that survived (*p=0.03*).

Conclusions:

These findings show considerable room for improvement in the optimal treatment of pertussis patients and should inform future pertussis guidelines. In particular, greater emphasis should be put on patients with symptoms lasting > 3 weeks, who were responsible for the majority of incorrect investigations and treatments. Furthermore, evidence suggests faster diagnosis of pertussis patients may lead to improved clinical outcome.

Systematic Review Registration:

NA

ESPID19-0586
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

The epidemiology of listeriosis in pregnant women and children in new zealand from 1997 to 2016: an observational study

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Background and Aims:

Listeria monocytogenes causes listeriosis and in resource–rich countries has the highest case-fatality rate of any foodbourne pathogen.The New Zealand (NZ) Ministry of Health publish food safety in pregnancy guidelines as part of a public health initiative to reduce infection in pregnancy. However the impact of listeriosis on children in NZ has not been studied. The aim of this study was to describe the epidemiological trends in disease notifications and hospital admissions due to listeriosis in pregnant women, infants and children in NZ.

Methods:

In this population-based descriptive study, routinely collected data on hospitalisation and notification rates were analysed from 1997-2016. Pregnant women aged 15-45 years and children <15 years were included. Trends over time were analysed and subgroup analysis was conducted for age, ethnicity and geographical location. Clinical outcomes, including morbidity and mortality were described.

Results:

In the 20-year study period there were 118 cases of listeriosis that resulted in hospitalisation (average annual rate 0.33/100,000), and 144 cases that were notified. Of the 118 listeriosis related hospitalisations, 84 cases (71.2%) were pregnant women and 34 cases (28.8%) were children. Children < 0 years (i.e. infected with *L. monocytogenes*at birth) were most commonly hospitalised (crude rate 1.69 per 100,000). Women (1.18/100,000) and children (0.36/100,000) identifying as Pacific Island ethnicity had the highest incidence of disease notification and hospitalisation.

Conclusions:

Listeriosis is a rare infection in pregnant women and children in New Zealand suggesting food safety messages for pregnant women have been effective. This is the first study to identify an increased risk of infection in Pacific Island women and their infants. Future public health messaging focusing around prevention of listeriosis should specifically target Pacific Island cultural groups.

Systematic Review Registration:

N/A

ESPID19-0576
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

New enzyme immunoassay for detecting naturally-acquired antibody against haemophilus influenzae type a in pediatric saliva

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Background

Haemophilus influenzae type a (Hia) has a particularly high prevalence in Indigenous communities of North America. Invasive Hia disease occurs primarily in young children (<2 years old), and manifestations include meningitis, bacteremia, pneumonia, epiglottis and septic arthritis. An Hia vaccine is in development, and an appropriate target population needs to be identified. The immuno-epidemiology of this disease, particularly Hia carriage and its transmission pattern are unclear and ideally require non-invasive studies. The aim of this study was to develop and utilize a new method for detection of anti-Hia IgA in pediatric saliva.

Methods

Pediatric saliva was collected from 12 healthy 2-7 year old Indigenous children undergoing dental procedures. Total IgA and Hia capsular polysaccharide (CP)-specific IgA were measured by enzyme-linked immunosorbent assay. Total protein was quantified using a modified version of Micro Lowry protein assay. Hia CP-specific IgA was expressed as arbitrary units (AU), based on absorbance measurements, and normalized to total salivary IgA levels. All assays were done in duplicate.

Results

Total salivary protein varied between 1,582-8,943 µg/ml saliva. Total IgA levels were 83-680 µg/ml saliva. Total IgA represented 3.3% to 13.7% of total salivary protein. Hia CP-specific IgA was detected in 11/12 (92%) samples, with a median of 13.4 AU Hia-CP IgA/total IgA (range 1.0 to 96.3). By comparison, adult samples had 36-44 AU Hia-CP IgA/total IgA.

Conclusions

We have developed a new assay for detection of anti-Hia specific IgA antibodies in saliva, with sufficient sensitivity to detect low levels of antigen-specific salivary IgA in healthy, unvaccinated children. This approach will help to clarify the epidemiology of Hia carriage and transmission, and thereby identify potential target populations for vaccination.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0254
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

2-years of automated data extraction from primary-care-pediatricians' computers: french pediatric ambulatory research in infectious diseases (pari)

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Background and Aims:

Infectious diseases account for 50-70% of ambulatory pediatric daily practice. In order to improve the diagnostic performance of primary-care pediatricians by providing real time data on epidemiology of several infectious diseases, we have set up a national surveillance network, PARI (Pediatric and Ambulatory Research in Infectious diseases) using an automated data extraction from the primary-care-pediatricians' computer. The participating pediatricians were specifically trained in diagnostic and treatment of infectious diseases and the use of rapid diagnostic tests.

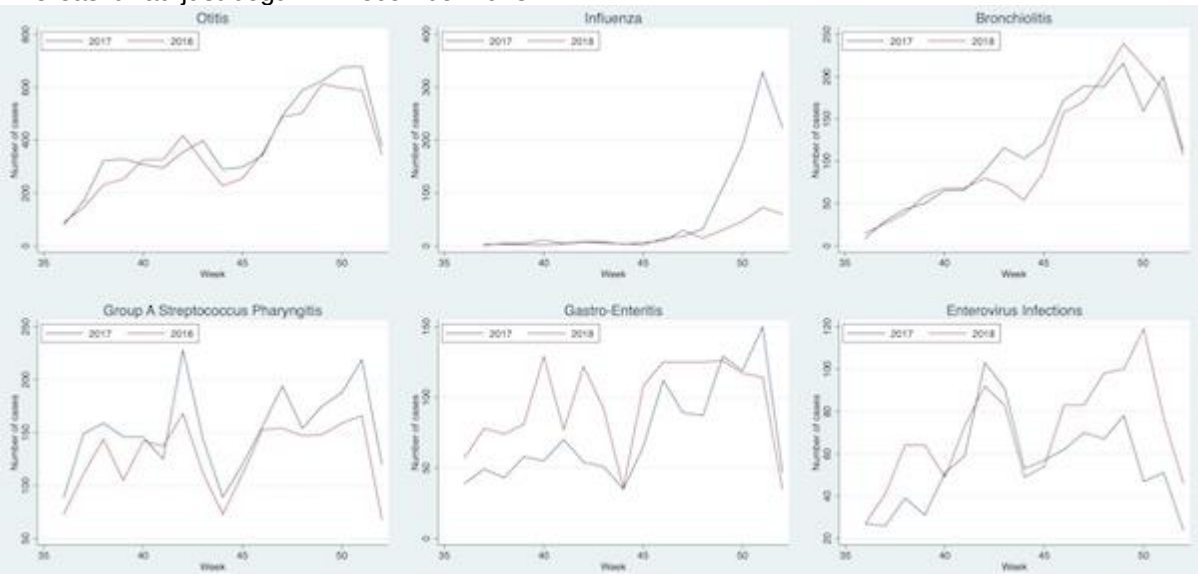
Methods:

We daily prospectively collect anonymized data (age, sex, height, weight, daycare attendance, vaccines, diagnosis and prescriptions) of children with infectious diseases in 82 primary-care-pediatricians using the same software (Axi5-Infansoft®, CompuGroup Medical).

Results:

Between September 2017 and December 2018, data on 25,923 patients, 37,033 consultations, 51,568 diagnoses, 176,331 vaccines and 161,654 drug-prescriptions were collected. Mean age at diagnosis was 3.0 ± 2.9 years and boys accounted for 57.1%. Frequencies of the different infectious diseases were weekly and automatically provided on a dedicated website as graphs for all pediatricians, to allow them to monitor the epidemiology of the diseases, locally as well as at national level. If the epidemiology over the two years was identical for otitis, bronchiolitis, group A S*treptococcus* pharyngitis, gastro-enteritis and enterovirus infections, the peak for influenza had already been reached by the end of December in 2017,

whereas it had just begun in December 2018.



Conclusions:

For the first two years of this study, the seasonal distribution of the pediatric infectious diseases is perfectly stackable, except for influenza diseases. These robust results validate the PARI network as an efficient and reliable tool for monitoring infectious diseases and enforce the impact of this automated surveillance on the pediatricians' practice and public health.

Systematic Review Registration:

NA

ESPID19-0093
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Ausvaxsafety surveillance of adverse events across the national immunisation program infant schedule

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H Quinn1, C Glover1, A Pillsbury1, C Damon1, K Macartney1 on behalf of the AusVaxSafety consortium 1National Centre for Immunisation Research and Surveillance, Westmead, NSW, Australia Background: Most childhood schedule points in the Australian National Immunisation Program (NIP) contain several vaccines. Receipt of multiple vaccines at one visit can be a concern for parents. AusVaxSafety conducts nationwide active vaccine safety surveillance for vaccines on the NIP. We analysed rates of adverse events following immunisation (AEFI) in infants receiving DTPa-hepB-IPV-Hib, 13-valent pneumococcal conjugate and rotavirus vaccines. Methods: De-identified, parent-reported AEFI were collected through text message solicitation by the data monitoring platform SmartVax. Data were analysed for the period 1 July to 31 December 2018 for infants aged 1–8 months. AEFI rates were calculated for each infant schedule point (2, 4, and 6 months). Longitudinal analysis was conducted to follow individual infants at each of the schedule points. Results: Among 24,880 participants, reported AEFI rates were lower at 2-months (9.1%) and 6-months (7.2%) compared with 4-months (12.3%). The AEFI profile was similar for each schedule point, with irritability, fever and injection site reactions most frequently reported, in <5% of infants. Data for all 3 schedule points were available for 1,816 infants. An AEFI at the 2 month schedule point was reported for 134 (7.4%) of the infants; 66 (49.3%) of these infants did not have any further reported AEFI. Conclusion: Parent-reported AEFI rates following the NIP schedule were low and within expected ranges. Over half of infants with a reported AEFI after dose 1, did not have another AEFI after dose 2 or dose 3. This provides reassurance to parents that immunisation following the NIP infant schedule is safe.

ESPID19-0036
Science and Educational Track

E-Poster discussion session 11 - Public health and epidemiology - Station 07

Google searches accurately forecast rsv hospitalizations

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Background and Aims:

Hospitalization of children with respiratory syncytial virus (RSV) is common and costly. Traditional sources of hospitalization data, useful for public health decision-makers and physicians to make decisions, are themselves costly to acquire and are subject to delays from gathering to publication. Here we use Google searches for RSV as a proxy for RSV hospitalizations.

Methods:

Searches for “RSV” and numbers of RSV hospitalizations in WA, MD, FL, and CT were examined from 2004--2018. Running correlation coefficients and phase angles between search and hospitalizations were calculated. Various machine learning models were compared to assess the ability of searches to forecast hospitalizations. Using search data from all 50 US states, we use K-means clustering to identify RSV transmission clusters. We calculate the timing of the optimal timing of RSV prophylaxis initiation as the week beginning the 24-week period covering 95% of all RSV cases.

Results:

High correlations (>0.95) and low phase differences were seen between counts of hospitalizations and search volume in WA, MD, FL, and CT. Searching for RSV began in FL and radiated outward and three distinct transmission clusters were identified: the south and northeast, the northwest and Appalachia, and the center of the country. Calculated initiation dates for prophylaxis closely followed those calculated using traditional data sources (correlation = 0.84).

Conclusions:

This work validates searches as a proxy for RSV hospitalizations. Search query surveillance of RSV is a rapid and no-cost addition to traditional RSV hospitalization surveillance and may be useful for medical and public health decision-making.

Systematic Review Registration:

NA

ESPID19-1165
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Kinetics of the immune response to 2 versus 3 doses of primary immunisation with PCV13 and the effect of a booster dose in healthy infants

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Background

Different vaccination schedules of 2 and 3 doses of PCV13 with and without a booster are used worldwide. The current study aims to compare the immunogenicity of a 2+1 versus a 3+0 and a 3+1 PCV13 infant schedule.

Methods

31 children received PCV13 either as 2+1 (Group A, n=7), 3+1 (Group B, n=10) or 3+0 schedule (Group C, n=14). Sera were collected before and 1 month after the last dose. Serum IgG antibody concentrations for serotypes 1, 3, 9V and 19A were measured with the WHO pneumococcal ELISA. Antibodies and geometric mean concentrations (GMCs) were calculated as μg/ml.

Results

Group A children had significantly lower GMCs compared to group B pre (7.9 vs. 42.6, 1.7 vs. 6.4, 1.6 vs. 17.3 for serotype 1, 3 and 9V respectively, p=0.001) and post-booster for serotype 1 (14.5 vs. 49.9, p=0.007) and 3 (3.8 vs. 7.9, p=0.008). The fold increase of antibody titers where higher in group A compared to group B for serotypes 1, 3 and 9V. We also evaluated the 3rddose of PCV13 when given as primary immunisation or as booster. GMCs were significantly higher when it was given as booster for serotypes 1 (14.5 vs 10.5, p=0.035) 3 (3.8 vs.1.7, p=0.14) and 9V (23.1 vs. 15.3, p=0.08).

Conclusions

A 2-dose primary schedule maintains significantly lower antibody titers pre and post booster than a 3-dose primary schedule for serotypes 1, 3 and 9V. However, the booster dose induced higher fold increases in infants receiving the 2-dose primary schedule, possibly due to high pre-existing antibodies induced by 3 primary doses that inhibit the production of new antibody-secreting cells within the germinal centers. A 3rd dose of PCV13 induces higher antibody titers when given as booster.

Clinical Trial Registration (Please input N/A if not registered)

NCT03405805

ESPID19-0684
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

The serogroup b meningococcal vaccine 4cmenb elicits antibodies to meningococcus serogroup z

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Background

Neisseria meningitidis serogroup B vaccine 4CMenB (Bexsero) is recommended for complement deficient patients. These patients are also susceptible for infections with less common meningococcal serogroups including Z. Preliminary evidence suggests 4CMenB vaccine (Bexsero) has an extended impact on other meningococcal serogroups (W and X) and *N. gonorrhea*, via induction of cross-reactive antibodies. Triggered by a case of *N. meningitidis* serogroup Z (MenZ) invasive meningococcal disease (IMD) in a complement deficient patient, we tested whether 4CMenB induced cross-reactive antibodies against MenZ.

Methods

Case Report

A 6 year old girl (Patient A) presented with a MenZ IMD. Immunological workup demonstrated C8 deficiency. She received subsequent 4CMenB vaccine in accordance with current guidelines. Her 10 year old sister (Patient B) was subsequently also diagnosed with C8 deficiency and vaccinated with 4CMenB.

Laboratory experiments

N. meningitidis serogroup B strain H44/76 (MenB), *N. meningitidis* serogroup C strain C11 (MenC) and *N. meningitidis* serogroup Z clinical isolate from patient A were incubated with 5% pre- and post-Bexsero vaccination serum for 30 minutes and binding of IgG, IgM or complement C3 were determined by flow cytometry.

Results

Bexsero vaccine-induced IgG binding was clearly detectable for MenB, MenC and MenZ. No binding of IgM to MenB or MenC was observed, whereas this was detectable and induced post-Bexsero vaccination for MenZ. Binding of complement C3 to the bacterial surface was increased post-Bexsero vaccination for MenB, MenC and MenZ.

Conclusions

Bexsero vaccine-induced IgG binds and increases complement activation on the bacterial surface of MenB, MenC and MenZ, indicating cross-reactivity. The impact of 4CMenB vaccine may be extended to MenZ and may potentially offer protection against MenZ IMD via opsonophagocytic killing in patients with terminal complement defects.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0606
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

The impact of vaccination on acute bacterial meningitis in a well-defined child population

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Background and Aims:

Introduction of vaccines has dramatically changed the epidemiology, morbidity and mortality of acute bacterial meningitis (ABM).

We explored the impact of vaccination on childhood ABM in a well-defined, adequately vaccinated population in Crete, Greece during a 27-year period.

Methods:

All patients between 1 month and 14 years old with bacterial meningitis were included. A three-source capture–recapture method was used to estimate total incidence.

Results:

Between 1991 and 2017, there were 245 patients with proven (*n* = 227) or suspected (*n* = 18) bacterial meningitis. Before conjugate MCC vaccine was licensed in Greece for routine vaccination (2000), the average rate of MenC was 15.1% of the total meningitis cases while after the introduction of vaccination, the average rate fell to 4.31% (OR 0.29; 95% CI 0.11-0.75; *p* 0.01). MenB became afterwards the predominant serogroup (OR 0.44; 95% CI 0.22-0.91; *p* 0.03). The MenB meningitis incidence did not show any decreasing trend during the three-year period (2015-2017) following the implementation of MenB vaccine (IR 1.57; 96% CI 0.76-2.34 vs. 2.25; 95% CI -2.73-7.23). When comparing the pre- (1991-2009) and post-PCV13 (2010-2017) periods, there was a three-fold decrease in annual incidence of pneumococcal meningitis (2.69; 95% CI 1.67-3.71 vs 0.96; 95% CI 0.22-1.71; *p* 0.03). Universal vaccination against Hib resulted in elimination of the disease, with IR 2.17; 95% CI -0.74-5.07 before vaccination and 0.04; 95% CI -0.04-0.13 afterwards (*p*<0.0001).

Conclusions:

Our results elaborate the decrease of bacterial meningitis cases in children following conjugate vaccines with disappearance of Hib and significant drop in MenC and *S. pneumoniae*. Ongoing surveillance is needed for evaluation of the long-term impact of vaccines on meningitis epidemiology.

Systematic Review Registration:

n/a

ESPID19-0855
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Safety and immunogenicity of vaxelis™ in premature infants

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Background

The safety and immunogenicity of Vaxelis™ was evaluated in four Phase III, randomized, active-comparator controlled clinical trials (Protocols 005 and 006 in the US [Control: PENTACEL™] and Protocols 007 and 008 in the EU [Control: INFANRIX™ hexa]) and one Phase III clinical trial in the UK (PRI01C). The vaccine, studied in >6,800 children, has an acceptable safety profile generally similar to that of control vaccines (Xu, PIDJ, 2018; doi:10.1097/INF.0000000000002257). Here we evaluate the safety and immunogenicity of Vaxelis™ in premature infants.

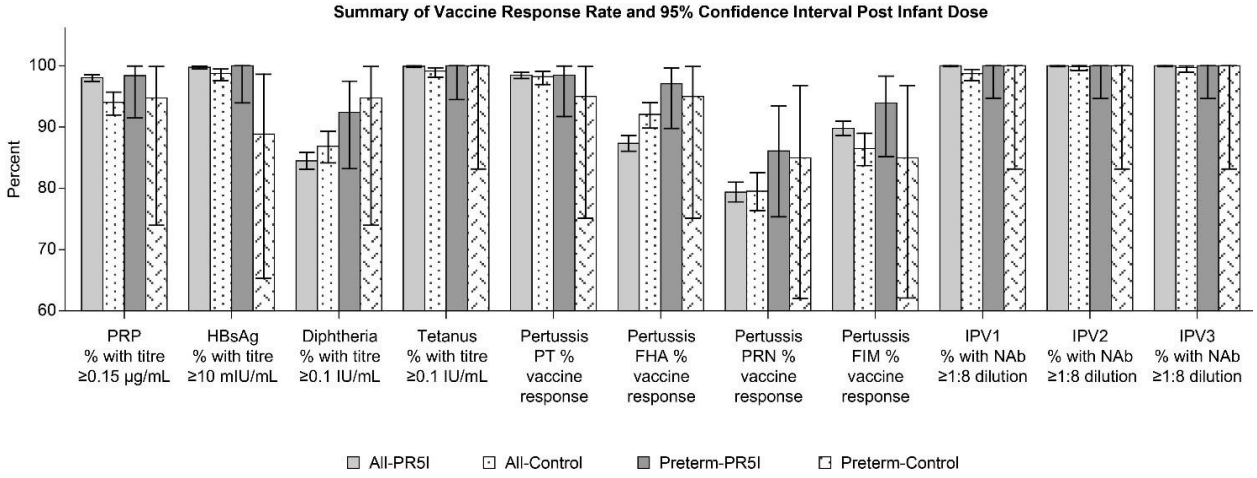
Methods

Premature infants were identified from these Phase III clinical trials using the prior medical conditions terms “premature baby/delivery” and/or “low birth weight baby”. Immunogenicity and safety data were summarized; no formal statistical comparisons were performed.

Results

Overall, 160 infants were considered premature (Vaxelis™=111; Control=49). In preterm infants the incidence of adverse events (AEs) on Day 1-to-15 post-vaccination was Vaxelis™=97.3%; Control=87.8%, solicited inject-site AEs Days 1-to-5 post-vaccination Vaxelis™=75.5%; Control=75.5%, and solicited systemic AEs Days 1-to-5 post-vaccination Vaxelis™=94.5%; Control=83.7% and was comparable to the incidence reported by all subjects of AEs (Vaxelis™=96.3%; Control=96.9%), solicited inject-site AEs (Vaxelis™=84.1%; Control=84.8%), and solicited systemic AEs (Vaxelis™=93.7%; Control=94.6%).

A high percentage of premature infants mounted protective immune responses to antigens contained in Vaxelis™. The figure below presents the response rates from Protocols 005+006 (other protocols are not integrated due to different vaccination schedules). Response rates in the preterm infants were in a similar range to the response rates of all infants for both Vaxelis™ and control vaccines (note overlapping 95% CIs).



Conclusions

These data support that the Vaxelis™ vaccine has similar safety and immunogenicity in premature and full-term infants.

Clinical Trial Registration (Please input N/A if not registered)

NCT01337167/NCT01340937

ESPID19-0842
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Pneumococcal conjugate vaccination provides similar estimates of vaccine effectiveness against late sequelae of acute otitis media irrespective of the age at vaccination

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[3]*National Institute for Health and Welfare, The Department of Public Health Solutions, Helsinki, Finland*

Background

Prevention of acute otitis media (AOM) by pneumococcal conjugate vaccines (PCVs) in early infancy has been hypothesized to reduce subsequent recurrent and complex AOM by preventing biofilm formation. We examined whether there are differences in long-term AOM-related outcomes in the Finnish Invasive Pneumococcal Disease (FinIP) Vaccine Trial in children vaccinated at different ages.

Methods

A post-hoc analysis was performed in FinIP, a cluster-randomized, double-blind trial that collected data on outpatient purchases for antimicrobials recommended for AOM and tympanostomy tube placements (TTP) from national registers as surrogates for AOM. In 2009-2010 children received 10-valent pneumococcal *Haemophilus influenzae* protein D-conjugate vaccine (PHiD-CV10, GSK) in 52 clusters or hepatitis B/A vaccine as control in 26 clusters according to 3+1 or 2+1 schedules (infants <7 months) or catch-up schedules (2+1 or 1+1 for children 7-11 and 12-18 months of age, respectively). PHiD-CV10 was introduced into the national vaccination program in Sep2010. We restricted the current analysis to the long-term follow-up period defined by age (24-71 months) and 4 calendar years (Jan2011-Dec2014) to limit the year-to-year variation between the different vaccination schedules. Negative binomial regression taking into account the cluster randomization was used in the analysis for parallel comparison of PHiD-CV10-vaccinated children to control-vaccinated children in different schedule groups.

Results

Mean ages, incidences rates and vaccine efficacy (VE) estimates in the defined follow-up period are presented in the table.

Table. Long-term vaccine effectiveness against tympanostomy tube placement and antimicrobial purchases in children 2 to 5 years of age vaccinated at different age periods

	Enrolment and first vaccine dose administered					
	<7 months of age		7-11 months of age		12-18 months of age	
	PHiD-CV10 (3+1/2+1)	Control	PHiD-CV10	Control	PHiD-CV10	Control
Number of subjects	20327	10200	3880	1907	6534	3126
Median age during the follow-up period, months (interquartile range)	44 (41-46)	44 (42-46)	49 (47-50)	49 (47-50)	51 (50-53)	52 (50-53)
Tympanostomy tube placements, rate/100 person-years	3.26	3.38	3.23	3.58	2.91	3.42
VE against tympanostomy tube placements, %	4 (-12 to 18)		7 (-20 to 28)		10 (-10 to 26)	
Antimicrobial purchases, rate/100 person-years	74.3	77.3	76.4	77.7	71.2	75.8
VE against antimicrobial purchases, %	4 (-3 to 10)		3 (-6 to 11)		6 (-2 to 14)	

Conclusions

The VE estimates were similar irrespective of the vaccination schedule used. However, the confidence intervals for the VE estimates were wide, precluding any firm conclusions.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT00861380 and NCT00839254

ESPID19-0655
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Pertussis vaccine effectiveness and duration of protection in manitoba, canada, 1992-2015: a nested case-control study

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Background and Aims:

Pertussis persists in Manitoba, Canada despite the universal availability of pertussis vaccines. Recent cases have included previously vaccinated individuals, raising concerns about declining vaccine effectiveness over time. We aimed to measure pertussis vaccine effectiveness (VE) and duration of protection in Manitoba.

Methods:

Using a nested case-control design, we linked all laboratory-confirmed cases of pertussis in Manitoba between April 1, 1992, and March 31, 2015 to the Manitoba Immunization Monitoring System (which registers all vaccines administered in Manitoba). Cases were matched on age, gender, geography, and number of physician visits in the previous year to up to five population-based controls and conditional logistic regression was used to estimate VE for both the whole-cell (wP) and acellular (aP) pertussis vaccines. Duration of protection was assessed using time since last pertussis dose as the predictor variable.

Results:

We included 321 eligible cases and 1503 matched controls. The VE estimates for up-to-date vaccination were 5% (95%CI, -41%-37%) for wP vaccine, and 82% (67%-90%) for aP vaccine. The VE of the aP vaccine was 88% (63%-96%) one to three years after the last vaccination. We were unable to assess duration past three years for either the aP or wP vaccines due to small case numbers.

Conclusions:

Receipt of any pertussis vaccine conferred protection against disease and VE estimates were higher for the aP than the wP vaccine. The aP vaccine provided high effectiveness lasting at least three years, but longer-term protection could not be assessed.

Systematic Review Registration:

N/A

ESPID19-0556
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

One decade with pneumococcal otitis media in children in slovakia during period 2008-2017

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Background and Aims:

Acute Otitis media (AOM) is a common childhood infection in children up to 5 years of age. Streptococcus pneumoniae, non-typeable Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pyogenes are the most frequently involved bacterial pathogens. After vaccination with pnemococcal conjugate vaccines (PCV) there was significant decrease of PCV serotypes although the replacement phenomenon has been observed by non-vaccine serotypes. In study area vaccination status of newborns is various due to various PCV vaccine availability (Prevenar, Synflorix or Prevenar 13).

Methods:

Goal of presenting study was to determinate AOM pathogens, detect antibiotic susceptibility and in case of *S.pneumoniae* performe serotyping by Quellung method. 2429 bacterial samples of children in age 0-5 year were acquired in to the study database with AOM. Middle-ear fluid was obtained by tympanocentesis or after spontaneous perforation for bacteriological testing. Time period of study was from January 2008 till december 2017 (10 years).

Results:

2429 bacterial samples in children up to 5 years of age were enrolled to the study database. *S. pneumoniae*, *H. influenza*, *S. pyogenes* and *M. catarrhalis and Turicella otitis* were identified. Serotyping was performed in 862 strains and manifested dominant role of serotype 19A, serotype 3, although replacement phenomenon of non-vaccine serotypes increased. Incidence of pneumococcal AOM in Bratislava self- governing region was evaluated.

Conclusions:

Reduction in some extent of pneumococcal OM was observed following to PCV. However, relatively high number of OM due to serotypes 19A and 3 persisted and increased 19A. A higher coverage of PCV containing these serotypes would bring significantly additional reduction of pneumococcal OM and its related antimicrobial resistance in Slovakia.

Systematic Review Registration:

not done

ESPID19-0498
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Evaluation of diphtheria-tetanus-acellular pertussis-polio-haemophilus influenzae type B in children who completed chemotherapy for acute lymphoblastic leukemia: a Canadian immunization research network study

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Background

Children with acute lymphoblastic leukemia (ALL) require prolonged chemotherapy, which may reduce immunity to vaccines received before diagnosis. Immunization recommendations post-chemotherapy vary across jurisdictions in Canada and worldwide. We evaluated the immunogenicity of diphtheria-tetanus-acellular pertussis-polio-Haemophilus influenzae type b (DTaP-IPV-Hib) vaccination among children who completed ALL chemotherapy.

Methods

We conducted a multi-center trial of children with ALL 6-12 months post-chemotherapy completion. We excluded children with infant ALL, relapsed ALL, and stem cell transplant recipients. Participants received DTaP-IPV-Hib and 13-valent pneumococcal conjugate vaccine (PCV) concurrently (PCV results were presented previously). Tetanus toxoid and pertussis toxin IgG levels were measured in serum collected before, and 2 and 12 months after vaccination. Geometric mean concentration (GMC) and GMC ratio were compared at 2 and 12 months post-vaccination versus pre-vaccination using linear mixed models.

Results

Seventy-one participants received DTaP-IPV-Hib and had serum available for analysis (mean age 9.2 years, SD 3.9). Participants were classified as having standard risk ALL (54%), high risk ALL (37%), or very high risk ALL (8%). Before enrollment, 51% of participants had received 4 doses of DTaP-containing vaccines and 32% had received ≥5 doses. Serology results are shown in the table.

	Pertussis toxin IgG (IU/ml)		**Tetanus IgG (IU/ml)**	
	GMC (95% CI)	**GM ratio (95% CI)**	**GMC (95% CI)**	**GM ratio (95% CI)**
Pre-vaccination	4.1 (3.7-4.6)	Reference	0.2 (0.1-0.2)	Reference
2 months post-vaccination	30.7 (22.3-42.3)	7.6 (5.5-10.5)	4.0 (2.6-6.2)	24.5 (16.8-35.8)
12 months post-vaccination	10.4 (7.8-13.9)	2.6 (1.9-3.5)	1.1 (0.8-1.5)	7.0 (5.2-9.3)

Conclusions

Children who completed chemotherapy for ALL demonstrated good IgG responses to pertussis toxin and tetanus toxoid following DTaP-IPV-Hib vaccination 6-12 months post-chemotherapy. Titers remained elevated through 12 months post-vaccination. Children with ALL would benefit from systematic DTaP vaccination post-chemotherapy.

Clinical Trial Registration (Please input N/A if not registered)

NCT02447718

ESPID19-0458
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

A multi-center, double-blind, clinical trial to assess the long-term immunogenicity of inactivated cell culture-derived influenza vaccine in korean children aged 6~35 months old

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Background

It is well known that influenza vaccine-induced antibodies decline over time, especially in younger children. This study aimed to assess the 6-month immunogenicity of cell cultured influenza vaccines in children aged 6 to 35 months.

Methods

Between Sep 2016 and Feb 2017, we conducted a double-blind, observational multi-center study to assess the persistence of immunogenicity of the influenza vaccine in healthy children 6~35 months of age at 9 hospitals in South Korea. For each subject, experiences of influenza-like illnesses (ILI) were collected during influenza season and serum samples were obtained at 6±1 months after vaccination. Blood samples were immediately stored at -70 °C until testing. HI test using chicken erythrocytes was performed according to WHO protocol.

Results

Total 124 children were enrolled, mean aged 27.7 months old. Eighty-one received ccQIV and 43 received ccTIV. Eighty-three got single dose and 41 did two doses of vaccine. Eight were excluded from immunogenicity analysis because of confirmed or suspicious influenza. The overall seroprotection rates at 6±1 months after vaccination were 88.7 % (H1N1), 93.7 % (H3N2), 36.6 % (B/Yamagata), 27.6 % (B/Victoria). The GMTs were 119.6 (H1N1), 186.4 (H3N2), 18.1 (B/Yamagata), 11.4 (B/Victoria). The seroprotection rates of ccTIV at 6±1 months after vaccination were 83.7 % (H1N1), 93.1 % (H3N2), 27.9 % (B/Yamagata), 25.6 % (B/Victoria). The GMTs were 100.3 (H1N1), 183.2 (H3N2), 13.8 (B/Yamagata), 15.2 (B/Victoria). The seroprotection rates of ccQIV at 6±1 months after vaccination were 91.4 % (H1N1), 94.8 % (H3N2), 41.3 % (B/Yamagata), 28.8 % (B/Victoria). The GMTs were 131.4 (H1N1), 195.0 (H3N2), 20.9 (B/Yamagata), 14.9 (B/Victoria).

Conclusions

The immunogenicity of influenza A was relatively persisting over 6 months in young children, but for influenza B, it seemed to decline quickly.

Clinical Trial Registration (Please input N/A if not registered)

na

ESPID19-0205
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Role of school nurses in adolescent immunization program in japan

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Background

Inadequate immunization coverage among adolescents is an important problem in many countries including Japan. Because school nurses (SNs) provide counseling to teens about health issues, we evaluated the effectiveness of an educational intervention for SNs to increase counseling for recommended vaccines.

Methods

We conducted an intervention study using postal questionnaires pre- and post-delivery of a vaccine education intervention targeting 249 Japanese SNs in 2017. The baseline questionnaire measured knowledge and attitudes about routinely recommended adolescent immunizations (Diphtheria Tetanus Toxoid (DT) and inactivated influenza vaccines (IIV)). All subjects were randomized to either the educational intervention (n=128) or control group (n=121). The intervention group received information sheets adapted from Vaccine Education Center materials. We mailed post-intervention questions to all participants and compared changes in knowledge and attitudes pre- and post-intervention between intervention and control groups.

Results

Overall, 66 (26.5%) and 65 (26.1%: n=31 intervention; n=34 control) SNs completed the pre- and post-intervention survey. Pre-intervention, 4.5 – 31.8% of SN's reported accurate knowledge about diphtheria, tetanus and influenza morbidity and mortality. Knowledge significantly increased in the intervention compared to control groups for diphtheria only (Table 1). At baseline, SNs had generally positive attitudes towards DT (81.3%) and IIV (71.2%) but few perceived having a role in or self-efficacy to counsel. There were no significant changes in attitudes in the intervention compared to control group, except self-efficacy to counsel about DT.

Table1: % Change in knowledge and attitudes

Knowledge		Pre-intervention	Post-intervention	
			Intervention	Control
morbidity	diphtheria	19.7	41.9*	26.5
	tetanus	25.8	45.2†	17.6
	influenza	24.2	32.3	26.5
mortality	diphtheria	12.1	38.7*	17.6
	tetanus	4.5	16.1	8.8
	influenza	31.8	41.9	32.4
Attitudes				
perceived role	DT	17.2	14.3	15.2
	IIV	41.5	38.7	39.4
self-efficacy	DT	25.0	46.4*†	24.2
	IIV	67.7	80.6	78.8

significant difference *Pre- vs Post-intervention †Post-intervention vs Control

Conclusions

In this small sample of SNs in Japan, knowledge about recommended vaccines and vaccine preventable diseases was low yet a targeted educational intervention did not significantly influence knowledge or attitudes about vaccine counseling. Future work can identify key barriers to vaccine counseling to inform development of more effective interventions.

Clinical Trial Registration (Please input N/A if not registered)

St. Marianna university 3622

ESPID19-0163
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Invasive pneumococcal disease among hospitalized pediatric patients in brazil before and after introduction of pneumococcal conjugate vaccine

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Background and Aims:

The objective of the study was to determine if the inclusion of the PCV10 in the Brazilian vaccination schedule was associated with a reduction of admission to intensive care unit (ICU) and mortality associated with Invasive pneumococal disease (IPD)

Methods:

The setting consists of two general university hospitals in São Paulo and Uberlandia both with an average 3,000 annual pediatric admissions. From January 1st, 2005, to December 31st, 2015, patients younger than 17 years old admitted to both hospitals due to IPD were included in the retrospective analysis. Case fatality rates and need for ICU was evaluated and compared between periods before vaccine introduction 2005-2009 (Pre-PCV10) and after vaccine introduction 2011-2015 (Post -PCV10)

Results:

We included 198 patients in the pre-PCV10 period and 62 in the post-PCV10 period. There was an important reduction of ICU admissions and fatalities due to IPD after PCV10 introduction. The number of intensive care admission was 20 per 10.000 pediatric admissions in the first period and was reduced to 5 cases per 10.000 in the second period. Mortality was reduced , from 6.6 per 10.000 pediatric admissions to 2 cases per 10.000. Both reductions were significant (P<0,001) Table 1

Table 1 Age, clinical diagnosis and complications of the patients

	Pre-PCV10 N	Post-PCV10 N
0 - 5 years	156	44
6 - 15 years	42	18
Meningitis	40	14
Pneumonia	114	29
Bacteremia	27	12
Other	5	4
Fatalities	20	6
Fatalities no meningitis	12	6

Conclusions:

After introduction of PCV-10 vaccine there was an important reduction (>50%) in number of cases hospitalized due to IPD and , a reduction of number of the fatal cases and ICU admissions

Systematic Review Registration:

pneumococcus
mortality
vaccine
10V pneumococcal vaccine

ESPID19-0094
Science and Educational Track

E-Poster discussion session 12 - Vaccine studies - Station 09

Effectiveness of maternal vaccination among infants aged <6 months hospitalised with pertussis

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H Quinn1, J Comeau1, H Marshall2, E Elliott3, N Crawford4, C Blyth5, A Kynaston6, T Snelling5, P Richmond5, K Macartney1, P McIntyre1 and N Wood1 on behalf of the Paediatric Active Enhanced Disease Surveillance (PAEDS) network 1National Centre for Immunisation Research and Surveillance, Westmead, NSW, Australia 2Vaccinology and Immunology Research Trials Unit, Women's and Children's Health Network, Adelaide, Australia 3Children's Hospital Westmead, Sydney, NSW, Australia 4Murdoch Children's Research Institute, Parkville, Vic, Australia 5Wesfarmer's Centre of Vaccines and Infectious Diseases, Telethon Kids Institute, Perth, WA, Australia 6Lady Cilento Children's Hospital, Brisbane, Qld, Australia
Background Pertussis remains one of the most challenging vaccine preventable diseases to control; the burden of severe disease and mortality lies with unimmunised infants. Maternal vaccination is the lead strategy for current pertussis control in this group. We report Australia's first national estimation of maternal vaccine effectiveness (VE) against pertussis hospitalisation in infants, using a test-negative design and data collected prospectively via the Paediatric Active Enhanced Disease Surveillance (PAEDS) hospital-based surveillance program. Methods Each infant case aged <6 months, presenting to hospital between July 2016 and December 2019 was matched to 1–3 controls by date of birth +/- 2 weeks and date of laboratory testing +/- 6 weeks. Maternal vaccination status was verified. Conditional logistic regression was used to estimate VE. Results Of 71 cases in infants aged <6 months with at least 1 matched control, 57 (80%) were eligible for inclusion in the analysis. Among cases, 40% (23/57) had a mother vaccinated in pregnancy, compared with 54% (82/151) controls. The adjusted VE in infants aged <6 months was 52.4% (95% CI: 0.7–77.1%). The VE was higher in admitted infants, aged <6 months (66.3%) and aged <2 months (84.2%). Of 14 intensive care unit admissions among included case infants, only 1 had a mother vaccinated in pregnancy, however the study lacked enough power to calculate VE for this subgroup. Conclusion Our result is comparable to other studies from the United States and England providing estimates of VE in infants. VE of maternal vaccination was higher in younger infants, where the most benefit from this strategy exists and supports efforts to encourage maternal vaccine uptake.

ESPID19-0329
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Central line-associated blood stream infections in paediatric haematology/oncology patients in iceland

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Background and Aims:

Central venous lines (CVLs) are an essential part of treatment for paediatric haematology/oncology patients. Central line-associated blood stream infections (CLABSIs) are a significant cause of morbidity and mortality, resulting in increased length of hospital stay and higher costs. This study describes the epidemiology, microbiology and risk factors for CLABSI in children with haematologic/oncologic malignancies in Iceland.

Methods:

Children diagnosed with malignant diseases during the nine-year period 2009-2017 and received a CVL during that period were included in the study. CVLs included were non-tunnelled CVLs, Broviac/Hickman catheters, implantable ports, midline catheters and peripherally inserted central catheters (PICCs). Characteristics of CVLs and patients were registered and information on potential risk factors and microbiology was collected. CLABSI was defined according to the Centers for Disease Control and Prevention (CDC) definition of CLABSI.

Results:

138 CVLs were placed in 89 children. Implantable ports were the most common CVLs (76/138), the majority were placed in the subclavian vein (124/138). Overall CLABSI rate was 0.24 per 1000 line-days (13 CLABSI episodes in 55,176 line-days), highest in 2011 (0.74/1000 line-days). If possible CLABSIs are included, the rate was 0.33 per 1000 line-days. No CLABSIs occurred for 4 consecutive years (2012-2015). *Staphylococcus aureus* was the most common pathogen, causing 53.8% of CLABSIs, followed by coagulase-negative staphylococci (30.8%). No episodes resulted in death, 9/13 CLABSIs resulted in CVL removal.

Conclusions:

We report very low CLABSI rates over a nine-year period, with 4 CLABSI-free years. Most CLABSIs were caused by staphylococci.

Systematic Review Registration:

ESPID19-1172
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Antibiotic prescription in paediatric outpatients: trends in a 8-year-period and bases for the stablishment of an antimicrobial stewardship program

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Background and Aims:

Antimicrobial resistance to antibiotics is a public health issue. Studies show that more than 80% of the antibiotics prescribed to children are prescribed in the outpatient setting, and up to 50% of these prescriptions are unnecessary. Strategies to optimize the antibiotic consumption are needed. However, information is lacking about antibiotic utilisation in our setting. Objectives: To analyze systemic antibiotic prescription and trends in paediatric outpatients in Cantabria Region (Spain).

Methods:

Observational, retrospective study of children <16 years old during an 8 year period (2011-2018). Data of antibiotic prescription were retrieved from the regional reimbursement database. Antibiotic consumption was calculated as Defined Daily Dose per 1000 inhabitant-days (DID), and annual prescription rate (APR) as number of prescriptions per 1000 person-years.

Results:

85 paediatricians from 42 Primary Health Centres were included, with data about 80475 children. The most prescribed antibiotic was amoxicillin (43.6%). Overall antibiotic consumption decreased from 12.4 to 9.5 DID. The APR decreased from 354 to 223 in amoxicillin, and from 210 to 132 in amoxicillin-clavulanate; cephalosporins also decreased, but azithromycin showed a two-fold increase in prescription rate over time. Seasonal peaks during winter months were pronounced for penicillins, macrolides and less for cephalosporins. There was a high variability among paediatrician prescription rates.

Conclusions:

Paediatric antibiotic prescription in Cantabria is high; however, time-trend analysis shows a slight improvement. We observed a high utilisation of broad spectrum antibiotics in winter months, which may suggest a misprescription for common non-bacterial conditions in children. Determinant factors affecting prescription in paediatricians are not well known yet. Thus, it seems necessary to incorporate specific antimicrobial stewardship programs in paediatric outpatients in our setting.

Systematic Review Registration:

Observational, retrospective study; data retrieved from regional reimbursement database from the Spanish National Health System.

ESPID19-0994
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Unnecessary antibiotic prescription and therapeutic failures in children who had throat swabs

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Background and Aims:

Group-A strep (GAS) tonsillitis is a clinical diagnosis. In UK practice, throat swabs are scarcely sent, while rapid antigen detection tests are not widely used.

The aim of the study was to identify how well Group A strep infection is identified in clinical practice, if they are appropriately treated, how many missed diagnoses are admitted and how many non-Group A strep infection receive antibiotics.

Methods:

Consecutive throat swabs performed at Bristol Children's Hospital from November 2017 to March 2018 were studied. Duplicates were deleted. 445 notes were reviewed and initial diagnosis, antibiotic prescription or not were identified. In two cases no notes could be found, and the diagnosis and treatment remained unknown. Patients who had underlying condition and were going to get antibiotics anyway were excluded.

Results:

Out of total 81 children with GAS tonsillitis, 61 (75%) were treated with antibiotics and 20 (25%) were not. Of 320 children that did not have GAS infection 207 (64.6%) received antibiotics. Statistically, the antibiotic usage did not differ between the GAS and the non-GAS group. Compared to none of the non-GAS group, 25 children with GAS infection (30%) were subsequently admitted to the wards

Conclusions:

This study demonstrates that there are difficulties differentiating those with GAS infection from those without, leading to the use of unnecessary antibiotics. A bedside diagnosis of GAS throat infection may have prevented admission in 25 children.

Given the above result an introduction of rapid antigen test is proposed for a pilot period, in order to determine whether it will reduce antibiotic use and the unnecessary admissions.

Systematic Review Registration:

non applicable

ESPID19-0909
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Risk factors for healthcare-associated infections after pediatric cardiac surgery

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Background and Aims:

Healthcare- associated infections (HAI) after pediatric cardiac surgery are significant causes of morbidity and mortality. The aim of this study was to identify possible risk factors for the development of HAI, after cardiac surgery in pediatric patients with Congenital Heart Disease (CHD) and their impact on the prognosis.

Methods:

We present a retrospective observational study of a single, tertiary Neonatal and Pediatric Cardiac Intensive Care Unit (PCICU). Seventy-nine (79) pediatric patients who underwent cardiac surgery due to CHD during the last 18 months were enrolled. Patients were categorized in 2 groups, with or without HAI. We identified four (4) common healthcare-associated infections (bloodstream infection, surgical site infection, pulmonary and urinary tract infection). Risk factors for HAI including age at surgery, preoperative and postoperative factors were compared.

Results:

We identified 28 cases of HAI (35.4%), including bloodstream infections (67.8%, 19/28 patients), pulmonary infections (7/28, 25%), surgical site infections (1/28, 3.5%) and urinary tract infections (1/28, 3.5%). The duration of prior hospitalization, colonization with resistant pathogens and non-cardiac comorbidities were identified as important risk factors for HAI after cardiac surgery. Other factors include the duration of mechanical ventilation (7.5 vs 3 days, $p<0.001$), CVC days(9.5 vs 5 days, p 0.004) and delayed sternal closure (17.8% vs 3.9%,p 0.03), as long as the presence of postoperative complications(28.6% vs 7.8%, p 0.014). We observed that HAI prolonged the LOS in of our study group (10 days vs 6, $p<0.001$).

Conclusions:

Postoperative healthcare-associated infections are major complications in pediatric patients with CHD who undergo a cardiac surgery, contributing significantly on morbidity and mortality in this special group of patients.

Systematic Review Registration:

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ESPID19-0647
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Audit of antibiotic prescribing and documentation for febrile paediatric emergency department attendances in a tertiary centre in the united kingdom

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Background and Aims:

This audit examines antibiotic prescribing behaviour for febrile children presenting to the emergency department (ED) in a tertiary centre in the United Kingdom with the goal of assessing antimicrobial stewardship. It describes antibiotic prescribing patterns and audits documentation of important information about antibiotic prescriptions.

Methods:

Data were prospectively collected for children with a febrile illness (temperature ≥ 38.0°C) and/or suspicion of infection. Electronic records, discharge summaries and paper notes were retrospectively reviewed for documentation of information about antibiotic prescriptions: antibiotic name, indication, dose, route, frequency and duration.

Results:

During the study period, 1345/3814 (35.3%) febrile patients received antibiotics. The decision to prescribe antibiotics was compared with the final diagnosis. Antibiotics were prescribed for 91.3% of “probable bacterial” diagnoses, compared with 6.2% of “probable viral”. However, in the group where it was unclear whether there was a bacterial or viral cause, 57.0% received antibiotics, which is disproportionate to the prevalence of serious bacterial infection.

229 attendances were selected for examination of prescription documentation. Antibiotic name and indication were recorded well, however dose, route, frequency and duration were recorded less often (average 39.9% for those discharged home and 58.2% for those admitted).

The initial audit was followed by a brief educational intervention. Re-audit is planned prior to presentation of this work.

Conclusions:

Antibiotics are commonly prescribed for febrile children presenting to ED. Many children with an uncertain diagnosis receive antibiotics despite the low prevalence of serious bacterial infection. Documentation of antibiotic prescribing was poor, especially for those patients who were discharged home from ED. Re-audit is planned after a brief educational intervention.

Systematic Review Registration:

N/A

ESPID19-0508
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

In-hospital antibiotic prescriptions for children with lower respiratory tract infections: a comparison between two secondary care wards

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Background and Aims:

Antibiotics are often prescribed in children with lower respiratory tract infections (LRTI). Antibiotic stewardship aims to reduce unnecessary (broad-spectrum) antibiotic use to prevent antimicrobial resistance. Regular evaluation of local antibiotic prescriptions supports adequate stewardship practices. We aimed to identify qualitative and quantitative differences in antibiotic prescriptions for LRTI in time and between 2 locations of a large secondary hospital.

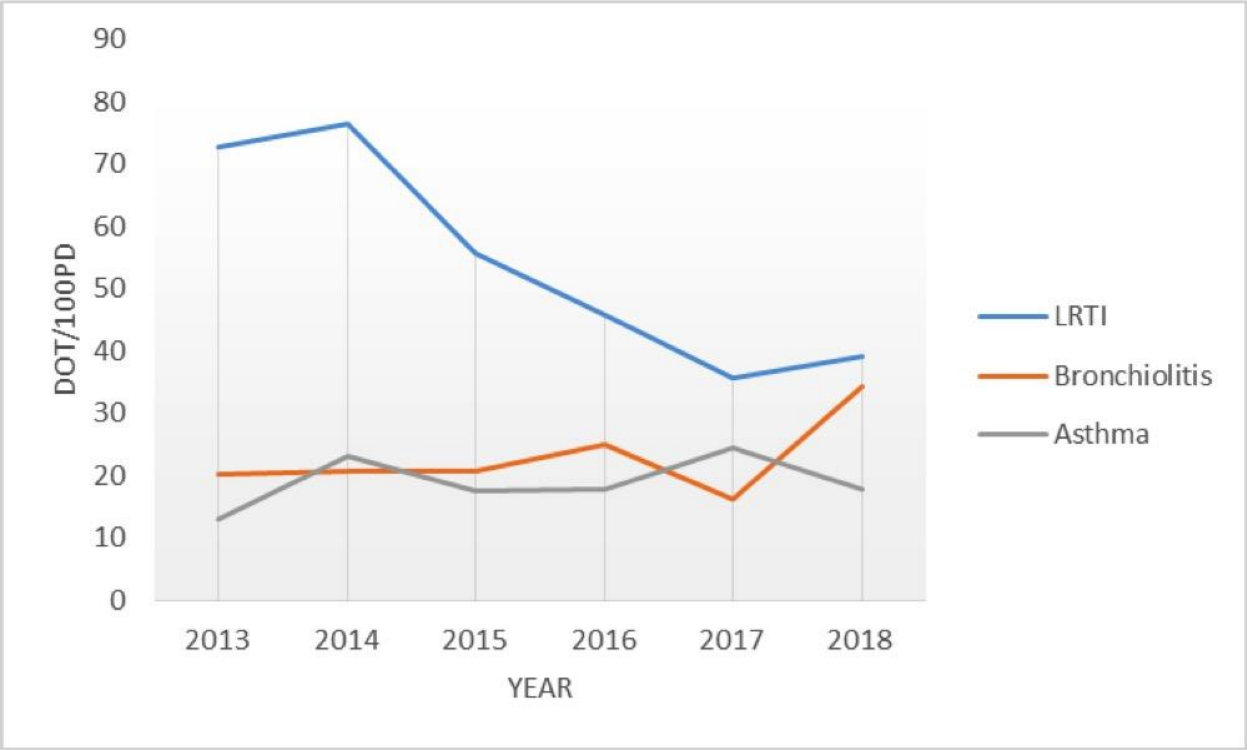
Methods:

A retrospective study of all in-hospital antibiotic administrations between 2013 and 2018 for LRTI(pneumonia), bronchiolitis and asthma admissions was performed. For ward 2 only antibiotic prescriptions from 2016-2018 were available. Outcomes were days of therapy per 100 patient days (DOT/100PD), class and route of antibiotics. Differences in time and between wards were estimated using regression/time series analysis and chi-square tests.

Results:

From 11.837 admissions, 25.6% was lower respiratory in origin. The proportion of patients prescribed antibiotics was 50.1% (LRTI); 23.1% (bronchiolitis); 17.7% (asthma). No time trend was observed for total DOT/100PD, class or route of antibiotic for ward 1. However, LRTI specific DOT/100PD on ward 1 decreased in time (2013: 72.7; 2018: 39.1; p=0.007, figure 1). On ward 2, there was an increase in penicillin and decrease in macrolide prescriptions for LRTI (p=0.045). Amoxicillin/co-amoxiclav ratio for LRTI within the penicillin group differed between the wards (55/45% vs. 73/27%;p=0.008). Macrolide use was higher for asthma compared to LRTI (~40

vs.~28%).



Conclusions:

A reduction in LRTI antibiotic prescriptions was observed. Differences between the wards were mainly related to class and spectrum. Although expected similar, patient case mix and severity was not assessed. Macrolide prescriptions did not change in time on one ward despite the protocol advising amoxicillin as the first choice. These data will be used to recommend rational antibiotic prescription practices.

Systematic Review Registration:

N/A

ESPID19-0451
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Molecular characterization of extended-spectrum beta-lactamases in escherichia coli and klebsiella pneumoniae in the pediatric population in qatar

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Background

Although extended-spectrum beta-lactamases (ESBLs) among *Enterobacteriaceae* is a major public health problem in the Arabian Peninsula, the molecular epidemiology of these enzymes in children is unknown. The aim of this study was to characterize sequence types (ST) and beta-lactamase (*bla*) genes in ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* recovered from clinical and screening specimens from pediatric patients at Sidra Medicine.

Methods

Whole genome sequencing of ESBL isolates was performed (January to July, 2018) on Illumina Miseq platform. STs were determined by in silico *multilocus sequence typing* (MLST), and resistance gene analysis was performed using ResFinder pipeline. Minimum inhibitory concentrations were determined by the BD Phoenix system and breakpoints were interpreted according to Clinical and Laboratory Standards Institute guidelines.

Results

Seventy-four ESBL producers were sequenced, 68 *E. coli* and 6 *K. pneumoniae*. Among them, 56 were recovered from screening specimens. CTX-M type enzymes were found in all of the isolates. CTX-M-15 enzyme accounted for 86%, followed by CTX-M-27 (7%). By MLST, *E. coli* ST 131 was the most prevalent clone (16%) followed by ST 1193 (9%). *bla*CTM-M-15 gene was detected in 64% and 83% of ST131 and ST 1193 types, respectively. The overall rates of resistance to gentamicin, ciprofloxacin and trimethoprim-sulfamethoxazole were 18%, 45%, and 70%, respectively. By contrast, only 3 isolates (4%) were resistant to piperacillin-tazobactam.

Conclusions

Our data suggest that the epidemiology of ESBLs in the pediatric population in Qatar is primarily dominated by CTX-M enzymes with a predominance of CTX-M-15. The worldwide pandemic multidrug-resistant *E. coli* ST 131 is the main circulating clone, followed by the emerging ST 1193. Of note, our data suggest that piperacillin-tazobactam may be a carbapenem-sparing option for the treatment of ESBLs infections in our setting.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0433
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Implementation of clinical pathway for acute pharyngitis in children: a pre-post study in an italian tertiary care children's hospital

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Background and Aims:

Acute pharyngitis is a common paediatric condition and represents a leading cause of admission to Emergency Department (ED). Pharyngitis is usually caused by viruses and only 37% of cases are estimated to be due to bacteria. Amoxicillin is the first line antibiotic whenever bacterial aetiology is confirmed. This study wanted to evaluate the impact of a Clinical Pathway (CP) implementation for therapeutic management of pediatric acute pharyngitis.

Methods:

We conducted a pre-post observational study at ED of Bambino Gesù Children's Hospital (OPBG), a 607-bed academic hospital in the Lazio Region (Italy). CP, a one-page decision support algorithm based on the use of McIsaac score, was implemented in December 2016. Patients with acute pharyngitis (ICD-9 CM code: 463) who presented to ED in the pre-intervention period (January-June 2016) and in the post-intervention period (January-June 2017) were identified using GIPSE (regional software for management of admission at ED). Proportions of patients treated with antibiotics in the pre- and post-intervention periods were compared through the $\chi 2$ test (or Fisher exact test, if applicable).

Results:

Five hundred and ninety-one (n= 591) eligible patients were included in the study: 366 in the pre-intervention and 225 in the post-intervention period. Demographic and clinical characteristics of patients did not differ in the pre- and post-intervention periods. No difference was observed in the proportion of patients treated with at least one antibiotic (94% versus 92%); however, the proportion of patients treated with amoxicillin significantly increased after the intervention (12.5% versus 71.0%), while the proportion of patients treated with amoxicillin/clavulanic acid and clarithromycin significantly decreased (from 72.0% and 9.6% to 21.3% and 4.8%, respectively).

Conclusions:

CP implementation significantly improved the choice of antibiotics prescribed in ED to treat pediatric pharyngitis.

Systematic Review Registration:

Not applicable

ESPID19-0424
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Antifungal stewardship program in a tertiary pediatric hospital

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Background and Aims:

Rising transplantation rates and complexity index of hospitalized pediatric patients have increased the need for antifungals, both for prophylactic and therapeutic strategies. Besides, increasing antifungal resistance and their high economic impact urge the need for antifungal stewardship programs (F-ASP). Antifungal prescription is monitored by the F-ASP group members on a basis of weekly audits. The aim of this study was to describe a bedside non-restrictive F-ASP in a tertiary care children hospital in Spain.

Methods:

Single-center modified point prevalence study over 3 months, with weekly retrospective data collection on antifungal use in hospitalized neonates and children (<18 years) receiving at least one systemic antifungal drug. Demographic and clinical data were collected. The quality of antifungal prescription was measured as the percentage of prescriptions considered to be necessary (indicated), appropriate (active) and adequate (correct dose, administration route and duration) by the F-ASP working group.

Results:

A total of 193 audits in 57 different children – 54% male, median age (IQR) 8.7 years (2.6-14.1), 9% neonates – were reviewed during the study period, accounting for 233 antifungal prescriptions. Reasons to start antifungal therapy were: prophylaxis (65%), empirical (20%), pre-emptive (2%) and targeted therapy (13%). Prescriptions were considered to be indicated and active in 92% and 99% of the cases, respectively. Dose, administration route and duration were adequate in 95%, 100% and 94% of the analyzed prescriptions. Disagreement with antifungal prescription was evidenced mainly in liver transplant patients and cardiac patients carrying ventricular-assist-device.

Conclusions:

Antifungals were mainly prescribed for prophylaxis in necessary, appropriate and adequate scenarios in our hospital. The F-ASP working group detected the need to initiate specific strategies aimed at the efficient use of antifungals in liver transplant patients and cardiac patients carrying ventricular-assist-device.

Systematic Review Registration:

ESPID19-0353
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

The profile of drug resistant bacteria in newborns having clinical sepsis and their outcome.

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Background and Aims:

The choice of antimicrobial therapy for neonatal sepsis is often empirical and based on the knowledge of local antimicrobial sensitivity pattern. The spectrum of organisms that causes neonatal sepsis and their resistance pattern changes over times Thus, this study was conducted to identify the organisms responsible for neonatal sepsis and their resistant pattern

Methods:

This prospective study was conducted in the NICU of BSMMU from October 2014-December 2017. During the study period, out of 1829 admitted patients, 559 blood samples from patients of clinically suggestive septicemia were evaluated. Only those who had a positive blood cultures were analyzed for this study.

Results:

Organisms were isolated in 124 (22.2%) of the collected blood samples. Only 11 cases were Early Onset Sepsis (EOS), remaining 113 were Late Onset Sepsis (LOS). Acinetobacter (46%) was found to be the most common organism in late onset sepsis followed by Klebsiella (37.9%) and E.Coli (6.4%). Most of the organisms in this study were resistant to 1st and 2nd line antibiotics. Colistin was the antibiotic with the highest sensitivity (93.5%) followed by Tazobactum- piperacillin (54.8%), and then Ciprofloxacin (44.3%), Netilmicin (43.5%) and Imipenem (41.9%). There is high prevalence of MDR and XDR organisms (78.8% and 51.1% respectively). Deaths in newborn due to XDR was proportionately higher compared to those in MDR, but the difference was statistically insignificant (45.3% vs. 33.3%, p=0.126).

Conclusions:

Gram negative bacteria, in particular Acinetobacter and Klebsiella are the leading causes of neonatal sepsis in our NICU. There is high prevalence of MDR and XDR organisms and infection with these organisms is associated with higher rate of mortality

Systematic Review Registration:

not applicable

ESPID19-0246
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Fluoroquinolone non-susceptible streptococcus pyogenes in japan

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Background

Streptococcus pyogenes (Group A streptococci : GAS) are known to cause a wide variety of human illnesses, some of which can be life-threatening. In particular, for children, GAS infections are an important cause of morbidity and mortality worldwide. Usually, penicillin is the first choice agent for the treatment of GAS infections. For patients with penicillin or beta-lactam antibiotics allergy, macrolide drugs are recommended as the first-line therapy. However, an increased prevalence of macrolide-resistant GAS (MRGAS) has been reported in many countries. Recently, some reports showed the fluoroquinolone non-susceptible GAS.

Methods

To reveal the rate of fluoroquinolone non-susceptible GAS, we investigated the minimum inhibitory test concentration (MIC), T-serotype, *emm* tying, and pulse field gel electrophoresis (PFGE) of 415 GAS strains isolated in Fukuoka southwest area of Japan between 2011 and 2013. We determined the fluoroquinolone non-susceptible that the MIC to TFLX was >1μg/ml.

Results

We identified 34(8%)quinolones non-susceptible GAS. In these strains, eight T-serotypes were detected. The predominant T-serotypes were T6 (11 isolates, 32.4%), TB3264 (7 isolates, 20.6%), T1 (6 isolates, 17.6%) and T4 (3 isolates, 8.8%). The predominant *emm* types were *emm*6 (14 isolates, 41.2%), *emm*89 (11 isolates, 32.4%) and *emm*75 (4 isolates, 11.8%). Molecular typing by PFGE classified 13 Molecular typing by pulsotypes and each pulsotype were quite different.

Conclusions

This result showed most of fluoroquinolone non-susceptible GAS strains have different origin. The *emm*89 that is known as cause of invasive GAS infection was one of the predominant subtype. That is a problem for the patients of beta-lactam allergy. In some countries fluoroquinolones can be used for children. Considering such a situation, continuous monitoring of quinolones non-susceptible GAS is necessary.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0239
Science and Educational Track

E-Poster discussion session 13 - Use of antimicrobials - Station 11

Clinical features and antimicrobial resistance of recurrent urinary tract infection in children with vesicoureteral reflux

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Background and Aims:

Vesicoureteral reflux(VUR) is risk factor of recurrent urinary tract infection(UTI) in children. When recurrent UTI occurs in VUR children, empirical antibiotic selection tends to be based on previous results. However, there is little evidence and research on this. The aim of this study is to investigate the clinical features and drug resistance of recurrent UTI in VUR patients and to establish therapeutic strategies.

Methods:

We retrospectively reviewed the medical records of children with VUR who had recurrent UTI from 2005 to 2018 at Severance Children's Hospital. We compared the clinical features between first and second UTI episodes. Relapse is defined when cultured pathogen is the same as the first episode. Reinfection is defined when cultured organism is different from the previous episode.

Results:

Among 78 VUR with UTI, 61(78.2%) had recurrent UTI (relapse 24, reinfection 37). The mean age at first UTI of the recurrent UTI group (12.1±21.4 months) was lower than that of the non-recurrent UTI group (21.5±28.2 months) (P = 0.039). Among recurrent UTI cases, the reinfection group had more bilateral VUR and prophylactic antibiotics used than relapse group(P = 0.046 and P = 0.027). In case of relapse, *E. coli* was most commonly isolated uropathogen(n = 13, 54.1%) followed by *K. pneumoniae* (n = 7, 29.2%). In *E. coli* relapse cases, antibiotics resistance increased during the 2nd episode in ampicillin, piperacillin/tazobactam, and cotrimoxazole (P < 0.001, P < 0.001, and P = 0.029).

Conclusions:

In VUR patients with recurrent UTI, reinfection were more frequent than relapse. In relapse cases, antibiotic susceptibility results of the 1st and 2nd episodes may be different. Antibiotics should be carefully selected, based on clinical presentation rather than previous culture results.

Systematic Review Registration:

N/A

ESPID19-0548
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

The respiratory microbiome and its association with infections and pneumococcal vaccine antibody response in a rural risk population of amerindian children

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[4]National Institute of Public Health and the Environment, Center for Infectious Disease Control, Bilthoven, The Netherlands
[5]Julius Center for Health Sciences and Primary Care- University Medical Center Utrecht, Epidemiology Infectious Diseases, Utrecht, The Netherlands
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Background

Infections of the respiratory (RTI) and gastrointestinal (GII) tract are still a major cause of childhood mortality. This is especially true for indigenous populations. Recent advances in high-throughput sequencing technologies have increased our understanding of the potential role of the microbiome in susceptibility to these infections and affecting response to therapeutic and preventive measures, such as vaccination. However, past work has mainly focussed on the role of the gut microbiome in mediating the immune response to vaccination and RTIs/GIIs.

Methods

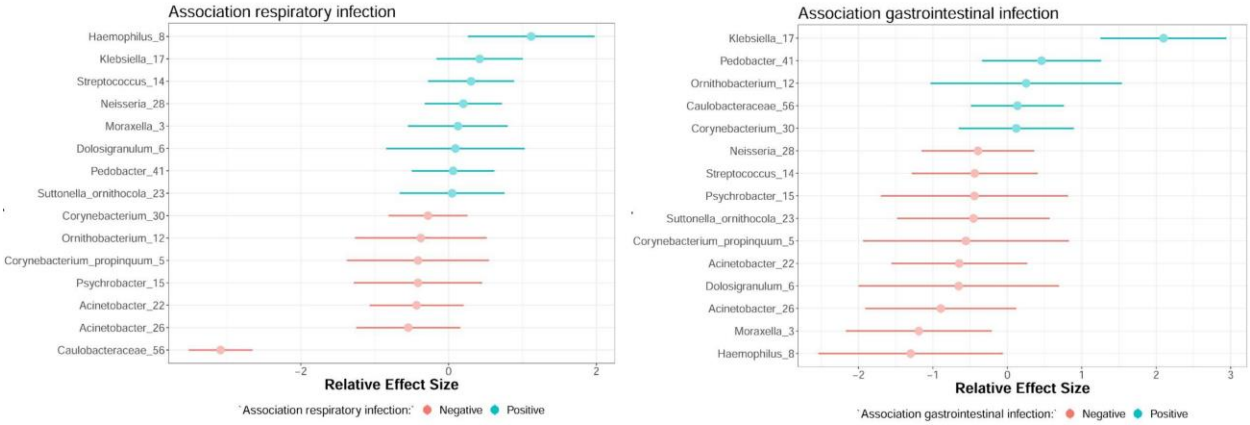
We studied nasopharyngeal microbiome profiles from 185 Warao Amerindian children residing in the Orinoco River Delta in Venezuela by using 16S-rRNA-based sequencing. Associations with RTIs/GIIs and pneumococcal vaccine response were determined by permutational multivariate analysis of variance, multivariable linear mixed effect models and random forest models.

Results

We found multiple different bacterial community profiles including some that are not commonly observed in Western populations. Interestingly, respiratory microbiome alpha diversity (Shannon index) was significantly decreased in children presenting GII symptoms ($p<0.01$). Furthermore, the relative abundance of *Klebsiella* spp. in the upper respiratory tract was significantly increased in children with diarrhea (23% vs. 0.3%, $p<0.001$). Finally, 42% of the variance in post-vaccination antibody levels was explained by a random forest model including age, nutritional status and six discriminatory bacteria, i.e.

Mycoplasma amphoriforme, *Acinetobacter*, *Moraxella*, *Haemophilus*, *Streptococcus* and *Bacillus*.

Genera that were significantly positively (blue) and negatively (red) associated with the presence of a A) respiratory infection or B) gastrointestinal infection. Overview of the relative effect size based on a mixed effect model adjusted for age on the top-15 most abundant genera. After Benjamini-Hochberg correction of p-values, the presence of *Caulobacteraceae* was negatively associated with RTI and Klebsiella showed a significant association with GII (all p<0.01).



Conclusions

Our findings underline the importance of studying respiratory microbiota in susceptible populations. We observed differences in community composition compared to children in high income countries. Moreover, we observed an association between nasopharyngeal microbiota and symptoms of acute infectious diseases as well as with pneumococcal vaccine antibody concentrations. Longitudinal studies are needed to understand the potential causal relationship between microbiota composition and symptoms or interventions.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0297
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Pneumococcal carriage density among nepalese children admitted to hospital with pneumonia.
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Background

We used nasopharyngeal samples from children with pneumonia to determine if higher pneumococcal density is more associated with proven or suspected pneumococcal pneumonia than with definite viral infection.

Methods

Between March 2014 and August 2016, 368 Nepalese children aged 2 months to 14 years admitted to Patan Hospital, Kathmandu, Nepal, with clinician diagnosed pneumonia had nasopharyngeal swabs analysed for pneumococcal density. DNA was extracted from the swab media and qPCR performed for pneumococcal autolysin (*lytA*). Respiratory viruses were detected by PCR of nucleic acids extracted from STGG. Children with pneumonia were classified into definite pneumococcal (N=6, sterile site culture positive for pneumococcus), probable bacterial (N=51, CRP>60 and end-point consolidation on CXR), probable viral (N=45, CRP≤60, normal CXR, and no virus detected), definite viral (N=81, CRP≤60, normal CXR and a virus detected), definite other bacterial (N=7 sterile site culture positive for pathogenic bacteria), and unknown bacterial or viral (not fitting other criteria) groups.

Results

Mean pneumococcal carriage density was significantly higher among children with definite pneumococcal pneumonia ($10^{5.67}$ copies/ml) when compared with children with; definite viral ($10^{3.21}$ copies/ml, $p<0.0001$), probable viral ($10^{3.59}$ copies/ml, $p<0.0001$), unknown bacterial or viral ($10^{3.38}$ copies/ml, $p<0.0001$), and probable bacterial pneumonia ($10^{4.59}$ copies/ml, $p<0.01$). When comparing children with definite pneumococcal pneumonia with definite other bacterial disease (only seven cases analysed), no significant difference in mean carriage density was detected ($10^{5.67}$ copies/ml vs $10^{4.11}$ copies/ml, $p=0.169$).

Conclusions

Pneumococcal carriage density is higher among children with confirmed pneumococcal pneumonia, when compared with children in other clinical categories. With further analysis of additional samples, especially those with confirmed bacterial disease, pneumococcal carriage density might be a useful adjunct for identifying pneumococcal pneumonia in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0172
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Pneumonia in children with sickle-cell disease in the pcv10 era: what has changed?

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Background and Aims:

Pneumonia is a leading cause of morbidity and mortality in individuals with sickle cell disease (SCD), considered a high-risk group for pneumococcal infection. Data on hospitalization in such patients lacks in the Brazilian population. We describe the effect of widespread PCV10 use on hospitalization due to pneumonia in children with SCD in a tertiary general hospital in São Paulo, Brazil.

Methods:

A hospital-based retrospective observational study was conducted and included children under 17 years with SCD and hospitalized due to pneumonia. Clinical Information was obtained from medical records and analyzed according to the pre-vaccination period (2005-2009) and post-vaccination period (2011-2015).

Results:

A total of 815 hospitalizations were identified among195 children with SCD – 386 before (average: 77.2/year) and 429 after PCV10 introduction (average: 85.8/year). 51.8% were male. An infectious cause was responsible for 43.8% (169/386) and 52.2% (224/429) of them when comparing periods. 119 (30,8%) and 137of such hospitalizations (31,9%) were due to pneumonia, respectively. When analyzing pneumonia-related hospitalization before and after the vaccine use, there were no changes in the median duration of hospitalization (6.0 days vs. 6.0 days). The median age decreased from 129 months to 87 months in post-vaccination era. Intensive care was neededin6.7% and 6,0% of children in both periods, respectively. Only four pneumonia-related deaths occurred during the study period: two before and two after PCV10.

Conclusions:

There were no differences in hospitalization rates, hospital length and hospitalization due to pneumonia before andafter PCV10 use in Brazil. ICU need and mortality rates were low in both periods. Younger children were more affected in the post-PCV10 era.

Systematic Review Registration:

Sickle cell disease
Pneumonia
Conjugated vaccines
PCV10

ESPID19-0702
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Il17f single nucleotide polymorphism rs763780 is associated with asthma at 11-13 years of age after bronchiolitis in infancy.

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Background

Interleukin-17F (IL-17F) is a fairly newly discovered cytokine that seems to play a crucial role in the pathophysiology of asthma. Several studies have appraised the association between *IL17F* gene polymorphisms and ashtma, but the results have been conflicting. The aim of this study was to evaluate the association between single nucleotide polymorphisms (SNPs) of *IL17F* rs763780(T/C), rs11465553(C/T) or rs7741835(C/T) and asthma after bronchiolitis in infancy in our prospective 11-13 years follow-up.

Methods

166 previously healthy full-term infants hospitalised for bronchiolitis at less than 6 months of age were invited to follow-up visits at 5-7 and 11-13 years of ages. At the follow-up visits asthma diagnoses and asthma presumptive symptoms, use of inhaled corticosteroids and atopy diagnoses were registered. Blood samples were obtained for *IL17F* rs763780, rs11465553 and rs7741835 determinations.

Results

No significant associations were found between children with *IL17F* SNPs rs11465553(C/T) or rs7741835(C/T) and clinical outcomes at 5-7 ot 11-13 years of ages. Instead, at the age of 11-13 years, children with the wild *IL17F* rs763780 genotype TT had used less inhaled corticosteroids (ICSs) between follow-ups from 5-7 to 11-13 years of ages (adjusted OR 0.28) than those with variant TC or CC genotypes. In addition, the children with the wild *IL17F* rs763780 genotype TT had less often doctor-diagnosed atopic eczema (adjusted OR 0.37) than those with variant TC or CC genotypes.

TABLE1.

Clinical characteristics of the 125 former bronchiolitis patients at the 11-13 years follow-up in relation to presence of wild vs. variant genotype of the *IL17F* rs763780 polymorphism.

Clinical characteristic	Wild genotype TT n=98 (%)	Variant genotype TC or CC=27 (%)	p value	OR (95% CI) for the wild genotype	aOR (95% CI) for the wild genotype
Current asthma	9 (9.2)	6 (22.2)	0.07		
Persistent asthma	5 (5.1)	4 (14.8)	0.08		
Use of ICSs in last 12 months	6 (6.1)	5 (18.5)	**0.04**	0.29 (0.08-1.03)	0.29 (0.07-1.17)
Use of ICSs at age 6-13 years	9 (9.2)	7 (25.9)	**0.02**	**0.29 (0.10-0.89)**	**0.28 (0.09-0.90)**
Doctor-diagnosed rhinitis	13 (13.3)	6 (22.2)	0.25		
Doctor-diagnosed atopic eczema	20 (20.4)	11 (40.7)	**0.03**	**0.37 (0.15-0.93)**	**0.37 (0.14-0.96)**

*aOR= OR adjusted for age, sex and RSV aetiology at age less than 12 months.

Conclusions

In this prospective long-term follow-up study we found preliminary evidence on the association between the *IL17F* SNP rs763780 and atopic asthma at 11-13 years of age after bronchiolitis in infancy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0564
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Association of viral load with disease severity in outpatient children with respiratory syncytial virus infection

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Background

Respiratory syncytial virus (RSV) is a major cause of acute respiratory infection and hospitalization in children. Several studies have examined the association between viral load and disease severity, but the results are conflicting, and most studies have involved only hospitalized children. There is little knowledge about whether viral load is associated with disease severity in outpatient children with RSV infection.

Methods

In a prospective cohort study of outpatient children, the children were examined at any signs or symptoms of respiratory infection. The parents filled out daily symptom diaries throughout the study. During each illness, nasal swabs were obtained for determination of the viral etiology. Detection of RSV was based on viral culture and RT-PCR. To explore the association between viral load and disease severity in children <10 years of age (n=201), we divided the children into two groups: higher viral load (Ct <27, n=106) and lower viral load (Ct ≥27, n=95).

Results

The duration of symptoms before viral sampling were similar between the higher and lower viral load groups. When analyzing the total duration of symptoms during RSV infection, children with higher viral load had significantly longer median durations of rhinitis (8.0 vs 6.0 days, p=0.001), cough (8.0 vs 6.0 days, p=0.34), fever (2.0 vs 1.0 days, p=0.018), or any symptom (10.0 vs 8.0 days, p=0.024) than those with lower viral load. No statistically significant differences were observed with respect to acute otitis media, pneumonia, or antibiotic treatment.

Conclusions

The duration of symptoms in outpatient children with RSV infection is positively correlated with viral load. Specific antivirals against RSV that would reduce the viral load might prove effective in shortening the duration of RSV illness in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0426
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Whole exome sequencing detects new host genomic susceptibility factors related to empyema caused by s. Pneumoniae in children

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Background

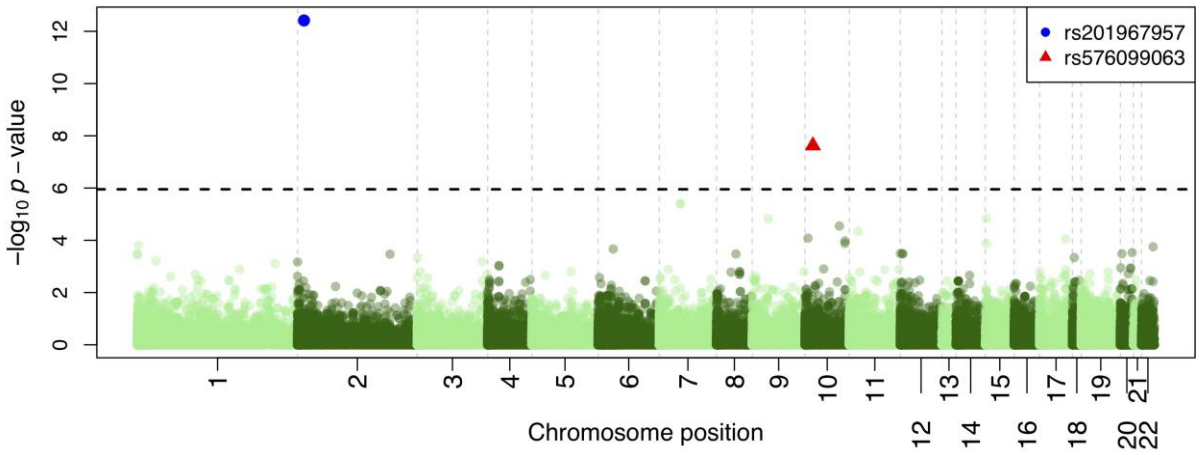
Pneumonia is the leading cause of death amongst infectious diseases. *Streptococcus pneumoniae* is responsible for ~25% of pneumonia cases worldwide, and it is a major cause of childhood mortality.

Methods

We carried out a whole exome sequencing (WES) study in eight patients with complicated cases of pneumococcal pneumonia (empyema). An initial assessment of statistical association of WES variation with pneumonia was carried out using data from The 1000 Genomes Project for the Iberian Peninsula as reference controls. In addition, to identify transcript signatures in patients with differing pneumococcal diseases we interrogated the GEO repository for the queries: 'Streptococcus pneumoniae' OR/AND 'pneumococcus' to validate the candidate genes obtained by the WES analysis.

Results

Association tests pointed to two nucleotide polymorphisms (SNP) as the best candidate variants associated to pneumococcal pneumonia: rs201967957 (gene *MEIS1*) and rs576099063 (gene *TSPAN15*). A burden gene test of pathogenicity signaled four genes, namely, *OR9G9*, *MUC6*,*MUC3A* and *APOB*, which carry significantly increased pathogenic variation when compared to controls. By analyzing various transcriptomic data repositories, we found strong supportive evidence for the role of *MEIS1, TSPAN15* and *APOBR* (encoding the receptor of the *APOB* protein) in pneumonia in mouse and human models.



Conclusions

Results from WES indicate that there are two SNPs statistically associated in empyema patients. In addition, this analysis also revealed four candidate genes with unexpected amounts of accumulated pathogenicity in pneumonia patients. The six genes are particularly interesting because they code for proteins that have been previously linked. WES emerges as a promising technique to disentangle the genetic basis of host genome susceptibility to infectious respiratory diseases.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0395
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Demographic, perinatal and childhood hospitalisation characteristics of hospitalised pertussis vaccine failure cases in new zealand: a case series study

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Background

Host characteristics that influence risk of pertussis vaccine failure are still not thoroughly understood. A greater understanding of host risk factors for pertussis vaccine failure has the potential to improve pertussis prevention strategies. We describe demographic, perinatal and childhood hospitalisation characteristics of paediatric pertussis vaccine failure cases.

Case Presentation Summary

A case series study design was used to describe all hospitalised cases of paediatric (5 months to four years old) pertussis vaccine failure occurring in New Zealand between 2006 and 2016. Hospitalisation, demographic and perinatal data was sourced from three large national data sets linked by unique identification number.

Of the 504,984 pertussis vaccinated paediatric population, 85 (0.2%) were hospitalised for pertussis disease during the study period. None were admitted to neonatal intensive care units or died from pertussis. Median age at pertussis hospitalisation was 15 months (Table 1). The median socioeconomic deprivation quintile was 4, indicating low socioeconomic status. Twenty-one (25%) cases were born prematurely; seventeen (20%) were of low or very low birth weight (less than 2500 g); and eleven (15%) had either a moderately low or very low five minute Apgar score (6/10 or less). Fifty-six (66%) had at least one hospitalisation between 92 days old and four years old; 70% were hospitalised for respiratory diseases not including pertussis.

Table 1 Case demographics

Characteristic	Value n=85
Median age at pertussis hospitalisation, interquartile range	15, 16
Socioeconomic deprivation (NZDep13) quintile median, interquartile range	4, 2

Learning Points/Discussion

Our findings suggest perinatal and demographic factors may influence risk for pertussis vaccine failure, but there is need to test these hypotheses statistically. Further work is being undertaken to identify predictive host factors for pertussis vaccine failure.

ESPID19-0368
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Mucosal immune response in the upper airways in children with complicated upper respiratory tract infections

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Background and Aims:

Respiratory tract mucosal immunity is seen as the first line of defense against pathogens and thus is linked to the characteristics of upper respiratory tract infections (URTIs). The survey objectives were to investigate airway mucosal immune response in children with primarily viral URTIs complicated by acute bacterial otitis media (ABOM) or rhinosinusitis (ABRS).

Methods:

120 children aged 3 to18 years were enrolled: 50 with recurrent (≥ 4 episodes of ABOM/ABRS per year) course of ABOM/ABRS (group I) and 70 with episodic one (group II). Levels of human cathelicidin (hCap-18/LL-37), lactoferrin (La), lysozyme (Lys) and secretory IgA (sIgA) were measured in oropharyngeal secretions twice during the disease and after recovery. The controls were 36 children with purely viral URTIs and 30 healthy children.

Results:

Measured beyond the infection, in group I levels of factors studied were comparable to ones in group II and in healthy children, except for Lys: 19.19 (16.80; 22.88) in group I vs. 26.58 (17.43; 34.98) pg/ml in group II and 40.37 (33.98; 43.81) pg/ml in healthy children ($p = .002$ and $p < .001$, resp.). The early response to bacterial infection in study groups was observed as a rapid substantial increase of hCap-18/LL-37 (25-50-fold rise) and La (7-13-fold increment) which considerably exceeded the response to viral URTIs (1-2-fold rise); the late response manifested as ascending Lys and sIgA levels (1-2-fold rise). Group I compared to group II showed significantly lower levels and amplitude of change of given immune factors during the disease, except for IgA. Levels of antimicrobial peptides showed an inverse correlation with the duration of catarrhal phenomena and total disease duration.

Conclusions:

Recurrent bacterial URTIs in children are associated with malfunction of airway mucosal immune mechanisms.

Systematic Review Registration:

N/A

ESPID19-0267
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Seasonality of respiratory syncytial virus hospitalisations (rsvhs) across 12 consecutive rsv seasons (2000-2001 to 2011-2012) in scotland

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Background and Aims:

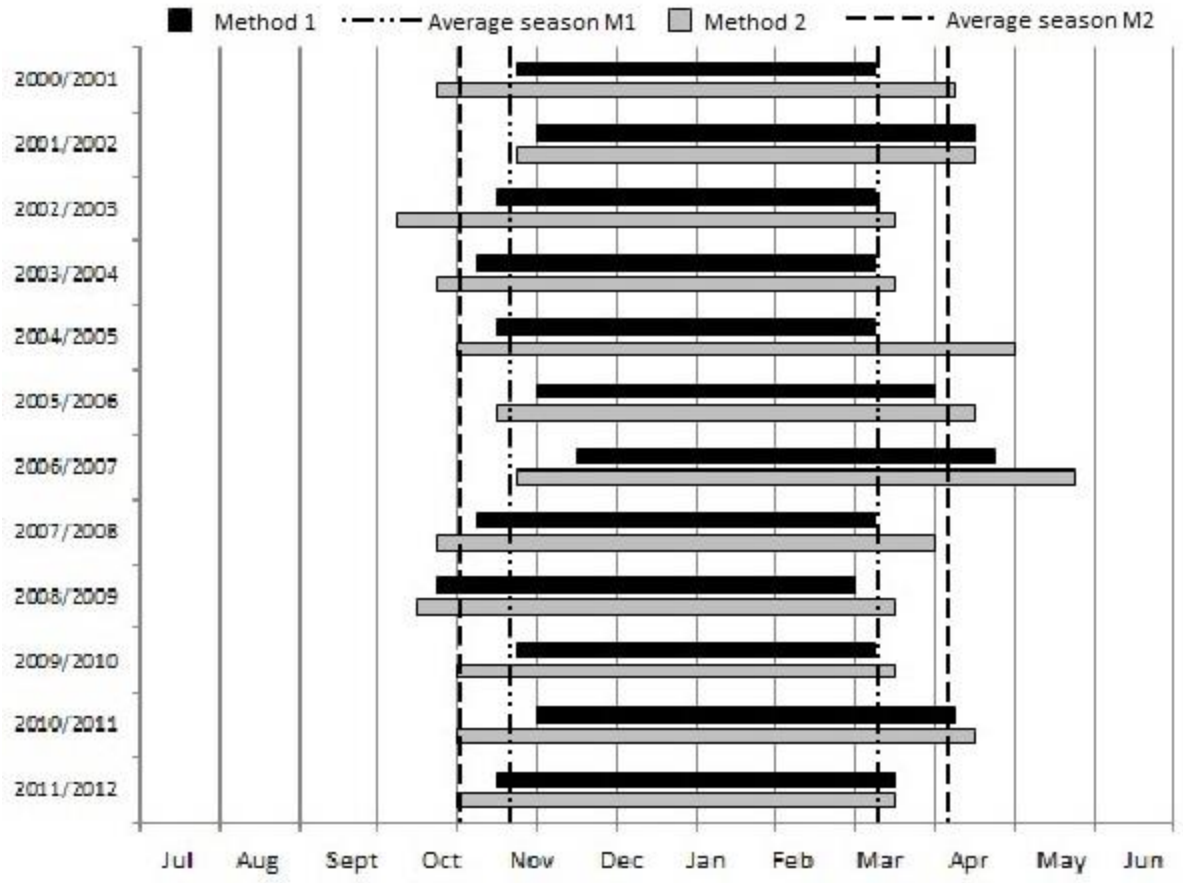
RSV causes a significant burden on paediatric services during autumn/winter; hence, it is important to know the timing of the RSV season in order to plan and manage healthcare resources effectively. This study assessed the seasonality of RSVHs across 12 consecutive seasons in Scotland.

Methods:

All RSVHs (ICD-10 codes: J12.1, J20.5 & J21.0) occurring during the first 2 years of life in children born in NHS Scotland hospitals between 2000-2011 were assessed. The RSV season was defined in weeks using two methodologies: M1. >1.2% of annual RSVHs occurred; or, M2. Admissions were twice the two-month pre-season median. Periodicity of timings was modelled and tested (Spearman correlation).

Results:

Of 623,770 children born 2000-2011, 13,362 (2.1%) had 14,632 RSVHs (23.1/1,000) over the 12 seasons. The RSV season ranged from early September to the end of May, though typically fell between October and March (Figure). The season start date varied by up to 7 weeks (M1: 7 weeks; M2: 6 weeks) and the end date by up to 9 weeks (M1: 7; M2: 9). Using M1, the RSV season had a relatively uniform length (median 20 [range 18-21] weeks), but showed a 4.5 year cycle in timing ($p<0.001$). There was a mean of 1,100 (range 910-1380) RSVHs *per* season and 91% of RSVHs occurred during the season. M2 demonstrated a longer season with a more variable timing (median 25 [range 22-28] weeks), but included 96% of RSVHs. During the season, RSVHs represented 8.5% of all inpatient admissions and 12.6% of intensive care admissions.



Conclusions:

The RSV season typically runs October-March, but can vary considerable across years and depending on how it is calculated.

Acknowledgements

Matthew Freddi (Strategen Ltd) for editorial services.

Systematic Review Registration:

N/A

ESPID19-0243
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Bacterial lysates as add-on therapy in pediatric wheezing and asthma: a systematic review and meta-analysis

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Background

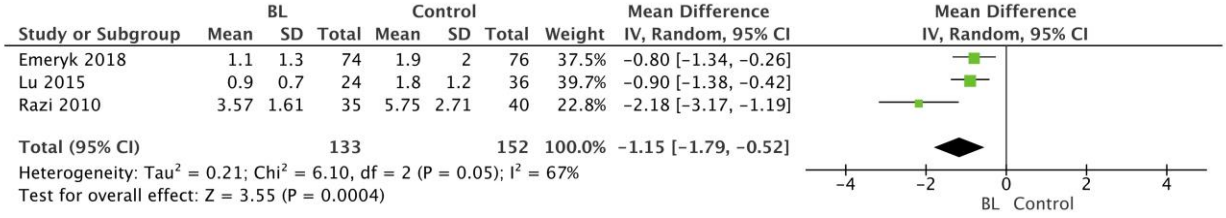
Wheezing or asthma exacerbations are the main cause of morbidity in pediatric obstructive lung diseases. Often, respiratory viruses are involved. Bacterial lysates, which are lyophilized bacterial extracts, act as non-specific immunomodulators and might prevent respiratory tract infections as shown in meta-analyses. Therefore, they also might prevent exacerbations. Mechanistic animal studies also show evidence for immunomodulation by regulatory T-cells resulting in downregulation of (allergic) Th2-cytokine responses and upregulation of Th1-responses. We aimed to assess the effect of add-on bacterial lysate therapy on exacerbation frequency in obstructive lung diseases.

Methods

We performed a systematic (English) literature review and meta-analysis using RevMan 5.3. Data was estimated using mean differences. Out of 98 screened articles; 24 studies were included; of which only 4 provided pediatric data; 2 on asthma in school children and 2 on wheezing in infants. The remaining studies described the effect of bacterial lysates in animals or COPD and will not be discussed here. Overall quality of the studies was low.

Results

Three articles were used for a meta-analysis. For childhood wheezing or asthma a median difference of -1.15 exacerbations (95%CI -1.79;-0.52;p<0.0004) was estimated (table 1). Additionally, the duration of symptoms, and antibiotic use was significantly reduced. Adverse events were equal between intervention- and control group. Pediatric human immunological data are scarce but 2 studies showed a significant increase in serum IL-10 and IFN-γand decrease in IL-4 and IL-17. Natural killer T-cells were higher after therapy.



Conclusions

Bacterial lysates can be considered as add-on therapy in children to prevent recurrent wheezing or asthma exacerbations. These data were confirmed by a recent Chinese study meta-analysis. Mechanistical data and larger studies will shed more light on which wheezing- or asthma phenotype benefits most.

Systematic Review Registration (Please input N/A if not registered)

Prospero CRD42017078141

ESPID19-0352
Science and Educational Track

E-Poster discussion session 14 - Respiratory - Station 13

Pneumococcal nasopharyngeal carriage dynamics in children <2 years, following pneumococcal conjugate vaccine (pcv) implementation in israel

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[2]Ben-Gurion University of the Negev, Faculty of Health Sciences, Beer-Sheva, Israel

Background and Aims:

The implementation of PCV resulted in a substantial decline in pneumococcal morbidity, while carriage rates remained relatively constant, due to increase in non-vaccine serotypes (replacement).

We assessed pneumococcal carriage rates dynamics in different clinical syndromes in children <2 years, following PCV introduction.

Methods:

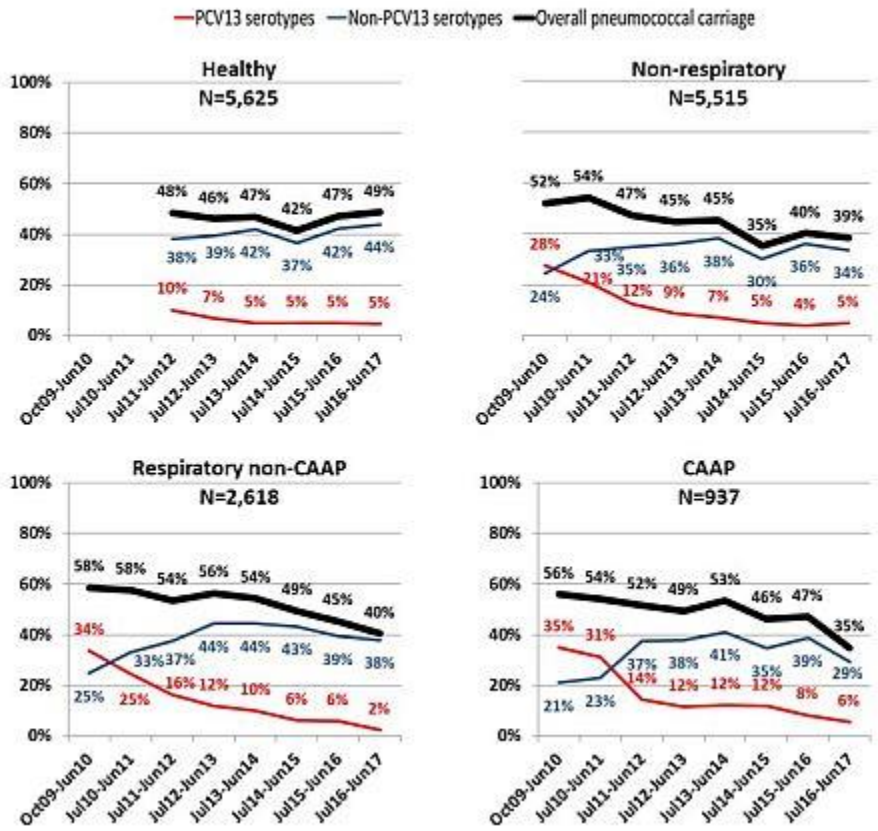
An ongoing prospective, population-based surveillance, conducted between October 2009 and June 2017, in Southern Israel. PCV7 and PCV13 were introduced to the Israeli National Immunization Plan in July 2009 and November 2010, respectively. Clinical syndromes were classified into 4 groups: healthy, non-respiratory illness, non-pneumonia respiratory disease, and community-acquired alveolar pneumonia (CAAP). The collection of cultures in healthy children started only in 2011. Continuous graphs were drawn (**Figure**), and rate ratios (RRs) with 95% confidence interval (CI) were calculated, comparing carriage rates in the early-PCV period (2009-2011) with the PCV13 period (2015-2017). RRs were adjusted for ethnicity, seasonality and antibiotic treatment in the preceding month.

Results:

Overall, 14,695 cultures were included. Carriage rates in healthy children remained stable throughout the study (RR=1.03; CI 0.92-1.14).

In contrast, carriage rates substantially declined in children with non-respiratory illness (RR=0.74; CI 0.68-0.81), non-CAAP respiratory disease (RR=0.71; CI 0.63-0.80) and CAAP (RR=0.71; CI 0.59-0.87). These trends were driven by ~80% reductions of vaccine serotypes, coupled with an increase in non-vaccine serotypes.

Figure. Dynamics of pneumococcal carriage in children <24 months, southern Israel, October 2009 through June 2017



Conclusions:

The sequential introduction of PCV7/PCV13 resulted in a substantial reduction in overall pneumococcal carriage rates in children with respiratory and non-respiratory diseases, while carriage rates in healthy children remained stable.

Systematic Review Registration:

N/A

ESPID19-1149
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Epidemiology of antimicrobial pathogens in bloodstream infections in a pediatric population

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Background and Aims:

Microbiological epidemiology is a simple though reliable tool in antimicrobial stewardship programs. Also, updated epidemiological data on frequently encountered bacterial pathogens is useful for deciding on empirical treatment. Bloodstream infections in a pediatric unit were analyzed to determine antimicrobial susceptibility trends over time.

Methods:

An ongoing active surveillance study in children aged under 16, from January 1st, 2010, through December 31st, 2018 was conducted in a tertiary-level Brazilian university hospital. All positive blood cultures were identified, and laboratory information was evaluated. Samples with the same pathogen within four weeks and polymicrobial culture were excluded.

Results:

A total of 2885 non-duplicate and non-polymicrobial pathogens were identified. Little variations in proportions occurred during the period. Gram-negative bacteria (GNB) were responsible for 19-28% of the identified pathogens, followed by gram-positive bacteria (GPB, 12-19%) and yeasts (0-6%). Candida albicans is the most frequent yeast (48.4%). Coagulase-negative staphylococci comprised 98.9% of the contaminants pathogens. Among GPB *Staphylococcus aureus* (49.4%), Streptococcus pneumoniae (13.8%), and Enterococcus sp. (11.8%) were the most prevalent. Klebsiella spp (32.9%), Acinetobacter spp (15.9%), Pseudomonas spp (14.3%), Escherichia coli (11.3%), and Enterobacter spp (10.7%) were the most frequent GNB

Conclusions:

Despite the variation of isolates numbers, little changes in proportion were seen along the years of evaluation. We provide substrate for empirical antibacterial therapy and data for antimicrobial stewardship programs to be implemented.

Systematic Review Registration:

Antimicrobial stewardship; Bloodstream infection; Bacterial resistance

ESPID19-1076
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Assessing antimicrobial use in hospitalized pediatrics patients in gaborone, botswana: a prospective cohort study

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Background and Aims:

Antimicrobial resistance is a global threat with alarming implications. While much is known about the status of antibiotic use in pediatric patients in high-income countries, there are minimal data on in low-to middle-income countries.We aimed to describe current prescribing practices in a hospitalized pediatric cohort at a large referral center in Botswana.

Methods:

From June 2018–October 2018 we conducted a prospective cohort study on pediatric patients admitted to Princess Marina Hospital, Gaborone. All children admitted to the medical and surgical wards aged up to 13 years were eligible for inclusion. After consent, the following data were abstracted; demographic, clinical, laboratory and microbiology, antibiotic use and drug availability. Stata v15 was used for analyses. Appropriate antibiotic use was defined as the correct choice and dose of agent for the diagnosis in question.

Results:

A total of 310 patients were enrolled; 62% on General Pediatrics and 36% on the Surgical service. The cohort was 57.4% male; 20% HIV-exposed and 4.1% HIV-infected. The most common reasons for admission were pneumonia, sepsis and gastroenteritis. Approximately 50% were prescribed at least one antibiotic, with 43% of antibiotic use deemed inappropriate on admission and 58% on discharge. Dosing was incorrect in 29% of cases on admission and 33% on discharge. Drug shortages affected almost 10% of patients. Overall, 81% of patients survived and 4% died from infectious causes. However, 15% were transferred to a different institution or had an unknown outcome.

Conclusions:

This prospective study on antimicrobial prescribing practices in Botswana revealed a heavy burden of antimicrobial use; a significant proportion of which was inappropriate either on admission or discharge. Antimicrobial stewardship training would be beneficial in standardize dosing and providing suitable alternatives when drug shortages are present.

Systematic Review Registration:

ESPID19-0938
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Aetiology of and antimicrobial resistance in childhood (≤5 years) central nervous system infections in malawi (2000-2017)

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Background and Aims:

Central nervous system (CNS) infections represent a significant burden of infectious disease in hospitalised children in sub-Saharan Africa. Recent data from our setting illustrate that antimicrobial resistance (AMR) in childhood bloodstream infection is an increasing and substantial problem. We describe trends over 18 years of bacterial CNS infections in children ≤ 5 years admitted to a large teaching hospital in Blantyre, Malawi, a malaria endemic setting outside of the epidemic “meningitis belt”.

Methods:

We determined the total number of cerebrospinal fluid (CSF) culture positive isolates between 2000 and 2017 (divided into 2000-2004, 2005-2008, 2009-2013, 2014-2017 for analysis) and associated antimicrobial resistance (AMR) profiles.

Results:

A total of 2,040 pathogens (Gram-positive (n=1036, 50.7%), Gram-negative (n=996, 49.3%)) were identified. There was an overall decline in total number of CSF pathogens over the 18-year period; 2000-2004 n=942, 2005-2008 n=470, 2009-2013 n=264 and 2014-2017 n=350. Significant reductions in CSF culture positive cases of *Haemophilus influenzae* (n=236, 25.2% vs n=6, 1.7%) and *Streptococcus pneumoniae* (n=373, 39.6% vs n=47, 13.4 %) were identified when comparing 2000-4 and 2014-2017. A notable increase in certain Gram-negative pathogens occurred during the same time periods; *Klebsiella* spp. (n=6, 0.6% vs n=49, 14%), *E.coli* (n=12, 1.27% vs n=43,12.29%) *and Acinetobacter baumanii* (n=0, 0% vs n=42, 12%). Resistance to ceftriaxone increased for *Klebsiella pneumoniae* from 20.0% to 95.8% and *E. coli* 0% to 62.8%.

	Time period								
	2000-2004		2005-2008		2009-2013		2014-2017		Total N
	N	%	N	%	N	%	N	%	
Gram-positives	439	46.55	313	66.60	125	47.35	148	41.71	1036
Group A Strep	7	0.74	4	0.00	5	1.89	3	0.86	19
Group B Strep	45	4.77	41	8.72	22	8.33	11	3.14	119
Streptococcus pneumoniae	373	39.55	254	54.04	65	24.62	47	13.43	739
Staphylococcus aureus	4	0.42	7	1.49	11	4.17	20	5.71	42
Other *Streptococcus* spp.	7	0.74	2	0.43	11	4.17	7	2.00	27
E. faecalis	2	0.21	5	1.06	6	2.27	12	3.43	25
E. faecium	0	0.00	0	0.00	5	1.89	46	13.14	51
All *Enterococcus* spp.	2	0.21	5	1.06	6	2.27	58	16.57	71
Listeria species	1	0.11	0	0.00	0	0.00	0	0.00	1
Leuconostoc	0	0.00	0	0.00	0	0.00	0	0.00	0
Gram-negatives	503	53.34	157	33.40	135	51.14	201	57.43	996
Acinetobacter baumanii	0	0.00	0	0.00	12	4.55	42	12.00	54
All *Acinetobacter* spp.	2	0.21	5	1.06	17	6.44	43	12.29	67
Citrobacter spp.	1	0.11	0	0.00	1	0.38	5	1.43	7
Enterobacter spp.	4	0.42	7	1.49	9	3.41	16	4.57	36
Escherichia coli	12	1.27	15	3.19	23	8.71	43	12.29	93
Haemophilus influenzae type b	238	25.24	24	5.11	13	4.92	6	1.71	281
All *Haemophilus* spp.	260	27.57	38	8.09	19	7.20	10	2.86	327
Klebsiella pneumoniae	5	0.53	7	1.49	25	9.47	48	13.71	85
All *Klebsiella* spp.	6	0.64	7	1.49	25	9.47	49	14.00	87
Neisseria meningitidis W135	0	0.00	3	0.64	2	0.76	8	2.29	13
Neisseria meningitidis group A	2	0.21	1	0.21	0	0.00	0	0.00	3
Neisseria meningitidis group B	0	0.00	1	0.21	0	0.00	0	0.00	1
Neisseria meningitidis	6	0.64	12	2.55	2	0.76	9	2.57	29
N. gonorrhoea	0	0.00	0	0.00	1	0.38	0	0.00	1
Proteus spp.	1	0.11	0	0.00	0	0.00	1	0.29	2
Pseudomonas aeruginosa	3	0.32	4	0.85	3	1.14	3	0.86	13
All *Pseudomonas* spp.	4	0.42	5	1.06	5	1.89	9	2.57	23
Salmonella Typhi	1	0.11	0	0.00	3	1.14	1	0.29	5
NTS	203	21.53	63	13.40	19	7.20	5	1.43	290
Serratia spp.	0	0	0	0.00	1	0.38	2	0.57	3
Shigella spp.	0	0	0	0.00	0	0.00	0	0.00	0
Vibrio spp.	0	0	0	0.00	0	0.00	0	0.00	0
Yersinia spp.	0	0	0	0.00	0	0.00	0	0.00	0
Other Gram-negatives[a]	3	0.32	5	1.06	10	3.79	8	2.29	26
Fungus	1	0.11	0	0.00	4	1.52	3	0.86	8
Candida	0	0	0	0.00	2	0.76	1	0.29	3
Cryptococcus	1	0.11	0	0.00	2	0.76	2	0.57	5
Yeast species	0	0	0	0.00	0	0.00	0	0.00	0
All pathogens[b]	943	100	470	100.00	264	100	350	100	2040

MRSA, methicillin-resistant Staph aureus; NTS, nontyphoidal Salmonella

[a]Includes *Aeromonas* spp., *Burkholderia* spp., Gram negative rods, *Moraxella* spp., *Morganella* spp., *Pantoea* spp., *Pasteurella* spp., *Raoultella* spp., *Sphingomonas* spp., *Stenotrophomonas* spp., spp..

[b]Excludes contaminants, including *Aerococcus* spp., alpha-hemolytic streptococci, *Bacillus* spp., *Clostridium* spp., coagulase-negative staphylococci, Diphtheroids, Gram positive rods, *Micrococcus* spp., skin flora also include Acinetobacter lwoffi

Conclusions:

The total number of bacterial CNS infections in hospitalised children at our tertiary referral hospital decreased over the last 18 years, reflecting the comprehensive roll out of conjugate vaccines in Malawi. However, there are worrisome increased numbers of Gram-negative pathogens resistant to first-line antimicrobials. These data mirror the rapidly expanding AMR in childhood bloodstream infections in our setting.

Systematic Review Registration:

N/A

ESPID19-0906
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Challenges in the implementation of the uk aware antibiotic classification in the treatment of paediatric infectious diseases

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Background and Aims:

As part of a multifaceted strategy to address antimicrobial resistance, a UK target is to achieve ≥55% total antibiotic consumption in the “Access” group of the modified “Access, Watch and Reserve” (AWaRe) classification. Amoxicillin-clavulanate, an antibiotic used as first-line treatment in many paediatric infections, was moved from the "Access" to the “Watch” category under this scheme. The aim of this prospective study was to measure the use of "Access" antibiotics at our institution to inform the feasibility of the national target.

Methods:

Between March 2016 and November 2018, antimicrobial prescription data were collected on all patients hospitalised at Evelina London Children’s Hospital as part of eight point-prevalence surveys (PPS). We performed a descriptive analysis using AWaRe category and indication. A chi-squared test for trend was used to evaluate whether the proportion of patients on antimicrobial agents decreased with time.

Results:

We analysed 728 prescriptions. On average, 38% of hospitalised patients were receiving an antimicrobial agent on the day a PPS was conducted, and this proportion remained stable through the study period ($p = 0.95$). In 2018, 21% of prescriptions were for medical prophylaxis and 8% for surgical prophylaxis. Between 42% and 55% (median 45%) of antibiotics were classified as "Access". The target of ≥55% was achieved in one of eight PPS. Amoxicillin-clavulanate was the most commonly prescribed antibiotic and accounted for 15-34% (median 25%) of all antibiotic prescriptions.

Conclusions:

There was no decrease in antimicrobial use during this period. Despite a probable overestimation of the proportion of "Access" antibiotics, the target (≥55%) was almost never reached. Amoxicillin-clavulanate was widely prescribed, making the proportion of "Access" antibiotics ≥55% of total antibiotic consumption a difficult target to consistently achieve in children.

Systematic Review Registration:

N/A

ESPID19-0746
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Greek medical students' perceptions, knowledge, and education about antimicrobial prescribing and resistance: a cross-sectional study

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Background and Aims:

Injudicious use of antibiotics is a major cause of antimicrobial resistance, which increases morbidity, mortality and health-care costs. WHO has highlighted the importance of undergraduate training in prudent antibiotic use. In Greece,a country burdened with high antibiotic consumption and resistance,little is known about students' knowledge on antibiotic prescribing. We aimed to assess Greek medical students' perceptions,knowledge, and education about antimicrobial prescribing and resistance(AMPR).

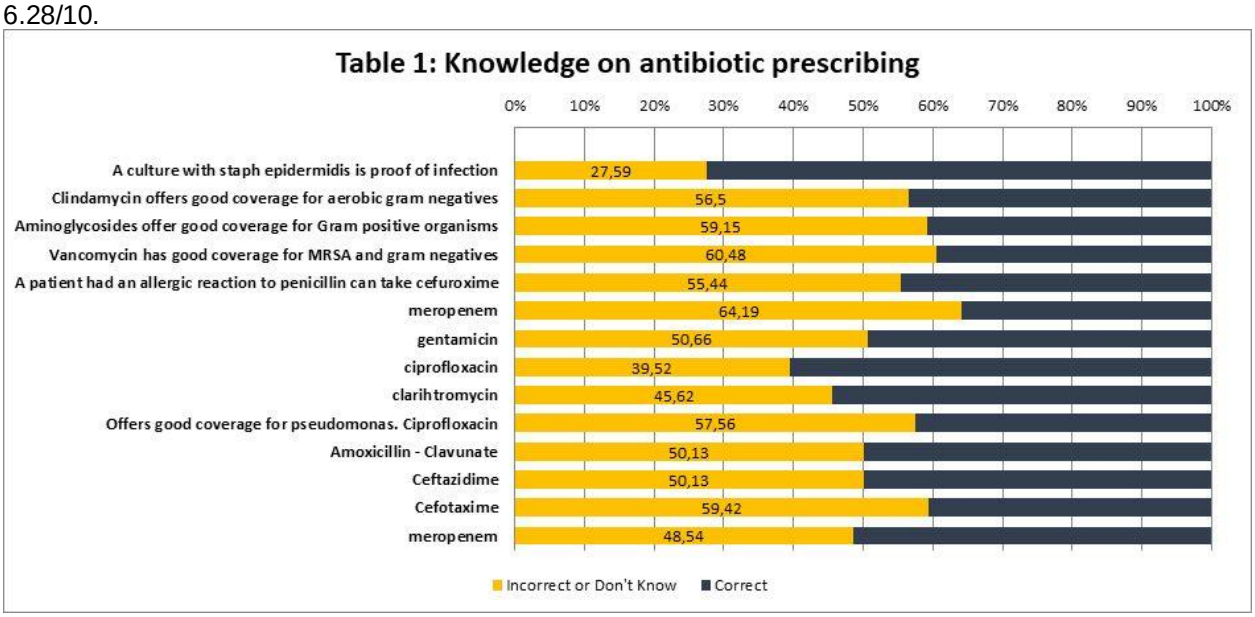
Methods:

A voluntary, anonymous, cross-sectional survey of final-year medical students was conducted in 6/7 medical schools in Greece, consisting of 40 questions on perceptions, knowledge, and education about AMPR. The survey was disseminated by HelMSIC(Hellenic Medical Students' International Committee) between 26/11/2018 and 7/12/2018.

Results:

The survey had a response rate of 60.3%(375/622). 71.5% had never heard the term Antibiotic Stewardship. 55% answered correctly to half or fewer of 14 questions on antibiotic prescribing(Table1). The majority failed to identify that vancomycin(59%) and clindamycin(57.8%) do not have good coverage for gram-negative bacteria. Students could not identify as inappropriate antimicrobials for an ESBL infection:amphotericin-B(84.3%),vancomycin(85.1%),linezolid(93.4%), or ceftriaxone(40%).Only 16% would prescribe amoxicillin to a fully immunized thirteen-year-old with community-acquired pneumonia. Throughout medical school respondents had been asked fewer than 5 times or not at all to choose: whether an antibiotic was needed(57.3%);the right antibiotic(48.5%); route,dose, and interval(71.2%);duration(62.3%); or the agent based on the culture results(67.4%). Self-reported confidence on 15 items regarding antimicrobial prescribing(on a scale from 1[not at all] to 10[totally]) was a mean of

6.28/10.



Conclusions:

We identified considerable gaps in knowledge of AMPR and inadequate practical training among Greek medical students, which impacts their confidence in these areas.These targets will educate the design of an intervention that could tackle Greece's problem of injudicious antimicrobial use and resistance at its root:the medical school.

Systematic Review Registration:

N/A

ESPID19-0607
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Disease related factors should be considered when prescribing systemic fluoroquinolones for children, results of a systematic review of pharmacokinetic studies

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Background

Resistance rates of fluoroquinolones are rapidly rising. As pharmacokinetics of antibiotics is affected by disease related and developmental factors, these factors should be considered when prescribing fluoroquinolones for children. Therefore, we conducted a systematic review of pharmacokinetic studies of systemic fluoroquinolones in children.

Methods

Pharmacokinetic studies of systemic fluoroquinolones, which were published before December 2018, were obtained from different major databases (PubMed, Embase, Cochrane Database of Systematic Reviews, Web of Science, Scopus, CINAHL, Embase). The structured search strategy was approved by an experienced librarian. Methodological quality was assessed, by 2 independent researchers, using the ClinPK checklist. Data are described both qualitatively and quantitatively.

Results

A total of 19 studies were included, in which pharmacokinetics of either levofloxacin, ciprofloxacin, moxifloxacin, trovafloxacin, ofloxacin, and gatifloxacin had been studied in children suffering different underlying diseases. Differences in pharmacokinetic profiles were found in different diseases, such as respiratory exacerbations of cystic fibrosis, neonatal sepsis, tuberculosis, complicated urinary tract infection, multidrug-resistant typhoid fever, postexposure inhalational anthrax, severe malnutrition, meningitis, and sickle cell anemia. For ciprofloxacin, renal clearance was decreased in children suffering complicated urinary tract infection, and volume of distribution was increased in children suffering cystic fibrosis. Levofloxacin is increasingly prescribed for treating multidrug-resistant tuberculosis, its maximum concentration (Cmax) is correlated with the mg/kg dose.

Conclusions

Disease related and developmental factors should be considered for the adequate dosing of systemic fluoroquinolones for children.

Systematic Review Registration (Please input N/A if not registered)

CRD42016039778

ESPID19-0396
Science and Educational Track

Independent E-Poster Presentations 01 - Antimicrobials - Stewardship and Resistance - Station 01

Implementing appropriate anti-pseudomonas drugs for post-tracheostomy respiratory tract infection (rti) by increasing the number of pediatric hospitalists

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Background and Aims:

Staphylococcus aureus and *Pseudomonas aeruginosa* are common causative organisms of post-tracheostomy respiratory tract infection (RTI). However, it is difficult to clinically distinguish whether the children who underwent tracheostomy are infected by bacteria or other organisms, and unnecessary broad spectrum antibiotics are often prescribed. The number of pediatric hospitalists in our hospital increased from 1 to 5 in April 2017. Our current study aimed to identify the effect of increasing the number of pediatric hospitalists on post-tracheostomy RTI.

Methods:

We conducted a retrospective observational study involving children who underwent tracheostomy and were admitted to our hospital due to RTI. May 2016 to March 2017 was defined as the pre-hospitalist ('Pre') period, while April 2017 to August 2018 was the post-hospitalist ('Post') period. The children admitted to the intensive care unit from the emergency room were excluded. Mann-Whitney test was performed for continuous variables. Chi-square test or Fisher's exact test was used for categorical variables. *P* -values under 0.05 were considered significant.

Results:

The frequency of use of anti-*Pseudomonas* drugs significantly decreased in the 'Post' group compared to that in the 'Pre' group (14% to 1%; p=0.011). The differences in the median age, the median values for hospital stay, positively gram-stained samples on admission, prevalence of *Pseudomonas*, and administration of antibiotics during hospitalization were not significant between the two groups. No patient died.

Conclusions:

The frequency of anti-*Pseudomonas* drug uses for post-tracheostomy RTIs significantly decreased on increasing the number of hospitalists in our hospital. This was because the hospitalists could work more closely with infectious disease doctors than before. Administration of antibiotics during hospitalization could have been reduced more. Future research should be conducted to use appropriate antibiotics for the children who underwent tracheostomy.

Systematic Review Registration:

Nothing

ESPID19-1070
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

A 21 year, single centre review of mucormycosis in paediatric haemato-oncological patients

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Background

Mucormycosis is a rare, life threatening fungal disease, primarily affecting severely immunocompromised hosts. Early diagnosis, correct and timely systemic antifungal treatment and surgical debridement remain the mainstay of successful treatment. However, because of its often acute onset and progression, the infection results in a fatal outcome in over half of cases.

Case Presentation Summary

We present a retrospective single centre case series of proven mucormycosis in paediatric haemato-oncologic patients between October 1997 and December 2018.

We identified 17 cases of mucormycosis. 41 percent were boys, the mean age was 10 years, 15 had haematological malignancies, and 2 had a solid tumour. 59 percent of patients survived. The lungs were the most common site (9/17) followed by skin infection (4/17). Four patients had disseminated disease, none of whom survived. One patient had Aspergillus coinfection, one basidiomyceta. The mean time to development of mucormycosis from the start of immunosuppressive treatment was 3.6 months. One patient developed wound infection without any prior immunosuppressive treatment. Over half of fatal cases (4/7) were diagnosed with mucormycosis post-mortem and did not receive antifungal treatment.

Localised infection, early debridement and treatment with amphotericin and posaconazole were associated with good outcomes. All surviving patients received long term posaconazole maintenance treatment.**Learning Points/Discussion**

In our cohort, patients developed mucormycosis at all stages of their treatment, including initiation. This highlights the necessity of early diagnosis and timely aggressive and combined surgical and systemic antifungal treatment. Mortality rates were in keeping with current data from paediatric haemato-oncological patients.

ESPID19-0777
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Kawasaki disease in slovenia – a 12-year experience from a university hospital

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Background and Aims:

The aim of the study was to assess clinical features and treatment in children with Kawasaki disease (KD) treated at the Department of Infectious Diseases, University Medical Centre Ljubljana.

Methods:

A retrospective analysis of children with KD treated at our institution between 1.6.2006 and 1.6.2018 was performed.

Results:

Of 103 children with KD, 90 (87%) had complete and 13 (13%) incomplete disease. Among the 13 incomplete cases, 5 were infants. The mean age was 45.4(±32) months and boys were more prevalent (61%). There were two incidence peaks in spring and autumn. The median time-to-referral was 5 days. The mean admission laboratory values were 136.6(±74.4) mg/L for CRP, 77.5(±28.6) mm/h for ESR and 14.5 $x10^9$($\pm 6.9 \times 10^9$)/L for WBC count, respectively. IVIG treatment was given to 96 (93%) children after a median of 7 days of fever. 88/96 (90%) patients responded to initial therapy, 9.4% (9/96) received another dose of IVIG, which was successful in 66% (6/9). Coronary artery abnormalities (CAA) were present in 26% (27/103) of children in the acute phase (ectasia, thickening of endothelium, aneurysm). At 6-8 weeks, CAA were present in 9.7% of children. At the end of follow-up (range 1.5 months-11.5 years, mean 12.8 months), 4.8% of children had demonstrable aneurysms. Aneurysms devloped in 3/10 patients who received IVIG after day 10, compared to 10/86 who received timely IVIG (p=NS). 1 patient died because of CAA complications.

Conclusions:

This is the largest series of KD patients from Slovenia. CAA were present in 4.8% of children at the end of the follow-up (mean follow-up time 12.8 months) which is comparable to the published data. Timely treatment reduces the incidence of aneurysms, although in our patients the difference was not significant.

Systematic Review Registration:

None.

ESPID19-0561
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Complement c9 deficiency: uncovering a complex family heirloom.

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Background

C9 complement component is part of the Membrane Attack Complex, and its deficiency results in a higher susceptibility to *Neisseria* infections. Although rare in people from European descent, C9 deficiency is the most common complement deficiency in Japan. However, patients with C9 may remain asymptomatic through their whole life, and recurrent infections are rare in this group.

Case Presentation Summary

A 1 year old patient of Chinese descent was referred to our Immunology Unit after a C9 deficiency was detected. The tests were performed after the patient had meningitis at 5 months (microbiological test were negative) and prolonged fever of one month with splenomegaly at 9 months. A genetic test was ordered and the mutation NM_0017.3:c.346C<T in the C9 gene was detected in heterocigosis. Both parents of the child were healthy but the paternal grandfather had meningitis in his childhood that resulted in deafness. The family was tested, both the father and younger sibling had the same mutation while the mother and the eldest were healthy. We started antibiotic prophylaxis with V penicillin and additional vaccines MenB and ACWY were administered.

Learning Points/Discussion

In our globalized world, entities that were common in one region can now be seen everywhere. C9 deficiency must be suspected in people of Asian descent with recurrent infections or meningitis. Genetic testing of the whole family must be performed when there are various family members affected and appropriate measures such as additional vaccinations and antibiotic prophylaxis should be taken.

ESPID19-1203
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Kawasaki disease with hepatobiliary involvement: rare complication

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Background

Kawasaki disease (KD) is the leading cause of acquired heart disease in paediatrics. In Argentina, the incidence is 4/100,000. We report a case of KD with hepatic alteration and a diagnosis based on the association of unusual symptomatology and late manifestation of the classic diagnostic criteria.

Case Presentation Summary

2 year-old male patient, with febrile convulsion 48hs before, admitted due to a 3-day history of fever, asthenia, distended and painful abdomen, jaundice and hand pruritus.

Admission laboratory: WBC 12500/mm3 (neutrophils 84%), platelets 272000/mm3, ESR 80mm/h, CRP 132mg/dl, AST 146U/l, ALT 377U/l, direct hyperbilirubinemia. Pyuria, chest X-ray with right lung base reinforcement. Abdominal ultrasound with cholecystitis signs. Negative blood and urine cultures. Recieved ceftriaxone 50 mg/kg/day and metronidazole 80 mg/kg/day for respiratory and abdominal infection.

He evolved by 18th day with fever, scrotum and lower limbs edema, jaundice, inflamed BCG scar and acral and genital peeling, so started treatment with gammaglobulin 2g/kg. Laboratory findings: important thrombocytosis, decreased hematocrit, leukocytosis, ascending direct hyperbilirubinemia, ALP and GGT, hypoalbuminemia, PT 41% and significant proteinuria. Abdominal ultrasound: enlarged liver, hydropic gallbladder with content, intrahepatic bile duct 4 mm. Negative serologies and PPD skin test. Good response to ursodeoxycholic acid, vitamin K and blood transfusion.

A later echocardiographic ultrasound showed ectasia and dilatation of the left coronary trunk (Z score +2.5) and all coronary arteries. Treatment started with ASA 50 mg/kg. Currently under follow-up.**Learning Points/Discussion**

In our country, less frequent clinical manifestations occur in 10-15% of cases and ar related to treatment-resistant forms of expression. In spite of that, we must know them and have it in mind in order to avoid atypical presentaton of KD to mean a delay in the diagnosis.

ESPID19-1162
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Prolonged course of a human bocavirus 1 respiratory infection in a charge patient with severe combined immunodeficiency treated with thymus transplantation

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Background

CHARGE syndrome is a rare, multiple congenital anomaly syndrome. In 90% of cases there is a dominant loss-of-function mutation/deletion of the CHD7gene. Besides the clinical signs included in the acronym, patients can have additional clinical features includingT cell lymphopenia.

More than 100 patients with profound Tcell deficiency due to congenital athymia have been treated with thymus transplantation until now with CHARGE syndrome accounting for between one quarter and one third of these. We present prolonged course of human bocavirus 1(HBoV1) infection in a CHARGE patient before and after thymus transplantation.**Case Presentation Summary**

The patient was diagnosed with CHARGE syndrome due to the characteristic dysmorphic features a few days after birth. A mutation in CHD7 gene was confirmed. Lymphocytes were normal in the neonatal period and severe Tcell deficiency only became apparent at the age of 5months when HBoV1 infection caused acute respiratory failure. Additional infections resolved on appropriate antimicrobial therapy but HBoV1 infection persisted with increasing viral load that caused prolonged tachypnea, increased respiratory effort and longterm oxygen requirement. He received thymus transplantation at 13months of age in London. HBoV1 viral load continued to increase to a maximum level of CT9,5 when he was admitted to ICU and at the age of 14months and ventilated for more than a month. 2.5months post transplantation his respiratory disease improved to such extent that he was breathing independently, with normal breathing effort. At the same time we observed a significant decrease in HBoV1viral load to CT31,2 and in virus viability with negativisation of CTmRNA. He remains profoundly T cell lymphopenic as expected at this stage after thymus transplantation.

Learning Points/Discussion

The significant reduction in HBoV1 load may be the first sign of immune reconstitution following thymic transplantation.

ESPID19-1080
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Chronic relapsing demyelinating disorder

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Background

Acute disseminated encephalomyelitis (ADEM) is a rare and mostly monophasic demyelinating disorder of the central nervous system, often in posinfectious, parainfectious, postvaccinal clinical situations. Multiphasic disseminated encephalomyelitis (MDEM), describes two episodes separated by at least 3 months. When more than two episodes are registered it is classified as chronic demyelinating disorder, once the designation recurrent ADEM was eliminated. Immunoglobulin might be considered as a treatment in MDEM.

Case Presentation Summary

An african girl, previously healthy, presented at 3 years 11 months with headache, loss of vision, ataxia and bilateral papilledema with nonatrophic optic nerves. The MRI supported the diagnosis of ADEM, she was treated with steroids and recovered completely within months. Six months later she presented bladder incontinence, global hypotonia and sleepiness, and MRI showed new demyelinating lesions in other territories. She was treated with corticosteroids and rituximab. Seven months later she had a new relapse, with deterioration on MRI. She was submitted to a third cycle of rituximab and started anticonvulsants. Six months later she had her fourth relapse, with fever, exanthema, vomiting, headache, hemiataxia and global hypotonia. EBV was identified by PCR in the CSF. Coronavirus HKU1 and Rhinovirus were also detected by RT-PCR in respiratory secretions. Symptoms were controlled with steroids and she started monthly immunoglobulin infusions. She remains stable with no evidence of new white matter lesions on MRI and no signs of recurrence for the past five months.

Learning Points/Discussion

Relapsing demyelinating disorders are rare, disabling, unpredictable and controversial. Immunoglobulin was apparently effective on preventing relapses in this patient, even though it is not formally recommended.

ESPID19-0570
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Immunity to polioviruses in immunocompromised children

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Background

Children with primary and secondary immunodeficiency are at increased risk of infectious diseases caused by vaccine preventable pathogens. Protection, especially against poliovirus, is important in immunocompromised patients because of low coverage vaccination against poliomyelitis in Ukraine. We report the data of immunity to polioviruses in children with immunodeficiency after vaccination or passive immunization with intravenous immunoglobulin.

Methods

We assessed serum anti-Polio IgG levels in 51 HIV-infected children, 55 children with primary immunodeficiency (30 of them - patients with severe hypogammaglobulinemia on replacement therapy with intravenous immunoglobulins), 12 children with rheumatic diseases on immunosuppressive therapy compared to 25 healthy controls of similar age.

Results

Among healthy controls, 56% had anti-Polio IgG level > 12 U/ml, which has been considered an immunological correlation of protection against poliomyelitis, in comparison to 52,9% HIV-infected children, 68% children with primary immunodeficiency without hypogammaglobulinemia and 91,6% children with rheumatic diseases on immunosuppressive therapy. Only 16% of patients with severe hypogammaglobulinemia had protective trough level of anti-Polio IgG despite regular replacement therapy by intravenous immunoglobulins. Among all patients, the antibody level did not differ significantly between groups and from those of healthy controls.

Conclusions

In our study we have found a lack of protective immunity against polioviruses in most children suffering from primary hypogammaglobulinemia. Such individuals may be at risk of developing poliomyelitis if exposed to wild-type or vaccine-derived type of polioviruses.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0287
Science and Educational Track

Independent E-Poster Presentations 02 - Immunology & Compromised Host - Station 03

Phagocytic activity of blood monocytes from children with bacterial inflammation of the stomach

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Background

Bacterial infection of children is one of the factors in gastric and duodenal erosions and ulcers pathogenesis.The aim of the research is studying of blood monocytes functional activity inchildren with gastric and duodenal erosions and ulcers.

Methods

Blood monocytes, extracted from blood in 44 children with gastric and duodenal erosions and ulcers. The 1st group was represented by H. pylori high dissemination. As for the 2nd group, the patients showed low bacterization.

First of all, we carried out tests of luminol- and lucigenin-dependent hemiluminescence. Further stage of the research was to identify CagA-positive strains of H. pylori in the patients.

Results

Studying chemiluminescence activity of blood lymphocytes in the patients with anti-CagA antibodies we found the true increase of the time of reaching the peak, the intensity and the area under the curve in spontaneous process in luminol-dependent response and the time of reaching intensity peak and the intensity of spontaneous chemiluminescence reaction, lucigenin being an activator. So we marked the increase of the activity of oxygen-dependent phagocytosis of blood monocytes in children with H. pylori associated with gastric and duodenal erosions and ulcers related to H. pylori increased bacterization. The growth of H. pylori dissemination results in the higher stage of stomach mucosa inflammation. Therefore active phagocytes generate more intensively the formation of active forms of oxygen, free radicals and the products of peroxide oxidation. CagA-positive strains of H. pylori, as a rule, are associated with the higher level of inflammatory activity than CagA-negative ones.

Conclusions

Result of such influence the functional activity of monocytes increases, because they are ”professional” phagocytes. The ability to perform phagocytosis is better expressed in them as compared to other leukocytes.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0952
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Bacterial gram stain distribution and it association with risks factors in late onset neonatal sepsis

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Background and Aims:

Late-onset sepsis (LOS) in newborn is a healthcare-associated infection and a major cause of neonatal mortality. Gram-negative bacteria are less common in LOS than gram-positive, but are associated with higher mortality.

Methods:

Retrospective observational study performed on a Brazilian NICU between 2011 and 2016. We included all newborns admitted due to LOS and bacteremia. For categorize the episodes by gram stain, we excluded duplicated strains and non-coincident gram in repeated episodes of LOS.

Results:

We included 107 newborns admitted in NICU, which had 148 episodes of LOS. In 2011 and 2014 gram-negative were more common and in 2012 and 2013 they were less common in incidence than gram-positive (Graphic). There were two LOS episodes in n=41 newborns and 78% (n=32) had coincident gram in the two episodes, therefore the final number of analyses was 46% (n=45) for gram-negatives and 54% (n=53) for gram positives. There were no statistically significant association between gram stains and risks factors for LOS (gestational age at birth, low weight at birth, use of central venous catheters, use of parenteral nutrition) or death in 30 days.(Table)

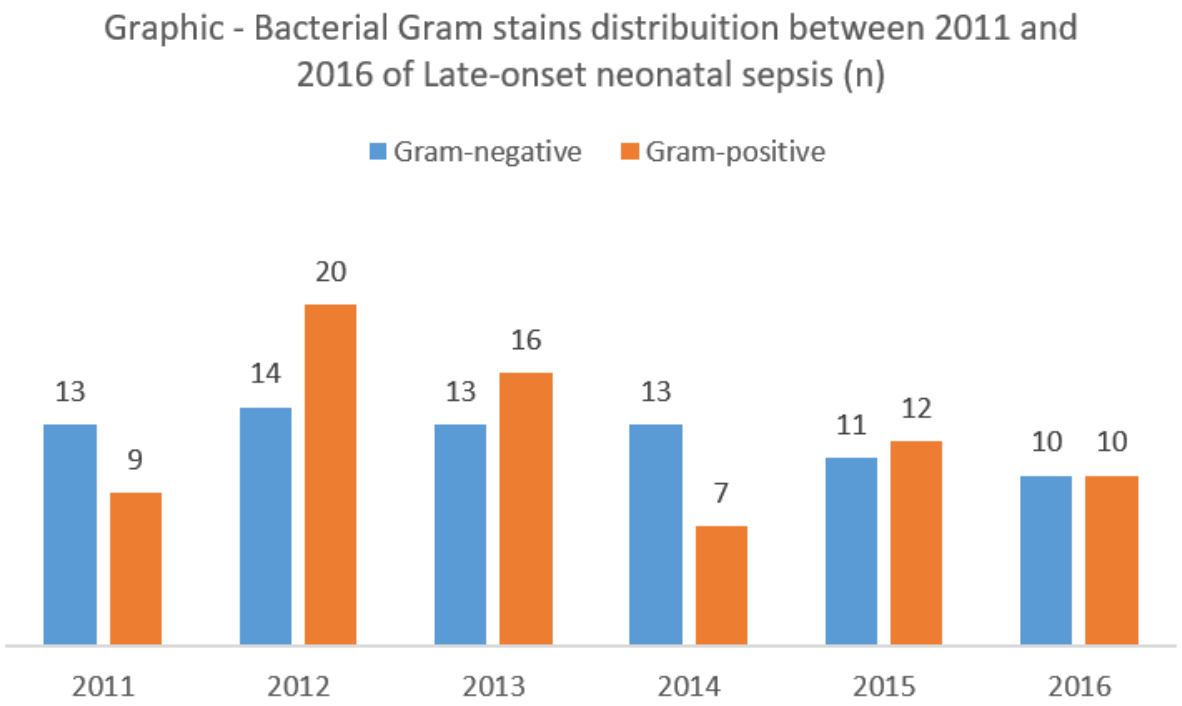

Table – The association of gram classification and risks factors for LOS or death in 30 days in late-onset neonatal sepsis

	GRAM NEGATIVE N=45	GRAM POSITIVE N=53	P
GESTATIONAL AGE AT BIRTH			0,56
>38 WEEKS	6(13,3%)	26(49%)	
30-38WEEKS	19(42,2%)	9(17%)	
<30WEEKS	20(44,4%)	18(34%)	
LOW-WEIGHT			0,49
<2500G	24(58,5%)	28(68,3%)	
<1000G	17(41,5%)	13(31,7%)	
CENTRAL VENOUS CATHETERS	36(80%)	42(79,2%)	1,00
PARENTERAL NUTRITION	32(71%)	39(73,6%)	0,96
DEATH IN 30 DAYS	15(33,3%)	12(22,6%)	0,34

Conclusions:

The bacterial distribution according gram classification over the years in this study showed stable gram-negative and oscillating gram-positive incidence. However it could not be changed with modifying knowing risks factors, because no assotiation was demonstrated. The continuous surveillance monitoring of LOS is an important for the adequate management of this patients.

Systematic Review Registration:

N/A

ESPID19-0732
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Bilateral adrenal abscess caused by resistant gram negative bacteria: report of two cases

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Background

Adrenal haemorrhage is not uncommon in neonates but the development of an adrenal abscess is extremely rare. The classical symptoms are abdominal mass, anaemia and prolonged jaundice which are associated with fever, vomiting and feeding difficulties.We present two cases of bilateral suprarenal abscess and their successful management with drainage and with intravenous antibiotics results in a successful outcome.

Case Presentation Summary

A 20 day old male baby(delivered at term by normal vaginal delivery) presented with intolerance of feeds, increasing abdominal distension and pallor* 5days. Investigations showed marked leucocytosis WBC count 18,900/cu.mm, raised CRP andultrasonogram showed bilateral suprarenal masses 4.9 × 3.5 cm and 4.7 × 2.9 cm on the right and left side respectively. US guided aspiration grew ESBL producing *Klebsiella pneumoniae*sensitive to carbapenems, aminoglycoside and colistin. **Case 2:**A 28-day-old female baby, weighing 3.2 Kg (term caesarean section delivery) was admitted with history of intermittent fever since birth. Investigations showed persistent leucocytosis 23,800/cu.mm and CRP (6.2 mg/dl).CECT showed bilateral suprarenal areas 6.8 × 4.6 cm and 2.5 × 1.8 cm on right, left side respectively.US guided aspiration was done and bacteriological cultures grew NDM1 expressing *Escherichia coli*sensitive to aminoglycoside, colistin and tigecycline.In both our patients the abscess resolved with US-guided percutaneous drainage and aggressive antibiotic therapy. First case was treated with meropenem and colistin* 14 days, second case was treated with high dose meropenem and amikacin for 14 days and followed serially at 1,3,6 months.

Learning Points/Discussion

Both our patients had a history of prolonged labour, meconium aspiration with perinatal hypoxia.Early and accurate diagnosis of the condition based on perinatal history, clinical examination, and radiographic evaluation is essential because of high rate of lethal outcome with delayed therapy and avoid unnecessary laparotomy.

ESPID19-1178
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Two cases of severe neonatal infection associated with multifocal joint infection caused by 'haemophilus quentini'

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Background

Following introduction of the *Haemophilus influenzae* serotype B vaccine, nontypable *H. influenzae* (NTHi) are the dominant cause of invasive infection caused by Haemophilus species. Biotyping of invasive NTHi in children has not associated distinct clinical syndromes with specific biotypes.

H. quentini is a proposed species forming part of the *H. influenzae* biotype IV group. It has been associated with neonatal infection and isolated from the female genito-urinary tract. We report two cases of severe neonatal infection associated with multifocal joint infection caused by '*Haemophilus quentini',* a clinical syndrome not previously described.

Case Presentation Summary

Case 1

Nine day old term infant presented with reduced leg movement; afebrile and clinically stable. However, he consequently deteriorated. An organism initially identified as *H. influenzae* was isolated from CSF following a full septic screen. Imaging confirmed bilateral subdural collections and septic arthritis five large joints. *Haemophilus* species PCR on joint fluid was positive and sequencing identified the organism as *H. quentini.*

Case 2

Eleven day old term infant presented with fever, drowsiness and diarrhoea. She required fluid resuscitation and was transferred to PICU. Imaging identified disseminated infection; subcutaneous lumbosacral collection; septic arthritis of hips, elbows and shoulders bilaterally and renal abscesses. An Gram negative cocco-bacillus was isolated from blood cultures and reported as *H. haemolyticus.* PCR, and subsequent sequencing, of joint fluid identified the organism as *H. quentini.*

Both children had extensive immunological investigations, which were normal.

Learning Points/Discussion

Standard laboratory techniques cannot distinguish *H. quentini* from NTHi or *H. haemolyticus.* These cases highlight a benefit of PCR and sequencing of invasive Haemophilus species. We suggest that increased awareness of the pathogenic potential of Haemophilus species is necessary to prevent this organism being overlooked in maternal and infant samples.

ESPID19-1031
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Pilot study: gut colonisation with resistant organisms in septic neonates treated with vancomycin

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Background

Antibiotic exposure interferes with normal gut flora in neonates and may lead to colonisation with resistant organisms, e.g. vancomycin resistant enterococci (VRE) and coagulase negative staphylococci (CoNS) with reduced vancomycin susceptibility (RVS). This pilot study aimed to define the methods for screening babies for colonisation with these organisms.

Methods

Stool/rectal swabs were screened from 10 septic neonates who were treated with vancomycin and participated in the NeoMero trial (https://clinicaltrials.gov/ct2/show/NCT01551394?term=neomero&rank=2). Mannitol salt agar (MSA) was used to assess staphylococcal colonisation (up to 10 colonies selected). MSA with the addition of vancomycin [4 micrograms/mL (MSAV4)] was adopted to screen for CoNS with RVS and VRE Brilliance agar (VREBA) was used to screen for VRE. MALDI-TOF was used for organism identification. Vancomycin MIC was determined for *Enterococcus* spp. and CoNS with RVS. BHI screen agar for heteroresistance screening was performed on CoNS with RVS.

Results

7/10 babies were colonised with 2 or more *Staphylococcus* spp.; most commonly *S. epidermidis* (Figure).

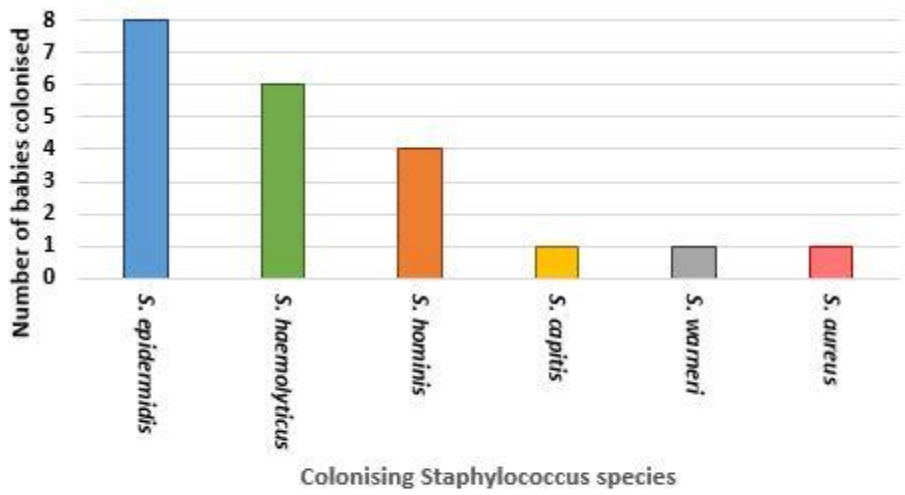

Figure - Staphylococcal species colonising the gut of septic neonates treated with vancomycin

3/10 babies demonstrated growth of CoNS on MSAV4. 1 baby was colonised with *S. hominis*, 1 with *S. haemolyticus* and 1 with *S. haemolyticus* and *S. hominis*. All *S. haemolyticus* isolates were heteroresistant by BHI screen agar, and MICs were all 4mg/L. None of the *S. hominis* isolates were heteroresistant; MICs were all 1mg/L.

4/10 babies demonstrated growth of *Enterococcus* spp. on VREBA; none of these were VRE.

Conclusions

20% of babies had gut colonisation with CoNS with RVS; this is of concern as the gut is a common source for organisms that cause invasive disease. False positive results on VREBA were common and so further optimisation of the methodology is required. A larger study will be performed to explore this further.

Acknowledgements: NeoMero Consortium.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0911
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Clinico-demographic profile of neonates with sclerema managed with dvet: experience over 4 years from tertiary care hospital in india

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Background and Aims:

Severe sepsis with sclerema has high morbidity and mortality. Various adjunctive therapies including double volume exchange transfusion (DVET) have been tried with insufficient evidence and uncertainty regarding therapeutic benefit. Clinical profile of neonates with sclerema undergoing DVET was analysed.

Methods:

From Jan'15 to Dec'18, neonates with features of sepsis admitted to neonatal unit were tracked and clinico-demographic profile of neonates with sclerema was recorded. DVET using 180 ml/kg of citrated fresh blood (<48 hours) was performed. The success of therapy was adjudged by resolution of sclerema and/or improvement of clinical features.

Results:

Over the study period, 53544 neonates were delivered and 10994 (20%) required admission with 60% (n=6577) being preterm. Overall incidence of sepsis was 23% (n=2473) with sclerema developing in 13% (n= 317). Mean birth weight and gestational age of neonates with sclerema was 1226±391 grams and 31±3 weeks respectively. Three-fifths developed sclerema within first 72 hours of life and 40% thereafter. Major morbidities observed were RDS (74%), shock (71%), IVH any stage (40%) and HsPDA (30%)(Table 1). Incidence of culture positive sepsis was 33% with two-thirds (64/105) being Multidrug resistant.

DVET was successfully performed in 80% with two-thirds requiring a single DVET (n=170) and one-thirds multiple DVETs. Sixty percent neonates undergoing DVET survived to discharge. Major causes of death were septic shock (82%) and pulmonary bleed (36%). On Multivariate analysis risk factors for higher risk of mortality despite DVET included: GA ≤ 28 weeks, requirement of PPV during birth resuscitation, HsPDA, IVH (grade 3 or more) and AKI. Feeding mother's own milk was protective.

Table: 1 Clinico-demographic profile of neonates with Sclerema

	N= 317
Male	60.3%
Small for gestation age (SGA)	38.5%
LSCS	40%
Antenatal steroid coverage (including partially covered cases)	47%
Requirement of PPV during birth	36.6%
Chorioamionitis	4.1%
Early onset sepsis	77.3%
Late onset sepsis	36%
Culture positive sepsis	33%
Respiratory distress syndrome	74%
Need for Surfactant replacement therapy	38.5%
Need for invasive ventilation	68.5%
Shock and circulatory compromise	71%
HsPDA	30.3%
IVH (any stage)	40%
IVH (Grade 3 or more)	8.8%
Pulmonary bleed	14%
NEC (any stage)	10.4%
NEC (Stage 2b and above)	4.7%
AKI	12%
DVET Received	80%
Single cycle of DVET	67.2%
Overall survival	55.2%

Table 2: Multivariate analysis of Risk factors associated with increased risk of mortality despite DVET in neonates with Sclerema

	Odds Ratio	95th Confidence interval		P value
		Lower Limit	Upper Limit	
Hemodynamically significant (Hs)PDA	1.933	1.013	3.689	0.046
IVH grade 3 or more	4.359	1.202	15.801	0.025
AKI	2.795	1.189	6.572	0.018
Need for PPV resuscitation at birth	4.142	2.188	7.842	0..0001
BW≤1000 grams	2.262	1.174	4.361	0.015
Use of Mothers own milk	0.033	0.011	0.098	0.0001

Conclusions:

Double volume exchange transfusion may serve as an effective adjunctive therapy in neonates with sclerema who are at high risk of morbidity and mortality.

Systematic Review Registration:

None

ESPID19-0412
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Breast milk may prevent adverse outcome in multidrug resistant blood stream inections in newborns

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Background

Multidrug-resistant (MDR) Blood Stream Infection (BSI) is a serious problem in neonatal intensive care units (NICU). The objective was to find the incidence of MDR BSI and its outcome and whether breast milk improves the survival.

Case Presentation Summary

Medical records of newborns admitted in the period between January and December 2013 were reviewed. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, breast milk intake, ventilator use etc. was retrieved. BSI was defined as positive culture from blood specimens. Multidrug-resistance was defined as per definitions proposed by the joint initiative of ECDC and CDC (2011). The outcomes of the patient were defined as survived, or died. Data analysis was performed using SPSS Version 20.0. Factors were evaluated using Univariate Analysis.

Results: Sixty nine out of (6.8%) out of total of 1012 blood cultures sent grew organisms. Forty three (62.3%) were MDR. Sixty percent (26) of babies with MDR BSI died. Administration of breast milk significantly reduced the mortality in MDR BSI (Fig
1).

Table 1. Univariate analysis

Variable	EBM (n=18)	No EBM (n=25)	O.R	Confidence interval		P Value
Male Sex	11	12	1.70	0.49	5.82	0.39
Birth Weight (grams)	1398 (657)	1429 (620)	1.00	0.99	1.00	0.87
Gestation (weeks)	31.50 (3.87)	32.92 (3.67)	0.90	0.76	1.06	0.22
Ventilation	6	21	10.50	2.46	44.78	0.001
Vasopressors	13	21	2.01	0.45	8.92	0.45
APGAR <7 at 1 Min	2	5	2.00	0.34	11.70	0.68
Surfactant	2	7	3.11	0.56	17.19	0.26
Death	5	21	13.65	3.09	60.30	0.000

Breast milk could be given irrespective of birth weight, gestation, asphyxia, surfactant administration.**Learning Points/Discussion**

Multidrug-resistant blood stream infection occurs at high rates in sick neonates in the NICU and carries high mortality. Breast milk may have protective effect.

ESPID19-0343
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Clostridium difficile in infants, are they only reservoirs?

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Background

Symptomatic infection by Clostridium difficile has increased its incidence in the population in recent years. Neonates and infants younger than 12 months have high colonization rates and can act as reservoirs, but rarely develop symptomatic disease.

Case Presentation Summary

Six-month-old male infant without previous hospitalization who was referred to the Emergency Department due to constipation, fever and moaning for 4 days, besides cough and rhinorrhea. Treatment with amoxicillin was completed the previous week for acute otitis media. Physical examination showed continuous moaning, distended tympanic abdomen and superficial tachypnea with subcostal retraction and hypoxemia. Hemogram and serum biochemistry was normal, RCP: 14.8 mg/dL, Procalcitonin: 1.13 ng/mL. Thoracoabdominal radiography: diffuse distension of abdominal loops with presence of distal gas. Virus PCR in nasopharyngeal sample: RSV positive. Bronchiolitis and abdominal pain of unknown etiology were the diagnosis in the admission. Due to persistence of moaning and increase of greenish stools on the second day of hospitalization, abdominal ultrasound, without pathological findings, and PCR of multiple pathogens in faeces, positive for Clostridium difficile toxin A/B, were performed. He received oral metronidazole (10mg/kg/8h) and intravenous fluid therapy, experiencing clinical improvement in the following 24h. Negative stool culture for common enteropathogens, negative blood culture were obtained. He was asymptomatic 20 days later.

Learning Points/Discussion

The interest of this case lies in the presence of a history of previous antibiotic therapy with amoxicillin, widely used in pediatrics and not usually associated with C. difficile infection, the age of the patient in whom the symptomatic disease is not usual , as well as the excellent response to antibiotic treatment, which emphasizes the importance of taking this possibility into account in the presence of abdominal distension and diarrhea in infants outside hospital.

ESPID19-0077
Science and Educational Track

Independent E-Poster Presentations 03 - Neonatal infections - Station 05

Human parechovirus type 3 infection in newborn infants with sepsis-like illness: 3 cases observed in a short period of time in a single insitution

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Background

Human parechoviruses (HPeVs) are newly recognized RNA viruses, similar to Enterovirus and usually cause mild respiratory or gastrointestinal symptoms. In newborn and young infants aged less than 3 months, HPeV type 3 (HPeV-3) can provoke sepsis-like illness and central nervous system infection, leading to neurological sequelae.
They are rarely investigated and therefore probably underestimated.

Case Presentation Summary

We present 3 cases of full-term newborn infants with HPeV-3 infection.
They were admitted from home to the pediatric department of our hospital in the second half of November – first half of December 2018. They were born in 3 different hospitals. The median age at onset of symptoms was 13 days. They all developed sepsis-like illness with fever, feeding difficulties and irritability.
The patients had normal values of CRP and procalcitonin, normal white blood cells or mild leukopenia. No CSF pleocytosis was observed. The diagnosis of HPeV infection was made by detecting HPeV with real-time PCR in CSF. These HPeV strains belonged to type 3.
One patient required hospitalization in a NICU, due to worsening of clinical conditions.
Broad spectrum antibiotics (ampicillin and netilmicin) were administered to the 3 patients for 48-72 hours, discontinued after negative blood and CSF culture.
The outcome for the 3 newborn babies was spontaneously favorable after 48 hours, with apyrexia and improved clinical conditions.

Learning Points/Discussion

The early diagnosis of HPeV infection in febrile newborn infants could reduce unnecessary treatment with antibiotics and extended hospitalization and could prevent nosocomial transmission.
Real-time RT-PCR has become an essential diagnostic technique and should be used for the early diagnosis of HPeV infection.
The management of HPeV infection is limited to supportive care and there are no effective antiviral drugs against HPeV, therefore establishing specific antiviral therapies are important goals.

ESPID19-0914
Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

Vaccination coverage against measles, hepatitis b and influenza among health care professionals in crete, greece

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Background and Aims:

Vaccination of healthcare professionals (HCPs) is strongly recommended as a major preventive tool against vaccine-preventable diseases (VPDs) but implementation remains low in many countries. Our aim was to evaluate immunization status, particularly to measles, hepatitis B and influenza, in HCPs of all levels of healthcare settings (primary to tertiary) in our area.

Methods:

A cross-sectional multicenter study that included 18 primary care centers and 3 hospitals. Data were obtained using a standardized questionnaire and vaccination records were assessed when available.

Results:

The study included 2,240 HCPs (24.2% men, median age 47, range 21-67 years). Immune against measles were 67.5% (1,510/2,236) either from reported natural illness (42.7%), confirmed complete 2-dose MMR vaccination (21.2%) or serologically proven immunity (3.6%). Vaccinated against hepatitis B were 60.9% of HCPs (1,355/2,225) and 91.1% of them (1,235/1,355) had evaluated their anti-HBsAg titres. Only 5.1% (6/116) of HepB vaccine non-responders had repeated a 3-dose schedule. Influenza vaccine uptake was 36.2% (807/2,232) for the 2017-2018 period. However, 50.6% of HCPs (1,107/2,186) never received the influenza vaccine the last five years while only 16.7% (366/2,186) of HCPs were receiving influenza vaccine annually. HCPs from primary care centers had higher influenza vaccine uptake and lower hepatitis B vaccine uptake compared to HCPs from hospitals (influenza: 49.8% vs 33.2%, hepatitis B: 43.1% vs 65.3% respectively, $p<0.0001$).

Conclusions:

Low vaccination coverage was noted for measles, hepatitis B and influenza in HCPs in all health care facilities in our area despite the strong national recommendations. Different rates are noted in primary care facilities and in tertiary hospitals. Robust occupational policies and rigorous interventions at each healthcare facility are required.

Systematic Review Registration:

N/A

ESPID19-0186
Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

Outbreak response immunization against diphtheria in east java province in indonesia 2018

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Background and Aims:

There has been a high number of diphtheria cases in East Java, one of the leading provinces in Indonesia since 2011 with population of 35 million people. The government performed a three-round outbreak response immunization (ORI) in 2018 to reduce the new cases significantly. The ORI was conducted on February, June, and November 2018. The aim was to report a surveillance study of ORI in East Java Province in 2018

Methods:

The reports were collected from 38 districts on daily, weekly, and monthly basis. Descriptive calculation and reports include the coverage on the districts, sub-districts, and community health centers in the region. Name, age, sex, and address for every vaccinee were collected. ORI covered children aged 1-19-year-old regardless of the previous immunization history. DPT, DT, and Td vaccines were used based on the age of the children. The minimal expected coverage was 90%.

Results:

For the first, second, and third round, the overall coverage was 97%, 94.19%, and 93.20%, respectively. The absolute numbers of the coverage were 10,508,354 (1), 10,234,005 (2), and 9,961,057 (3) children. Even though the target was passed, the distribution of the districts and subdistricts were not similar. One, three, and twelve districts could not reach the minimum limit on the first, second, and third round, respectively. Most of those failed districts were located on the north and eastern part of the province. The impact of these ORI was not rapidly seen since the number of diphtheria cases for the 2018 (753) was higher than the last three years (2015:319, 2016:350, and 2017:460).

Conclusions:

The coverage of three round ORI were above the minimum target but in unbalanced distribution. We need several months to analyze the impact.

Systematic Review Registration:

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ESPID19-1013
Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

Varicella-related healthcare resource use among the pediatric population in jordan

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Background and Aims:

Although varicella can be prevented with effective and well-tolerated vaccines the exact burden is not well-quantified in many settings. Numerous countries in the Middle East/Levant region are using varicella vaccines, and to facilitate evidence-based decisions about prioritizing varicella vaccination in Jordan, we examine varicella-associated health-care resource utilization (HCRU).

Methods:

A hospital-based, multicenter, retrospective chart review study of patients 0-14 years in Jordan from 2013-2018 assessed clinical complications among those with a primary varicella diagnosis, along with varicella-associated HCRU (outpatient/inpatient visits, tests/procedures, and medication use).

Results:

140 children with varicella (78 outpatients, 62 inpatients), were included, with a mean (SD) age of 4.4 (3.2) and 4.0 (3.8) years, respectively. No outpatients reported any varicella-related complications, while 51.6% of inpatients experienced at least one. The most common complications were skin and soft tissue infections (21.9% of patients with complications), pneumonia (18.8%), encephalitis (12.5%), sepsis (12.5%), and cerebellitis (9.4%). HCRU was higher for inpatients compared to outpatients, including prescription medication use (93.5% vs. 6.4%, respectively), tests/procedures (67.7% vs. 2.6%), and consultations with allied medical professionals (17.7% vs. 0.0%). Over-the-counter (OTC) medications, were used more frequently by outpatients (59.7% vs. 96.2%). The mean (SD) duration of hospitalization for inpatients was 5.6 (5.1) days. More than 55% of prescription medications administered to inpatients were antibiotics. Total (direct and indirect) costs of treatment (95% CI) were USD 66.05 (64.05,68.05) per outpatient and 648.52 (455.56, 1373.84)) per inpatient.

Conclusions:

Varicella in children is associated with considerable burden to the healthcare system in Jordan, and may be responsible for 1,000-12,000 courses of antibiotic treatment per year, and annually costs approximately 11,500,000 USD. These results support varicella vaccination to both reduce HCRU burden and limit use of antimicrobials.

Systematic Review Registration:

Not Applicable.

ESPID19-0852
Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

Case fatality rate of imd in children & adolescent/young adults' population in europe: results from a systematic literature review

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Background

Invasive meningococcal disease (IMD) is a serious bacterial infection caused by *Neisseria meningitidis*. Almost all cases are caused by one of six serogroups (A, B, C, W, X, Y) who vary temporally, geographically and with age. Although IMD is a preventable disease, it continues to be a global public health concern particularly in children & adolescent/young adults (0-24 years old) due to its epidemic potential, mortality and sequelae. We aimed to conduct a review of IMD's serogroup case fatality rate (CFR) in EU-27 countries.

Methods

A systematic review of PubMed, EMBASE and Cochrane Library databases was conducted (publication date 2000 to January 2018) to characterize the burden of IMD in Europe. Here we report the results on CFR for the population 0-24 years old according to serogroups and age.

Results

Out of 106 included papers with CFR data reported in all age groups, 53 presented data in the 0-24 years olds' population from 13 EU countries. Data reported covered the period from 1974 to 2016. The CFR range for all serogroups in 0-24 years olds was 0.0-42.7%. The CFR range for A, B, C, W & Y serogroups was respectively 2.0-14.3% (based on 2 estimates in Greece); 0.0-23.5%; 0.0-50.0%; 0.0-16.7% and 0.0-33.3%. We observed differences according to serogroups and age groups. Serogroup C had the highest CFR for <1 year, 5-14 and 15-24 years' groups.

Conclusions

IMD is a severe infectious disease with a high CFR. Serogroup C had the highest CFR in most age groups. Recent surveillance data reported an increasing number of W and Y cases with significant CFR. Vaccination policies (against A, B, C, W135, Y serogroups) are necessary to prevent this infection and reduce associated mortality.

Systematic Review Registration (Please input N/A if not registered)

CRD42018084136

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Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

A prospective genotype surveillance for pediatric enterovirus infection in jeollabuk-do province, january – december, 2018

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Background and Aims:

Human enteroviruses (HEVs) are major pathogens causing various pediatric morbidity such as nonspecific febrile illness, herpangina, hand-foot-and-mouth disease (HFMD), aseptic meningitis, encephalitis, myopericarditis, etc. Most enteroviral infections are self-limited, but fatal cases could also be reported in outbreaks of specific enterovirus types. We aimed this study to see which genotypes were prevalent in each type of HEV infections.

Methods:

From January through December, 2018, stool, pharyngeal swab, and/or cerebrospinal fluid samples from suspected enterovirus infected children were collected using “Pathogen Surveillance for Enterovirus Infection” program operated by Korea Centers for Disease Control and Prevention, and the viruses were genotyped using RT-PCR for HEV at Jeollabuk-do Institute of Health and Environment Research.

Results:

A total of 124 samples, including 37 from Chonbuk National University Hospital, were tested for HEV and 68 were found positive. Coxsackie virus A (CA) were 39 (CA10 25, CA6 6, CA4 2, CA9 1); coxsackie virus B5, 7; echovirus, 13 (E30 8, E11 2, E3 1, E13 1, E25 1); and enterovirus 71, 2; and untyped 7. Clinical diagnosis of the 2 cases of enterovirus 71 were hand-foot-and-mouth disease. While the pathogen found in most case of HFMD and herpangina was coxsackie virus (33 of 35 and, 10 of 13 respectively), that in most cases of aseptic meningitis was echovirus (11 of 17). No fatal cases were reported.

Conclusions:

Although variable genotypes of HEV were found in Jeollabuk-do Province, 2018, coxsackie virus were more prevalent in HFMD and herpangina cases and echovirus in aseptic meningitis. Genotype surveillance system could provide detailed data for analysis of HEV outbreaks and its control.

Systematic Review Registration:

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ESPID19-0569
Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

Severe pneumococcal meningitis in well-vaccinated infants in catalonia. An emergent trend? A three case report.

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Background

The incidence of invasive pneumococcal disesase (IPD) has decreased for all-age ranges sincethe introduction of conjugate anti-pneumoccocal vaccines. However, several studies reveals aproportional increase in cases owing to non-vacunal serotypes.One year after the stablishment of systematic vaccination with VNC13 in Catalonia, we couldsee the same trend in our environment, with a higher aggressiveness in some cases.We report three cases of fulminant pneumococcal meningitis admitted in our centre from11/2017 to 04/2018.

Case Presentation Summary

We present three infants with similar ages (10-14 months) and epidemiological conditions(healthy, well-vaccinated with VNC13, good environment, assistance to nursery) who wereadmitted in our Pediatric-ICU service (a third level Hospital), in the clinical context of 48h-evolution fever and drownises with low GCS. They had pancytopenia with high acute phasereactants in the blood test and pathologic CSF. All of them had a withering evolution, dyingwithin the first 48h because of cerebral edema and transtentorial herniation, in spite ofantibioteraphy and intensive care suport. Two of them had a positive blood and CSF culture forS.Pneumoniae 15B/C and the third infant had a positive PCR for *S.Pneumoniae* in themeningeal necropsy sample.

Learning Points/Discussion

Despite the high rates of vaccination coverage in our country, IPD are an active and severissue. The incidence of invasive infection due to non-vacunal serotypes are proportionalygreater than vacunal ones, specially in meningitis disease. In our patients, a severeaffection has been observed. It could be an early sign of a new behaviour on the emergentserotypes, not previously involved in IPD.We conclude that an acute epidemiological surveillance and further research is necessarywithin in the next years to develope new strategies in prevention efforts.

ESPID19-0518
Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

Molecular characterization of invasive streptococcus pneumoniae isolated in pre (2005-2009) and post (2011-2015) 10-valent pneumococcal conjugate vaccine introduction in brazil

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Background and Aims:

Brazil introduced the 10-valent pneumococcal conjugate vaccine (PCV10) in the national childhood routine immunization program in 2010. The aim of this study was to characterize genetic lineages of invasive *Streptococcus pneumoniae* (Spn) strains isolated in the pre and post-PCV10 introduction periods.

Methods:

Were selected 688 *Spn* isolates (n=350 pré-PCV10 and n=338 post-PCV10) from IPD obtained through national laboratory-based surveillance, of all ages, corresponding an approximately 10% of the strains in the serotypes: PCV10, additional PCV13 (3, 6A and 19A) and prevalent non-PCVs (6C, 8 e 12F). The isolates were serotyped by Quellung, resistance profile was determined according CLSI and the molecular characterization was performed by MLST. The sequence-type (ST) was determined at MLST website and clonal complexes (CC) by eBURST software.

Results:

Were identified 182 STs, clustered in 33 CCs and 30 singletons, with 16 international clones. Was remarkable at pre-PCV10 the vaccine serotypes (VT) clones presence (pre-PCV10 n=164/198, 82.8%; post-PCV10 n=84/163, 51.5%) and of post-PCV10 non-vaccine serotypes (NVT, pre-PCV10 n=34/198, 17.2%; post-PCV10 n=79/163, 48.5%). Pre-PCV10 VT CCs most important were CC156/14 (n=75) and 9V (n=14) associated to Spain^{9V}-3 and CC90/6B (n=11) to Spain^{6B}-2, both MDR. At post-PCV10 NVT CCs were frequently, CC180 (n=33, Netherlands^{3}-31), CC53-12574 (n=20, Netherlands^{8}-33) and CC218 (n=29, Denmark^{12F}-34), and 2 major STs were resistance related, ST320/19A (n=15, DLV-Taiwan^{19F}-14) and ST386/6C (n=10, DLV-Poland^{6B}-20).

Conclusions:

The molecular study identified the large diversity and the spread of international clones in Brazil. After long-term using the PCV10 were observed the reduction of VT clones and CCs and increase of NVT clones and CCs, highlighting the ST320/19A and ST386/6C both related to antimicrobial resistance.

Acknowledgment: To the Global Pneumococcal Sequencing Project for the WGS of part of samples used in this study.**Systematic Review Registration:**

N/A

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Science and Educational Track

Independent E-Poster Presentations 04 - Populations Studies - Station 07

10 year experience with higher-valent pneumococcal conjugate vaccines in children: from promise to proof?

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Background and Objective

With the introduction of the first pneumococcal conjugate vaccine (7-valent PCV, PCV7) in 2000, pneumococcal disease in children became one of the most important vaccine-preventable diseases. From 2009, PCV7 was gradually replaced by higher-valent PCVs (HVPCVs: PHiD-CV/PCV13 which include protein conjugates of 10/13 serotypes, respectively) to extend serotype coverage and thereby increase vaccine impact. We evaluated whether 10 years of HVPCV use had the intended impact on pneumococcal disease burden in vaccinated populations worldwide, and whether this impact was comparable for both HVPCVs.

Methods

We analysed publicly available datasets (from publications and national surveillance networks) available before PHiD-CV/PCV13 until ≥2016, reporting: invasive pneumococcal disease (IPD) incidences, pneumonia rates, and pneumococcal disease mortality in children aged <5 years, as well as vaccine coverage. We compared data (as published or estimated from graphs) between the period pre-HVPCV introduction and the period post-HVPCV introduction to assess HVPCV impact.

Learning Points Discussion

− Datasets from 8 countries suggest that since HVPCV introduction, an average reduction of 45% in IPD incidence in children has occurred.

- In Sweden where the impact of both HVPCVs can be assessed in a similar setting, a comparable impact on IPD was observed for both HVPCVs.

− Based on meta-analysis and modelling publications, the reduction in pneumococcal pneumonia observed after PCV7 introduction has continued after HVPCVs introduction.

− Pneumococcal disease mortality in children decreased by approximately 35% from the 450,000 deaths estimated in 2009.

− HVPCV coverage has increased globally over the past decade and reached ≥90% in 50% of countries with data available. Efforts to increase vaccine coverage may further enhance HVPCV impact on pneumococcal disease.

Funding: GlaxoSmithKline Biologicals SA

ESPID19-0110
Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Determinants of health seeking behaviour of mothers in treatment of upper respiratory tract infection in children in a satellite community in akure, ondo state, nigeria

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Background and Aims:

Signs and symptoms of Upper Respiratory Tract infections (URTI), though common among children, may be precursors for serious ailment such as Pneumonia. Parental response to signs and symptoms of Upper Respiratory Tract Infection (URTI) is mixed while reasons influencing actions are steeped in cultural/environmental influences. Modifiable barriers in seeking treatment for under-5 URTI in the study population has not been determined.

Aim is to determine the Health-seeking behaviour of mothers in the treatment of childhood Upper Respiratory Tract Infections and to identify predictors of proper health seeking behaviour.

Methods:

A cross-sectional study involving administration of semi-structured questionnaire on Knowledge of signs and symptoms, perception about causes, health-care seeking practice, identification of modifiable barriers in seeking treatment for childhood URTI and, assessment of service characteristics as a cue to action for health care seeking behaviour was conducted. 200 mothers at the Basic Health Centre Orita Obele, Akure, Ondo State were involved. SPSS (version 23.0) was used to analyse the data collected.

Results:

Majority of mothers used home remedies and self-medication for their children for treatment of cough (80%) and catarrh (82%) while almost all (95%) would visit health facility from the outset for children with earaches/ ear discharges.

Children whose ailment are considered as severe or persisting beyond 24 hours were more likely to see a physician than children whose ailment was not considered severe.

No demographic variables of the mothers were statistically significant between those who would seek immediate medical attention for the three symptoms of URTI and those who would not

Conclusions:

Perceived severity of ailment encourages visits to health facilities while financial limitation and anticipated poor treatment by health workers were the modifiable characteristics which discouraged some parents from visiting health facility

Systematic Review Registration:

none

ESPID19-1125
Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Coronavirus in a pediatric population

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Background and Aims:

Human coronaviruses (HCoV) are a group of virus identified in respiratory infections, but also in enteritis and colitis in younger children. The HCoVNL63 and HKU1 serotypes are emergent virus but poorly characterized in the pediatric age.

Methods:

Descriptive study of coronavirus infection in children hospitalized between 2015 and 2018. HCoVRNA was detected by RT-PCR of respiratory secretions. Demographic, clinical and laboratory parameters were studied.

Results:

Coronavirus was identified in 147 (4%) of 3509 samples: HCoV-OC43 (65), HCoV-NL63 (33), HCoV-HKU1 (26), HCoV-229E (20), and non identified serotype (3). The highest number of cases occurred in 2016/2017 (63,9%), between December and April (78%) with peak in March (20%). Median age was 1 year old. 69/147 (46,9%) children had underlying chronic disease: neurological (21), atopic (22), respiratory (10), congenital heart (10), hematologic (10) and others (30). The diagnosis were upper respiratory infection (54), bronchiolitis (44), viral pneumonia (24), meningoencephalitis (8), gastroenteritis (11) and febril convulsion (5). 26,5% had bacterial secondary infection: pneumonia (23) and acute otitis media (16) and 39% others complication: hypoxemia (44) and acute respiratory insufficiency (14). 10,2% were admitted to the ICU and 10/15 were chronical patients. Co-infection occurred in 80,9% cases: rhinovirus (41), adenovirus (34), RSV (30), bocavirus (25), parechovirus (21), metapneumovirus (12), influenza A/B (10), parainfluenza (10) and enterovirus (2). The median of hospitalization was 7 days. HCoV-NL63 and HCoV-HKU1 infections occurred in underlying chronic disease (21,7%) and were associated with complications (43%).

Conclusions:

HCoVs were infrequently detected in the studied population but may have significant complications associated at younger ages and chronic disease. Emerging new viruses have been associated with more complications mainly in chronic disease. The role of coinfections is not yet well established.

Systematic Review Registration:

N/A

ESPID19-1101
Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Influenza virus in a level iii pediatric center: 2017-2018

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Background and Aims:

Influenza, a seasonal infection generally considered benign, can occur with complications.

Methods:

Retrospective study from September 2017 to June 2018 10 months). Social, demographic, epidemiological and clinical data were evaluated. Influenza virus was detected by polymerase chain reaction in respiratory secretions.

Results:

There were 68 cases, with a median age of 4.5 years (51% <2 years). The peak incidence occurred in January and February (75%). There was an initial circulation of the H1N1(n=34) and H3N2 (n=10), followed by Influenza B (n=25), considering that the strains that circulated were not covered by the vaccine. 40/68 (59%) patients had a known chronic disease: neurological (8), haematological (6), asthma/recurrent wheezing (6), and/or another risk factor (20). Only 4/68 (5.9%) were vaccinated with the trivalent vaccine (H1N1, H3N2 and B Vitoria strain). Respiratory symptoms were the most common (70%) presentation symptoms. Complications occurred in 26/68 (38%) patients: bacterial co-infection (21), pneumonia (12), otitis (6), bacteraemia (1) and Toxic Shock Syndrome (2). Other complications included hypoxemia (12), pleural effusion (3), atelectasis (2) and pneumothorax (1). A sepsis death was recorded, in a liver transplanted patient. Influenza nosocomial infection occurred in 24%. The median length of hospital stay was 7.6 days, corresponding to direct daily costs of 4134€ per patient.

Conclusions:

Influenza virus is a serious illness at early ages and in patients with chronic diseases, with high costs. As verified in previous studies, the vaccination of risk groups is still insufficient .Quadrivalent vaccine may be an asset in the future.

Systematic Review Registration:

N/A

ESPID19-0902
Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Antibiotics in uncomplicated peadiatric infections in the emergency department: what do parents think?

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Background and Aims:

Most paediatric consultations in the emergency department (ED) are because of infectious disease episodes. The misuse of antibiotics in self-limiting infections of viral origin is a major contributor to antibiotic resistance. Antibiotics have no efficacy in the treatment of viral infections, but are nevertheless often prescribed by paediatricians for their treatment. We hypothesize that parental perceptions and demands might also contribute to the consideration of paediatricians to prescribe antibiotics. Therefore it is important to explore the perceptions of caregivers towards this practice to develop further educational interventions.

Methods:

We observed discharge conversations of children with a suspected infection who visited the ED of a general paediatric hospital. After 7-10 days a semi-structured interview with parents was conducted. Thematic analysis was performed on qualitative data by two researchers independently.

Results:

We observed 70 discharge conversations and interviewed 55 parents after 7-10 days. Most parents were not in favour of antibiotic prescription (65%). Reasons not to want antibiotic prescription were previous negative experiences, side effects, or not wanting to use too much medication in general. Also, 1 in 5 parents wanted the child to fight the infection naturally. In general, parents trust the paediatricians' decision and judgement concerning the indication for antibiotic prescription. Parents do not only want information about antibiotic treatment, but also the diagnosis, pathogen (viral/bacterial), the expected course and safety netting.

Conclusions:

In the Netherlands parental perceptions about antibiotic prescriptions are to a great extent in line with those of the paediatrician. Parents have trust in the paediatricians' decision and will follow their advice, as long as complete information about the (mis)use of antibiotics in self-limiting viral infections is provided.

Systematic Review Registration:

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ESPID19-0366
Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Acute bacterial otitis media and rhinosinusitis in children: some aspects of mucosal immunology, microbiology, antimicrobial susceptibility and use of antimicrobials

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Background and Aims:

Bacterial upper airway infections are the most common reason for ambulatory antibiotic use, which might be inappropriate. Respiratory tract mucosal immunity status may influence the pattern of these infections. Thus, the survey objectives were to investigate microbiology of pediatric acute bacterial otitis media (ABOM) and rhinosinusitis (ABRS) in association with innate mucosal immune response, and actual patterns of antibiotic use.

Methods:

We enrolled 214 children (6.0 (3.7; 12.0) years) with ongoing ABOM or ABRS: 86 children with ≥ 4 episodes of ABOM/ABRS per year (group I) and 128 children with episodic ABOM/ABRS (group II). Preceding patterns of antimicrobial use, nasopharyngeal/middle ear exudates cultures and antibiotic susceptibility of agents were studied, as well as dynamics of lysozyme (Lys), human cathelicidin (hCap-18/LL-37) and lactoferrin (La) concentrations in oropharyngeal secretions during the disease episode.

Results:

Self-prescription of antimicrobials was habitual in 100.0 % of families in group I vs. 25.8 % in group II: 2.0 (0.0; 2.3) vs. 0.0 (0.0; 0.1) times per year, resp. ($p < .001$); Internet forums were the main source of information for parents. Microbiology failure rate was 34.9 % in group I vs. 19.7 % in group II ($p = .008$). In group I twice higher rate of resident bacteria isolates (e.g., St. aureus) in the absence of the typical pathogens was obtained ($p = .006$). S. pneumoniae and St. aureus strains of group I demonstrated lower ampicillin susceptibility. St. aureus and H. parainfluenzae residency were both linked to modified respiratory innate mucosal immune response.

Conclusions:

Recurrent ABOM/ABRS are associated with relatively low rate of detection of typical pathogens, and antimicrobial misuse, and altered respiratory mucosal immunity. Reduced ampicillin susceptibility of pathogens and resident bacteria in these patients is a matter of concern.

Systematic Review Registration:

N/A

ESPID19-0296
Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Epidemiology of respiratory infection in paediatric: 3 years retrospective study in malaysia

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Background

Epidemiology of acute respiratory infection (ARI) helps formulate prevention policies. However, literature on related information from tropical countries is limited. The objective of this study is to study the epidemiology of acute respiratory infections in Malaysia.

Methods

4205 positive nasopharyngeal swab specimens from paediatric patients (age <18) with respiratory tract infections were collected from 2015-2017. 19 respiratory viruses and 3 bacterial were identified qualitatively by PCR method using Luminex NxTAG RPP reagent kit.

Results

Enterovirus/Rhinovirus (24.4%) were the most common pathogens detected in ARI samples, followed by Influenza (17.1%), RSV (16.8%), adenovirus (10.6%), parainfluenza virus (7.8%), Bocavirus (7%), human Metapneumovirus (hMPV, 6%) and Coronavirus (3%) in the descending order. 79% of the ARIs were caused by single infection, 18% and 3% co-infection with 2 and 3 pathogens, respectively. Among these respiratory pathogens, RSV showed the most pronounced seasonal variation with peak activity from June-October. Others like influenza infection happens throughout the year. RSV and Enterovirus/Rhinovirus were the most common viruses causing ARI in toddlers below 4 years, whereas influenza affected mostly pre-school children below 6 years old, with an admission rate of 43%. Bacterial ARI caused by Mycoplasma pneumoniae and Chlamydophila pneumoniae were much lower compared to viral pathogens, at 0.5% and 0.02% respectively.

Conclusions

Influenza is one of the main causes for ARI in pre-school children after Enterovirus/Rhinovirus. With this new data, public health authorities should look at introducing influenza vaccination to pre-school children below 6 years to reduce child morbidity as well as the economic burden to family and society. Parents should also consider vaccinating their children before travelling to tropical countries.

Systematic Review Registration (Please input N/A if not registered)

N/A

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Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Retropharyngeal and parapharyngeal abscess in children: case series

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Background

Suppurative infections of the neck (peritonsillar, retropharyngeal and parapharyngeal abscesses) are rare in children but they are potentially very serious. In approximately one-half of cases there is an association with antecedent upper respiratory tract infection, and one-fourth of cases is secondary to pharyngeal trauma. These infections are usually polymicrobial, with predomination of group A streptococcus (GAS), *Staphylococcus aureus*, and respiratory anaerobes.

Case Presentation Summary

A total of 18 cases of suppurative neck infections in patients <18 years of age were treated in University Hospital for Infectious Diseases in Zagreb in the past 10 years (2000-2018). There were 8 cases of retropharyngeal abscess, 4 cases of retro- and parapharyngeal abscess, and 6 cases of parapharyngeal abscess. In our study 50% of cases were caused by GAS, 22% by other common pathogens (1 *S. aureus*, 1 *S. mitis*, 2 mixed infection) and 28% remained etiologically unproven. Most common symptoms upon presentation were fever (95%), neck stiffness (67%), and difficulty swallowing (56%) with record of antecedent respiratory illness in 95%. In 83% of patients CT/MRI were performed. 17 patients were treated with combination of beta-lactam antibiotic and clindamycin, and surgical treatment was performed in 83% (15 patients). All patients fully recovered, without sequelae. We noticed a raise in cases in the last three years, with 14 patients (78%) treated in this period (2016-2018)

Learning Points/Discussion

Although suppurative neck infections are rare in children, they must be considered in febrile child with neck stiffness and difficulty swallowing. CT or MRI of the neck should be performed in order to confirm diagnosis. We noticed a considerable rise in number of cases in the last three years, but the reasons for this remain unclear, and requires further investigation.

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Science and Educational Track

Independent E-Poster Presentations 05 - Upper Respiratory Infections & Influenza - Station 09

Childhood otitis media: relationship with daycare attendance, harsh discipline, and maternal depression

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Background and Aims:

Stressful life has been linked to developmental problems and poor health in children. However, it is unclear whether mental stress in children is also related to otitis media (OM). As part of a long-term study on surveying the characteristics of childcare and development, we analyzed the relationship between OM and sources of mental stress in children, such as maternal depressive mood and harsh discipline.

Methods:

We analyzed the data of 1998 children from the 2013–2014 "Kids in Taiwan: National Longitudinal Study of Child Development & Care Project" at the age of 3 years. Using bivariate and multivariate logistic regression models, we tested several risk factors as potential independent predictors of two outcomes: parent-reported child health and rate of OM development.

Results:

The proportion of children who had ever developed OM in the first 3 years of their life was 12.5%. Daycare attendance (odds ratio [OR]: 1.437; 95% confidence interval [CI]: 1.037–1.989), maternal depressive mood (OR: 1.940; 95% CI: 1.329–2.832), and harsh discipline (OR: 1.094; 95% CI: 1.027–1.165) were correlated with the parent-reported rate of OM.

Conclusions:

The rate of OM in children was associated with measures of childhood mental stress, including daycare attendance, maternal depressive mood, and harsh discipline. These findings suggest that providing psychosocial support to both parents and children might be a novel strategy for preventing OM.

Systematic Review Registration:

N/A

ESPID19-1157
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Haemophilus influenzae fulminant sepsis in a healthy baby: should we investigate for an underlying illness?

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Background

After the universal introduction of *Haemophilus influenzae type b* (Hib) vaccines, there has been a dramatic reduction in the number of Hib invasive diseases cases. However, non-b serotypes have increased and were responsible for sixty percent of invasive infections caused by *Haemophilus influenzae* (Hi) species.

Infection with Hi may lead to asymptomatic carriage or clinical disease, including pneumonia, bacteremia, sepsis and meningitis.

Case Presentation Summary

A three-month-old boy was admitted to hospital because of low grade fever (38.2ºC), mild irritability and vomits. He had been two hours earlier vaccinated against rotavirus. He was a healthy boy well immunized at two months, apart from pathological newborn screening and history of hearing impairment secondary to menigitis in his paternal grandfather.

Initial laboratory data showed no increase in white blood cells or CRP. Ten hours after admission, Gram negative rods were isolated in the blood culture and cefotaxime was started. Eight hours later, a focal seizure was observed and treated with good response. Cerebral CT was normal, but laboratory data showed WBC 4,440/µL, CRP 114 mg/L, metabolic acidosis and coagulopathy. Cerebrospinal fluid was not performed in view of the baby´s rapidly deteriorating condition with an apnea attack requiring mechanical ventilation, supportive measures such as inotropic drugs, sedation and intensive-care-unit transfer.

Owing to intracranial hypertension signs and seizures despite treatment, a cerebral-CT was performed showing hydrocephalus and empyema.

Learning Points/Discussion

Severe outcomes even with appropriate antimicrobial therapy and supportive care have been reported in infants, mostly six months of age or younger, and may also be caused by age-dependent limitations in T-

cell responses, incomplete schedules immunization against Hib or underlying illness.
We should be aware that children with invasive Hi infections presented with a mild and nonspecific illness may progress rapidly.

ESPID19-0800
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Invasive trichosporonosis due to trichosporon asteroides masquerading as a soft tissue sarcoma in an infant

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Background

Trichosporon spp, an ubiquitous yeast, causes superficial dermatologic infections in normal hosts and rare cases of disseminated disease among immunocompromised patients. Neonatal cases are exceptionally rare. Invasive trichosporonosis is a life threatening opportunistic fungal infection in an immunocompromised host and rarely causes invasive infection in the healthy individual. Empiric amphotericin B is not recommended as it may cause recurrence or partial response.

Case Presentation Summary

A four-month-old baby presented to Pediatric surgery OPD with chief complaints of gradually progressive swelling over right cheek since two weeks which started after minor trauma. On examination the swelling was 7cm x 8 cm, mobile, non-tender, erythematous, slightly indurated. Laboratory blood investigations were normal. Incisional biopsy specimen was sent to mycology and histopathology laboratories. Histopathology showed inflammatory cells with well-formed granulomas and fungal elements suggestive of fungal etiology. Mycology investigation: KOH wet mount showed no fungal elements. However, dry, rough, cream-coloured colonies grew on SDA after 3 weeks of incubation. Gram stain from colonies showed budding yeast cells with pseudohyphae and arthroconidia. Based on urease production, sugar assimilation, growth at 42°C, the isolate was identified to be *Trichosporon asteroides.* In-vitro susceptibility of the isolate was determined by E-test method for amphotericin B and voriconazole. The isolate was found to be sensitive only to voriconazole (MIC 0.23 µg/mL). Baby was initiated on voriconazole with good clinical response for 6 months till cured with no recurrences on 2 year follow up.

Learning Points/Discussion

Our case highlights the importance of high clinical suspicion and intensive mycological investigations in a case of indurated soft tissue swelling in an otherwise healthy host. The mycology laboratory plays an indispensable role in identification and susceptibility of rare, invasive, yeast infections for timely management and better outcomes.

ESPID19-0155
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Pyomyositis and paravertebral abscess by s.Pyogenes

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Background

Pyomyositis is a purulent infection of skeletal muscle that arises from hematogenous spread, usually with abscess formation. The main pathogen is S.aureus and is not as frequent as osteomyelitis or septic arthritis

Case Presentation Summary

4 year-old-boy presented with 3 days of fever up to 41ºC, back and hip pain. The first diagnosis was spondylodiscitis and was admitted with intravenous cefazolin. The US and X-ray did not show any suggesting findings. The hemoculture was positive for S.pyogenes (twice), so cefazolin was changed to penicillin G plus clindamycin intravenous. At that point, the MRI showed myositis on the psoas and paravertebral muscles.

During the admission, presented cholestasis, treated with ursodesoxicolic acid and reactive arthritis in both knees.

The patient developed an abscess collection 1*1.5*4 cm with elevated acute phase reactants and was drained guided by US with exit of purulent material but negative cultures.

Finally was treated with 2 weeks of intravenous penicillin and 2 weeks of oral amoxicillin**Learning Points/Discussion**

Pyomyositis was a typical infection on the tropics, but the frequency is increasing in temperate climates as our country. Our patient had no risk factor as immunocompromised or other comorbidities.

Local complications as abscess formation and systemic complications such as cholestasis and reactive arthritis were described in our patient.

ESPID19-1142
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Fungal endocarditis in a child with complex cardiac background: a dilemma for the clinician

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Background

Fungal endocarditis is a rare and fatal condition. The diagnosis, particularly of prosthetic valve fungal endocarditis, can be extremely challenging. The optimum antifungal treatment remains debatable and treatment can be difficult due to biofilm formation. We present a case of Candida parapsilosis fungal endocarditis as an exemplar to highlight some of the challenges experienced with the management of this condition.

Case Presentation Summary

A 14-year-old boy presented with fever and discomfort in his chest. He had a background of valvar and supravalvar aortic stenosis, requiring multiple previous interventions. In situ were a prosthetic RV-PA conduit, and a prosthetic aortic root replacement with a mechanical aortic valve. Clinical examination did not identify any peripheral stigmata of endocarditis. Transthoracic echocardiograms and cardiac CT showed no vegetations but repeat blood cultures (BCs) drawn over a 6-day period grew Candida parapsilosis. He was started on IV micafungin (2mg/kg/day) for presumed fungal endocarditis. IV ambisome (1mg/kg/day) was added and increased to 3mg/kg/day due to persistently positive BCs. Blood cultures remained positive for 21 days post commencement of antifungal therapy. Further investigations showed no evidence of extra cardiac complications. Intracardiac prostheses were not removed due to extremely high surgical risk.He completed a 3-month course of IV antifungals - his ambisome was switched to oral fluconazole and IV micafungin was discontinued. As sterilisation of his prosthetic material cannot be certain, he continues on lifelong fluconazole treatment, with no evidence of clinical relapse.

Learning Points/Discussion

This case demonstrates the challenges with diagnosis and treatment of fungal endocarditis. In particular, while current guidelines recommend early surgical intervention, this may not be suitable for all patients, which is an added complexity. Current guidelines will be reviewed, and research gaps discussed.

ESPID19-1006
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Incidence and outcome of osteo-articular infection of shoulder in children- review over a period of 6 years.

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Background and Aims:

Background - Osteoarticular infection of shoulder is uncommon among paediatric patients in the developed world and is often associated with missed diagnosis or delayed presentation. The review aims to find the epidemiology and long term outcome of these patients.

Methods:

Method- Data was collected retrospectively for patients presenting with shoulder joint infections between 2010-2016 at Leeds Trust. A total of 19 out of 192 admissions for septic joint (9.89%) were found eligible. Outcomes of operative and non-operative management were noted.

Results:

Results- Among 19 patients, 52.6% were less than 1 year of age, predominantly females. Mean time for clinical presentation was 10.68 days, three patients had an initial diagnosis of Erb's palsy. All patients received antibiotics as per trust guidelines and cultures. Mean duration of antibiotic therapy was 6 weeks. Nearly 80% patients had operative intervention. Half of these patients had positive cultures, Streptococci and Staphylococcus aureus being the predominant pathogens. One of these patients grew N.meningitidis from the aspirate. Eighteen (94.7%) patients had evidence of proximal humerus osteomyelitis, of those, two had multi joint involvement. Over a mean follow up period of 21.3 months, about 90% patients had achieved subjective full range of movement(ROM).

Conclusions:

Conclusion- From our review, we concluded that osteo-articular shoulder infection is a disease of infancy and often has delayed presentation.Our cohort had a female sex and left side preponderance The condition has a strong association with proximal humerus osteomyelitis, requiring long term antibiotic treatment. Multi joint involvement is a poor prognostic factor for ROM. We suggest having a high index of suspicion in infants with restricted arm movements. Operative intervention for cases with radiological evidence of joint collection offers good outcomes and targeted antimicrobial therapy.

Systematic Review Registration:

N/A

ESPID19-0975
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Risk factors for in-hospital mortality of pediatric sepsis

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Background and Aims:

Severe conditions like septicemia, septic shock, and multiple organ failure are experienced frequently in pediatric intensive care units (PICU). Despite effective treatment approaches, sepsis can lead to mortality and long term disability. The aim of this study was to characterize the clinical presentation, pathogens, and factors affecting mortality in children admitted to PICU at an academic tertiary care hospital in Istanbul, Turkey.

Methods:

Medical records of patients aged 29 days to 18 years admitted to PICU at Bezmialem Vakif University Hospital from March 2012 to April 2018 were reviewed. Sepsis and septic shock were defined according to the 2005 pediatric consensus criteria. The primary outcome measure was mortality. Independent predictors such as age, underlying disease, etiology, and treatment were identified by multivariate regression analysis

Results:

Among 201 patients with sepsis 156 had septic shock. Median age was 4 years and median length of stay was 16 days. 45 patients died (22.5%). The mortality rates of septicemia and septic shock were 13% and 25%. The most common site of origin was respiratory system. 107 patients (53%) had underlying comorbidities. Microbiological growth was detected in blood culture in 74 (36.8%) patients. Patients who received mechanical ventilation, blood products, dialysis, and plasmapheresis experienced higher PICU mortality.

Conclusions:

Sepsis and septic shock are both very fatal diseases in the world. Particularly, children are affected more severely. In this study, high mortality rate of 22.5% may relate to the large number of hospital-acquired infections because of high-risk patients and prolonged duration of hospitalization. Nevertheless blood cultures were positive in the first 48 hours in 30 patients (community acquired sepsis) which is also significant. More studies are necessary to monitor long term effects of septicemia in surviving patients.

Systematic Review Registration:

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ESPID19-0439
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

Septic arthritis of the pubic symphysis

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Background

Pubic-symphysis septic arthritis is an infrequent pathology that requires a high index of suspicion for its diagnosis. The real incidence is unknown, with only isolated reports in the literature.

Case Presentation Summary

15-year-old boy referred to the emergency department for fever (39.6ºC) and bilateral inguinal pain that does not give up with metamizol and incapacitates walking. He did not have other symptoms, did not travel, did not ingest unpasteurized milk.

The examination revealed pain on palpation and active mobilization of the hip and inability to walk around due to pain.

A blood test was taken: 9330 leucocites with 88% neutrophils. PCR 22.5 mg / dl. An ultrasound and radiography of the hips was performed, with normal results. Given these findings empirical antibiotic therapy with cloxacillin IV was started.

After 24 hours, blood culture was positive for S.aureus. New analytical was obtained with an increase in CRP up to 33.6 mg / dl. Abdominal ultrasound, Chest x-ray, CT scan of the pelvis and abdomen were normal. Due to persistence fever and clinical worsening, antibiotic therapy was changed to cefotaxime and vancomycin. On the 4th day of admission, fever and increase of inguinal pain appear. Pelvic MRI scan is requested, showing arthritis in symphysis of the pubis without collections or signs of osteomyelitis. Treatment with vancomycin and rifampicin was optimized. On the 6th day, when new growth of sensitive S.aureus was obtained in another blood culture, antibiotics werechanged to cloxacillin and rifampicin. The pacient improved. 10th day cloxacilin was change completing six weeks with oral cefadroxilo with good evolution in control NMR.

Learning Points/Discussion

Pubic-symphysis septic arthritis is a rare entity described in young athletes that we should suspect in the presence of compatible clinical symptoms.

ESPID19-0300
Science and Educational Track

Independent E-Poster Presentations 06 - Systemic and Multi-organ Infections - Station 11

The epidemiology of pediatric acute septic arthritis and osteomyelitis at a tertiary hospital in japan

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Background and Aims:

We evaluated the etiology and clinical features of acute septic arthritis (SA) and osteomyelitis (OM).

Methods:

Medical records from patients < 15 years with SA or OM admitted to our hospital between 2000 and 2018 were retrospectively reviewed.

Results:

A total of 26 children were evaluated. Seventeen cases were SA (mean age: 2.2 years) and nine cases were OM (mean age: 7.4 years).
A microorganism was isolated in 10 SA patients (59%), and two OM patients (22%). In SA, *Staphylococcus aureus* was the most causative (60%; 10% were *methicillin-resistant*), followed by *Streptococcus pyogenes*, *coagulase-negative staphylococci* and *Haemophilus influenzae*. In OM, *Staphylococcus aureus* was only isolated.
The joints infected by SA were knee 48%, hip 18%, elbow or ankle 12%, and wrist or shoulder 5%. The bones infected by OM were tibia or femur 33%, and scapula, ilium, ischium or calcaneus 11%.
Compared with OM patients, SA patients were shorter durations of symptom on presentation (4 vs. 6 days), higher rates of fever on admission (82 vs. 44%), and shorter hospital stays (27 vs. 35 days).
The mean duration of total antibiotics for SA was 39 days (intravenously 30 days, orally 9 days) and for OM was 43 days (intravenously 30 days, orally 13 days).
Only one SA patient had a sequela of leg length discrepancy.

Conclusions:

The SA patients were more predominant and younger than the OM patients.
More than half of the OM patients did not have fever on the admission, which might be related to late admission.
S. aureus including MRSA was the most causative, thus the initial antibiotics should be selected considering MRSA infection.
The total durations of antibiotics and intravenous to oral antibiotic switch therapy need to be more investigated further.

Systematic Review Registration:

N/A

ESPID19-0880
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

The association between pneumococcal detection by pcr and radiographic or laboratory tests in community acquired pneumonia

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Background and Aims:

The polymerase chain reaction (PCR) methods can increase the identification of the etiologic diagnosis of community-acquired pneumonia (CAP), but it is not yet largely used in medical routine in Brazil. Other laboratory tests and risk factors are still used to provide an empirical diagnosis and antimicrobial use, such as white blood cells count, acute phase reactants or chest x-rays images.

Methods:

Retrospective observational study with children aged 1 month to 14 years between 2012 to 2018. All patients were admitted due to CAP and tested by lytA targeted PCR for Streptococcus pneumoniae detection. Chest X-rays were analyzed by radiologists, blindly.

Results:

We have included 110 patients with CAP, median age was three years (IQR=1-6 years), median length of stay was 12 days (IQR=7-21 days). Laboratory findings (leukocytosis, thrombocytosis, acute-phase markers) or the presence of pleural effusion had no statistically significant association with the pneumococcal identification by PCR. Image findings by chest x-rays that defines pneumonia were associated with pneumococcal detection by PCR. (table)

Table - Association between pneumoccocal detection by lytA targeted PCR, laboratory or chest x-rays findings and presence of pleural effusion in children admitted with community acquired pneumonia

	PNEUMOCOCCAL PCR DETECTED N=24	PNEUMOCOCCAL PCR NOT DETECTED N=86	P
CHEST RADIOGRAPH			0,01
NO ALTERATIONS	0	7(11,3%)	
OTHER INFILTRATE	0	14(22,6%)	
PNEUMONIA	20(100%)	41(66,1%)	
LEUCOCYTOSIS	9(47,4%)	26(37,7%)	0,61
THROMBOCYTOSIS	1(5,9%)	6(11,8%)	0,67
HIGH ACUTE PHASE REACTANTS*	12(100%)	45(88,2%)	0,58
PLEURAL EFFUSION	21(87,5%)	28(32,6%)	0,07

*Acute phase reactants: Erythrocyte Sedimentation Rate or C-Reactive Protein

Conclusions:

This study demonstrated the evidence of an association between pneumonia abnormalities on chest X-ray and pneumococcal detection by PCR, showing the importance of this image evaluation despite the results about leucocytes or acute-phase proteins, to a correct management of the CAP patients.

Systematic Review Registration:

N/A

ESPID19-0762
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

Community-acquired pneumonia in infants after introduction of the 10-valent pneumococcal conjugate vaccine: is there an impact due to the serotype replacement?

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Background and Aims:

The 10-valent pneumococcal conjugate vaccine (PCV10) was introduced in Brazil for routine immunization of infants at 2010 and has changed pneumonia hospitalization and mortality rate. However, the use of PCV10 results in serotype replacement and an increase in non-PCV10 serotypes diseases, with unknown clinical impact nowadays.

Methods:

Retrospective study analyzing two groups of patients diagnosed with community acquired pneumonia (CAP): G1 - Early-vaccine group (admitted in 2012 to 2014) and G2 - Late-vaccine group (admitted in 2015-2018) about clinical outcomes and pneumococcal detection by lytA targeted polymerase chain reaction.

Results:

Patients aged 1 month to 14 years were included in this study, n=45 (40 %) into G1 and n=68 (60%) into G2. Patients were analyzed in respect to age, sex, comorbidity, intensive care, complications and molecular agent detection. There was no statistically significant difference between the groups (table).

Table - Early and Late vaccine groups in children admitted due to Community-Acquired Pneumonia

	G1: EARLY-VACCINE N(%)	G2: LATE-VACCINE N(%)	P
AGE			0,61
≤ 2 YEAR	14 (12,5%)	23(20,5%)	
2 TO ≤ 5 YEARS	16 (14,3%)	20(17,95)	
5 TO ≤ 14 YEARS	13(11,6%)	26(23,2%)	
SEX			1,00
MALE	20 (17,7%)	32 (28,3%)	
FAMALE	24 (21,2%)	37(32,7%)	
PREVIOUSLY HEALTHY	27 (23,9%)	32 (28,3%)	0,17
ADMISSION IN INTENSIVE CARE UNIT	13(11,6%)	27(24,1%)	0,45
COMPLICATION: PLEURAL EFFUSION	21 (18,6%)	30(26,5%)	0,80
PNEUMOCOCCAL DETECTION BY POLYMERASE CHAIN REACTION	6(5,5%)	18(16,4%)	0,14

Conclusions:

Although the serotype replacement could increase the pneumonia burden by age, disease severity or pneumococcal detection as etiological cause of CAP, this study did not demonstrated significant association between the two groups, early or late vaccine, in pediatrics patients admitted due to CAP.

Systematic Review Registration:

N/A

ESPID19-1022
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

A case report on treatment of lower respiratory disease with low cost bubble-cpap system in a low- and middle-income country (lmic)

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Background

Continuous positive airway pressure (CPAP) has been proven effective in treatment of lower respiratory disease, but equipment and staff training are resource demanding, which makes it unavailable in many secondary healthcare facilities in LMICs. CPAP works by minimising the work of breathing (WOB) avoiding development of respiratory collapse. We report a case of low cost bubble-CPAP treatment in a LMIC.

Case Presentation Summary

A 6-month-old infant was admitted at Magunga District Hospital, Tanzania, with cough and difficulty in breathing (DIB). It presented with fatigue, respiratory rate (RR) of 108/min, and chest indrawing. Saturation was 84%, pulse 190/min, and temperature 39.8°C. Bilateral crepitation and wheezing were heard on auscultation. Clinical diagnosis was pneumonia. Bubble-CPAP was created from an oxygen concentrator, nasal prongs, and a sterile bottle, inspired by Trevor Duke's CPAP-guide (Figure 1). The expiratory tube was descended 5cm into sterile water where continuous bubbles appeared. Airflow was delivered at maximum 8L/min to avoid pneumothorax. Vital signs and quality of bubbles were closely monitored. Improvement of RR and pulse, hence lowered WOB, was achieved after optimising two parameters: 1) Using tubes with the largest diameter available, thus having lower air resistance in the system, 2) by fitting each cannula closely to the nostrils with tape, obtaining no air leakage. After five days

of treatment, the infant was discharged afebrile and no DIB.

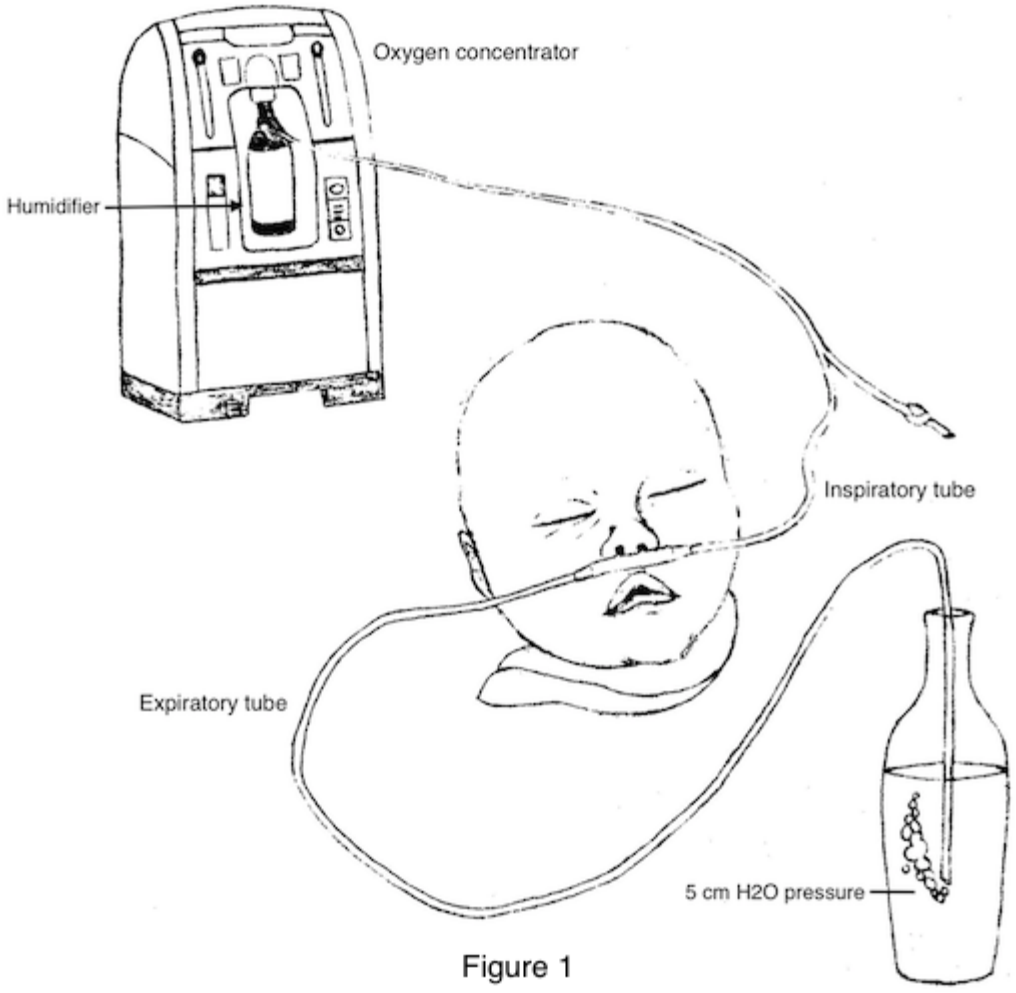

Figure 1

Learning Points/Discussion

It is possible to create a bubble-CPAP system from resources available in a LMIC secondary healthcare facility. To obtain effective treatment, a proper installation and close monitoring are necessary, especially on air leakage, since this is crucial for establishing the required pressure. The case emphasises the need for CPAP in secondary settings in LMICs to decrease under-five mortality due to respiratory infections.

ESPID19-0692
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

Hospitalization due to influenza or respiratory syncytial virus infection in infants and young children – a comparative, retrospective analysis

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Background and Aims:

Infections due to Respiratory Syncytial Virus (RSV) and Influenza virus (FLU) are leading causes of hospitalization in young children. Yet, there is little data comparing the two etiologies in terms of severity, survival, and antimicrobial consumption.

Methods:

We conducted a retrospective, single-center comparative analysis. All patients below 2 years of age hospitalized between 2015-2018 were searched for by ICD-10 codes. We compared length of stay, need for oxygen, intensive care, and antimicrobial consumption.

Results:

RSV infection was diagnosed in 298/364 patients (81.9%), FLU in 64/364 (17.6%), and RSV-FLU-co-infection in 2/364 (0.5%). Diagnoses were mainly made by SOFIA® rapid antigen tests (98% for RSV, 96.9% for FLU). Median age at presentation was lower for RSV (0.33 years; IQR 0.17-0.67) compared to FLU (1.0; IQR 0.5-1.4; $p<0.0001$), while sex was similarly distributed. Both, length of stay and length of oxygen need (5 days; 3 days), were longer for RSV than for FLU (4 days; 0 days). Transfer to ICU was necessary for 9/298 RSV patients (3.0%) and none of the FLU patients. Initial C-reactive protein (CRP) levels were marginally lower for RSV compared to FLU (7.2 mg/L vs. 8.3 mg/L), while maximum CRP levels were slightly higher for RSV (15.5 mg/L) than for FLU (13.6 mg/L). Antibiotic therapy was initiated in 86/298 (28.9%) of RSV and 14/64 (21.9%) of FLU patients, with similar lengths of therapy (mean 8.5 days).

Conclusions:

In our cohort of hospitalized children below the age of 2 years, RSV was associated with younger age and longer hospital and ICU stays. Although inflammatory parameters were similar for both groups, children with RSV infection tended to be treated with antibiotics more often, opening new possibilities for antimicrobial stewardship.

Systematic Review Registration:

n/a

ESPID19-0618
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

A multicenter study on the trends of complicated parapneumonic effusion admissions after pneumococcal conjugate vaccine introduction in greece

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Background and Aims:

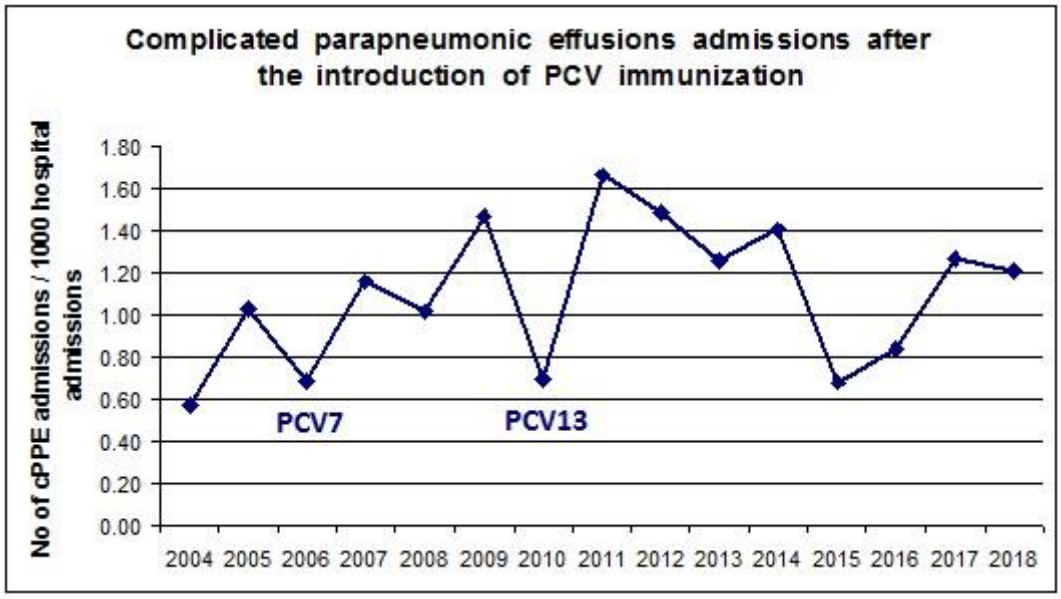
Parapneumonic effusion (PPE) is a common complication of community-acquired pneumonia. The most common cause of PPE is bacterial pneumonia due to *Streptococcus pneumoniae*. After the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), an increase in the incidence of PPE was recorded in some countries. The 13-valent PCV (PCV13) is expected to provide a wide protection against PPE. We aim to examine the impact of PCV introduction on the number of complicated parapneumonic effusion (c-PPE) admissions among children in our area.

Methods:

We analysed cases of pneumonia with PPE requiring chest tube insertion (complicated PPE, c-PPE) in the 3 public Children's hospitals in Athens between 01/01/2004 and 30/06/2018. Data were collected retrospectively before 2013 and prospectively thereafter. The annual incidence rate of c-PPE cases/1,000 general pediatric hospital admissions was recorded and the trend was examined with interrupted time series analysis.

Results:

A total of 374 cases of pneumonia with c-PPE were recorded-166 between 2004-2010 (period A) and 208 between 2011-2018 (period B). The annual incidence rate of PPE was increasing by 0.14 PPE/1000 admissions/year for the period A (p=0.006). After the introduction of PCV13 (period B) this rate was decreased significantly (β=-0.16,p=*0.041*). The increasing rate of period A was reversed and nowadays the annual c-PPE admission rate is decreasing by 0.02 PPE/1000 admissions/year. An interesting increase in serotype 3 was reported, from 1,8% of c-PPE cases in period A to 11.5% in period B (max 41% in 2017).



Conclusions:

A decreasing time trend in c-PPE cases among children was shown after the introduction of PCV13 in our area. Serotype 3 is nowadays a common cause of PPE. Continuous surveillance is required to confirm these findings over time.

Systematic Review Registration:

-

ESPID19-0175
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

Antibiotic usage among children admitted for community acquired pneumonia

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Background and Aims:

It had been observed that there was widespread use of broad spectrum antibiotic for the treatment of in-patient childhood community acquired pneumonia (CAP) but no recent formal audit was carried out to verify this observation. The study objective is analyse antibiotic usage among children admitted for CAP and factors associated with it.

Methods:

This is a retrospective audit study conducted in a district general hospital. Chest X-rays (CXR) performed on children aged 1 month-16 years old admitted in summer (1/6/2017-31/8/2017) and winter (1/12/2017–28/2/2018) were retrieved and reviewed along with their reports. Patients' admission data was collected from electronic discharge notes using a standard case report form in Excel format. Children with diagnosis of CAP supported by presence of CXR changes and/or clinical features of pneumonia were included.

Results:

118/1410 (8.4%) children were hospitalised in summer and 321/1508 (21.3%) in winter for CAP ($p<0.0001$; OR 2.96; 95% CI 2.36-3.71), of which 49 and 51 admissions were analysed respectively. 79% (79/100) received antibiotic; Co-Amoxiclav 37/79 (47%), Ceftriaxone 18/79 (23%), Amoxicillin 9/79 (11%) and Macrolide 9/79 (11%). Initiation, duration, choice and decision to use combination of antibacterial were not significantly associated with seasonal variation, presence of comorbidity and CXR appearance. Median age of children who received antibiotic was 2 years old and median age of children who did not was 1 year old ($p=0.01$). Prescription of Ceftriaxone was significantly associated with longer hospital stay and antibiotic duration (Figure 1).

Conclusions:

Use of first line narrow spectrum penicillin-based antibiotic e.g. amoxicillin for the treatment of uncomplicated CAP among hospitalised children was rare, in contrast to recommendations from national and international guidelines. Broad spectrum antibiotic (Co-Amoxiclav, Ceftriaxone) prescription was substantially high among children admitted for CAP.

Systematic Review Registration:

N/A

ESPID19-0159
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

The microbiology, antimicrobial management and outcomes of paediatric pleural empyema – a review of current literature

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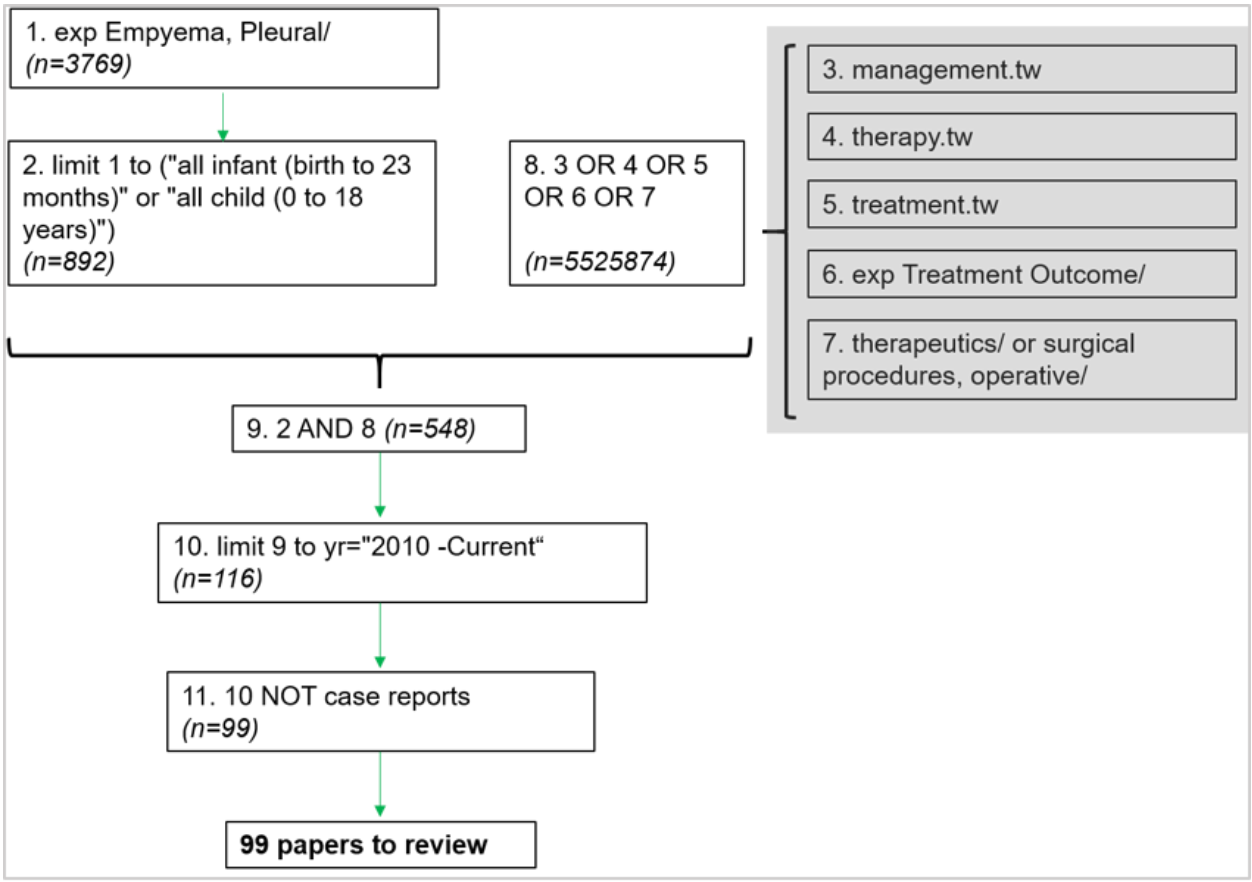
Background and Objective

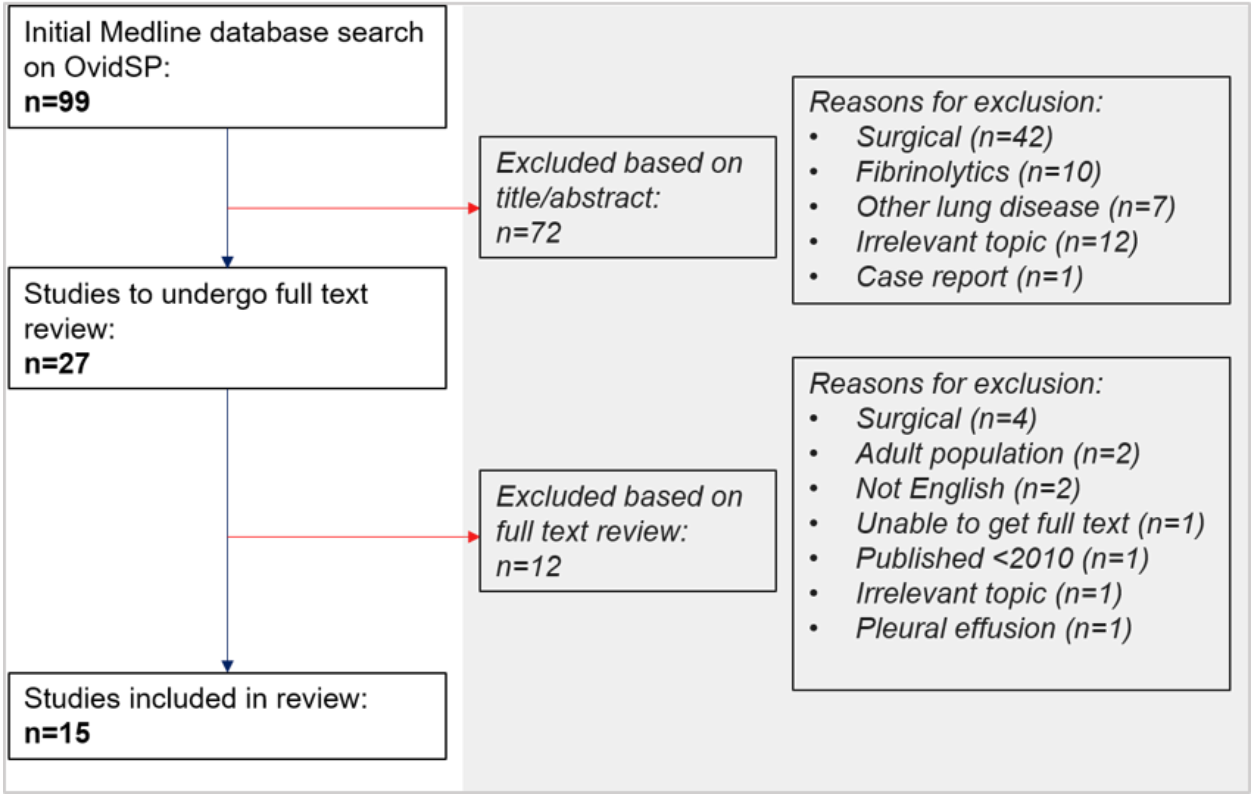
There is a lack of consensus amongst paediatricians regarding the length of antibiotic course in paediatric pleural empyema. This comprehensive review of the literature aims to provide insight into the microbiology and management of paediatric empyema. The aim of this study was to describe current management practices and identify knowledge gaps.

Methods

The MEDLINE database was searched using the OvidSP interface to identify papers relevant to the management of childhood empyema, published from 2010 to present. Two investigators independently reviewed the manuscripts. Discordance were settled by discussion.

Learning Points Discussion


1. exp Empyema, Pleural/ (n=3769)
2. limit 1 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)") (n=892)
8. 3 OR 4 OR 5 OR 6 OR 7 (n=5525874)
3. management.tw
4. therapy.tw
5. treatment.tw
6. exp Treatment Outcome/
7. therapeutics/ or surgical procedures, operative/
9. 2 AND 8 (n=548)
10. limit 9 to yr="2010 -Current" (n=116)
11. 10 NOT case reports (n=99)
99 papers to review


Initial Medline database search on OvidSP: n=99
Excluded based on title/abstract: n=72
Reasons for exclusion:
• Surgical (n=42)
• Fibrinolytics (n=10)
• Other lung disease (n=7)
• Irrelevant topic (n=12)
• Case report (n=1)
Studies to undergo full text review: n=27
Excluded based on full text review: n=12
Reasons for exclusion:
• Surgical (n=4)
• Adult population (n=2)
• Not English (n=2)
• Unable to get full text (n=1)
• Published <2010 (n=1)
• Irrelevant topic (n=1)
• Pleural effusion (n=1)
Studies included in review: n=15

Results:

15 papers were included. This literature review demonstrates:

- Of the pleural cultures, 26.32% were positive. Of those, 54.03% were *Streptococcus pneumoniae*, 11.55% *Staphylococcus aureus* and 8.96% *Streptococcus pyogenes* (n=573).

- Europe had the lowest mortality rate (0.79% (n=1071)), and the highest ICU admission at 50.03% (n=934). In the US there were higher rates of *Staphylococcus aureus* empyemas.

- In European studies 81.8% (n=1508) of cases had a chest drain inserted, but only 48.08% (n=15200) in the US. This could explain the lower mortality rate, increased rates of ICU admission and increased length of stay in Europe.

No studies specifically looked at length of antibiotic course in empyemas.

Discussion:

There is large worldwide variation in how paediatric empyema is defined and managed, as well as little evidence guiding the length of antibiotic therapy.

ESPID19-0048
Science and Educational Track

Independent E-Poster Presentations 07 - Pnuemonia - Station 13

Trial of respiratory infections in children for enhanced diagnostics (trend) study protocol: introducing a new algorithm for classification of etiology in studies on pediatric pneumonia

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[2]South General Hospital, Sachs' Children and Youth Hospital, Stockholm, Sweden
[3]Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden
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Background

There is a need to better distinguish viral from antibiotic-requiring bacterial infections in children presenting with clinical community-acquired pneumonia (CAP) to assist healthcare workers' decision-making and improve rational use of antibiotics.

Methods

Methods: Children 1-59 months with clinical CAP as well as healthy hospital-based asymptomatic controls will be included at a pediatric emergency hospital in Stockholm, Sweden. Blood (analysed for myxovirus resistance protein A (MxA) and C-reactive protein (CRP)) and nasopharyngeal samples (analysed with real-time polymerase chain reaction as gold standard and antigen-based MariPOC® respi test as well as saved for later analyses by a new recombinase polymerase amplification based point-of-care test) will be collected. A newly developed algorithm for the classification of CAP etiology will be used as reference standard.

Results

The overall aim of the TREND study is to improve the differential diagnosis of bacterial and viral etiology in children below 5 years of age with clinical CAP, by evaluating MxA as a biomarker for viral CAP and by evaluating an existing (MariPOC® respi) and a potential future point-of-care test for respiratory pathogens.

Conclusions

The findings from the TREND study can be an important step to improve the management of children with clinical CAP.

Clinical Trial Registration (Please input N/A if not registered)

The study is registered at clinicaltrials.gov (ID:NCT03233516) July 28, 2017.

ESPID19-1176
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

Unusual presentation of tuberculosis in a child with chronic otitis media

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Background

Tuberculosis (TB) of the middle ear is uncommon and usually occurs secondary to pulmonary TB via direct inoculation along the eustachian tube. It mimics chronic otitis media (OM) which is common in children and may lead to delayed diagnosis. Additionally, acid-fast bacilli (AFB) test may be falsely negative.

Case Presentation Summary

A 11-year old British male presented with a two-year history of ear discharge despite repeated courses of antimicrobial therapy, on a background of chronic OM. Examination under anaesthesia (EUA) revealed granulation tissue. Samples were negative for AFB and biopsy was suggestive of cholesteatoma. Temporal bone CT scan revealed infected mastoid cells with no bony destruction. A year later he underwent further EUA for persistent discharge; repeat samples were sent for AFB and histopathology. A chest X-ray requested due to high suspicion of TB showed extensive chronic changes with cavitation and a calcified focus on the right. Sputum examination demonstrated AFBs and he commenced quadruple TB therapy. Discharge from the ear and sputum subsequently grew mycobacterium tuberculosis.

He had no history of contact with TB and no significant travel history. Interestingly, aged 10 he underwent a hemicolectomy for acute Crohn's disease. He went into remission within several weeks and received no immunosuppressive therapy at any stage. Histology from his hemicolectomy was subsequently reviewed and had no AFBS, no granulomas and TB PCR testing was negative.

Follow-up post treatment revealed a well child with residual lung changes on chest x-ray and 50% conductive deafness on the left.

Learning Points/Discussion

- · Chronic otitis media may be a presenting feature of tuberculosis.
- · Patients with pulmonary TB and otitis media should be assessed for possible Tuberculous otitis.
- · Diagnostic delay may lead to profound deafness and other complications including facial palsy.

ESPID19-0871
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

A case of inflixtb – be aware!

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Background

Even though the incidence of tuberculosis is falling worldwide, it is still a major cause of death. Certain groups are more susceptible to this infection, including those receiving anti-TNFα.

Case Presentation Summary

A 17-year-old boy with Crohn's disease was on infliximab for 2 years. Before biologic therapy he had a normal chest x-ray and indeterminate IGRA and completed 9 months of isoniazid. He was admitted with a 2-week history of fever, dry cough and pleuritic chest pain. Physical examination was unremarkable. Chest CT scan showed an upper left lobe consolidation and countless micronodules. IV amoxicillin/clavulanate and co-trimoxazole were started. Fever persisted with rising inflammatory markers. *Mycobacterium tuberculosis* was identified on sputum samples. CSF analysis was normal. Miliary tuberculosis was diagnosed, quadruple therapy started (isoniazid, rifampicin, pyrazinamide and ethambutol) and biologic therapy stopped. Initial slight improvement was followed by progressive clinical and biochemical deterioration. Due to disseminated infection, oral intolerance and suspicion of immune reconstitution IV levofloxacin, amikacin and corticosteroids were introduced. Fever ceased within 3 days. He was discharged 2 weeks later on oral quadruple therapy (pyrazinamide total of 118 days), oral levofloxacin, IV amikacin (total of 96 days) and oral corticosteroids (currently tappering). Infliximab was reintroduced 5 months later. Outcome was good.

Learning Points/Discussion

Patients receiving infliximab are prone to tuberculosis reactivation with disseminated and atypical presentations. Tuberculosis screening prior to biologic therapy is mandatory. Aggressive treatment may be needed to control TB as these patients are highly susceptible to mycobacteria and may present severe forms as occurred in this case.

ESPID19-0643
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

Social costs of leprosy on children and young people: a systematic review

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[2]London School of Hygiene and Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom
[3]University of Bristol, Medical School, Bristol, United Kingdom

Background

Mycobacterium Leprae is a chronic, disabling infection that remains endemic in Brazil, India, and China, causing significant stigma and exclusion. The World Health Organisation highlights social factors, poverty, and lack of education as both consequences of leprosy infection and risk factors for ongoing transmission. Alongside improving diagnosis and treatment, identifying and reducing these social costs remains an important priority towards mitigating the impact on children and young people.

Methods

A search was performed using medline, embase, LILACs, Global Health, Ind-Med, African Index, Pakmedinet up to 15/12/2018 for papers measuring social costs on children and young people. *Mycobacterium leprae*, Hansen's disease and leprosy were combined with terms incorporating disability, isolation, stigma, quality of life, education, income, and housing. Studies were included that measured social outcomes associated with leprosy in the child or a direct family member; studies were excluded if they were qualitative, ecological or lacked description of the outcome or population.

Results

The total search count for abstracts and titles was 3639, with 101 included studies for full text screening and 8 found to be included. This will be independently screened by a second author prior to final reporting of the data, then data will be extracted. Children report increased grade 2 disability (WHO criteria), loss in household income, reduced schooling or absolute drop out, separation from family members and social support, and impaired quality of life.

Conclusions

Though poorly addressed in the literature, leprosy has wide ranging social impacts on children's home, economic and educational lives. By addressing these, policy makers can strategically reduce the vicious cycles in affected communities where ongoing stigma, discrimination and isolation contribute to ongoing transmission and the negative burden of disease.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESPID19-0493
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

Central nervous system tuberculosis: three different cases in our pediatric department

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[2]Università degli Studi di Padova, Padova, Italy

Background

Children with primary TB infection present a higher risk of progression to TB disease, if compared with adults. The development of severe TB disease, such as CNS TB or miliary TB, dramatically increases in children under age five .

Case Presentation Summary

We report three cases of children presenting TB disease with CNS involvement . The first child ,3 years old, presented multiple cerebral tuberculomas , the second, 1,5 year old , presented TB meningitis , the third ,4 years old, had both meningitis and tuberculoma. The youngest one developed a permanent emiparesis , the two others had a good outcome .

All these children were born in Italy, two of them with family immigrating from TB-endemic regions , and the youngest with frequent travels in these regions .

No household contact was reported in Italy and we presume that the children were infected by visiting friends or relatives in TB- endemic countries .

Learning Points/Discussion

The diagnosis of CNS involvement in TB disease, burdened by high morbidity and mortality ,can be difficult in developed countries where the TB incidence rate is low , due both to the early aspecific clinical manifestations and the slow progression of disease. This is why a high clinical and anamnestic suspicion and epidemiological features play a significant role in the early diagnosis and treatment, leading to a better long-term clinical outcome. In order to prevent the CNS and miliary TB in children a BCG vaccine should be offered to children born in the developed countries who immigrated from countries with high TB incidence . In this context the system of early detection of Latent Tubercolosis Infection in families at higher risk should be implemented.

ESPID19-0357
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

Tuberculosis or lung tumor? Atypical presentation of a pulmonary tuberculosis by micobacterium bovis

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[1]Hospital Universitario Fundación Jiménez Díaz, Pediatrics, Madrid, Spain

Background

Tuberculosis (TB) is caused by one of several mycobacterial species that belong to the Mycobacterium tuberculosis complex. The most representative bacterium is Mycobacterium tuberculosis. Other human pathogens are M. africanum, and M. bovis.

Case Presentation Summary

Three-year-old child in follow-up for two repeated pneumonias since 8 months, both in the middle lobe. CT was performed observing an inflamatory lesion in the right lower lobe with involvement of the intermediate bronchus and obstruction of the middle and the lower one, mantoux was 10 mm. Clinically asymptomatic except for persistent cough. Fibrobronchoscopy was indicated and antitubercular treatment with isoniazid, rifampin, ethambutol and pyrazinamide was initiated. PCR in a fibrobronchoscopy specimen was positive for M bovis, pathological anatomy compatible with tuberculosis and Ziel-Nielsen was negative.

Two months of treatment were completed with four drugs. Subsequently four months with isonized and rifampicin with good evolution.

An extension study was carried out on family members, all negative. No travel, no contact with animals, no intake of unpasteurized dairy products was reported.

Learning Points/Discussion

M. bovis belongs to the TB complex. Although it is usually associated with consumption of unpasteurized dairy products, a stay in an endemic country or immunosuppression, it can also affect previously healthy individuals

ESPID19-0309
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

Pott's disease in a 3 years old italian child

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Background

Tubercular spondylodiscitis is the most common type of skeletal TB, more frequent in children than adults. It is rarely reported in developed countries.

Case Presentation Summary

A 3 years old Italian child referred to our center to an history of back pain, intermittent fever and walking deficiency started two months before and with progressive worsening and non-responding to common anti-inflammatory treatments. Back spine X-rays didn't show particular alterations, whether blood test revealed high level of C-reactive protein and leukocytosis. Anti-tubercular tests (Quantiferon and Mantoux) done during admission came positive, and a specific magnetic resonance showed an extended L1-L2 spondylodiscitis. An anti-tubercular treatment was started with isoniazid, rifampicin and pyrazinamide for two months, then carried on with isoniazid and rifampicin for other seven months, with a slow clinical improving. An imaging repeated during follow-up showed a reduction of L1 (body vertebrae) and of the inter-somatic space between L1-L2, with no other signs of spondylodiscitis at the end of the treatment. The patient is now undergo to specific orthopedic follow-up, with the necessity of a specific corsept to stabilize column and walking.

Learning Points/Discussion

Diagnosis of tubercular spondylodiscitis in children coming from developed countries, with no history of TB and travel or living in developing countries, is rare and very difficult, but an early recognition could lead to a positive outcome. Incidence of TB is increasing in developing countries, mostly due to immigration. Back pain, in particular when associated to walking deficiency, has to be considered a serious problem in children with no benefits from common treatments.

ESPID19-0018
Science and Educational Track

Independent E-Poster Presentations 08 - Tuberculosis - Station 01

Bedaquiline and delamanid in children with xdr tuberculosis – what is prolonged qtc?

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Background

Background: Bedaquiline (BDQ) and Delamanid (DLM) are being increasingly used with improved outcomes in the older population with extensively drug resistant (XDR) tuberculosis (TB). Due to insufficient evidence in children, at present BDQ has been advised only for those above 12 years of age, and DLM for ages 6 and above. Both drugs are known to cause prolonged QTc on electrocardiogram (ECG) and require intense monitoring with hospitalization in the initial days.

Case Presentation Summary

We report two children (13 years old female with fibrocavitatory TB and 8 years old male with chest wall abscess along with scalp abscess) with XDR-TB, who were put on BDQ and DLM along with other second line anti-TB drugs. In the girl, the treatment regimen consisted of capreomycin, high dose Mfx (HMfx), Clofazimine (Cfz), cyclcoserine (Cs), PAS, amoxicillin-clavulanic acid along with imipenem-cilastin apart from BDQ and DLM. In the boy, the treatment regimen consisted of Cfz, Cs, HMfx, PAS, meropenem, linezolid, amoxicillin-clavulanic acid along with BDQ and DLM. Measurement of QTc is usually done by the Bazett's formula. However, both our patients had prolonged QTc on Bazett's formula (QTcB) and needed withholding of BDQ and DLM for 10 days. None of them were symptomatic at that time. However when Qtc was monitored by Fridericia's formula (QTcF), the QTc was normal. Hence the drugs were restarted and both of them tolerated the medicines without any adverse effects.

Learning Points/Discussion

Guidelines should emphasize the correct formula for monitoring QTc thereby preventing unnecessary withholding of the medicines. Since most of the automated ECG machines calculate the QTc by Bazett's formula, it is necessary to measure the QTcF based on the Fridericia's formula. BDQ and DLM appear to be safe in children.

ESPID19-0612
Science and Educational Track

Independent E-Poster Presentations 09 - Global Health - Station 03

Respiratory complication in typhoid fever: a case report

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Background

Typhoid fever is a systemic disease caused by the Gram negative bacillus *Salmonella typhi*. Approximately 10% of cases develop complications, the majority of which are abdominal. The choice of antibiotics for the management of typhoid fever should be guided by the resistance patterns of the place of likely acquisition due to increasing drug resistance to first line agents.

Case Presentation Summary

A previously well, fifteen-year-old girl presented with a five-day history of fever and profuse vomiting. *Salmonella typhi* (resistant to ciprofloxacin, chloramphenicol, and azithromycin) was isolated from her blood culture after 48 hours incubation, and treatment with ceftriaxone was commenced. Despite the treatment, she remained persistently febrile and after three days she developed severe respiratory distress requiring high flow nasal oxygen therapy. A chest radiograph demonstrated bilateral pleural effusions associated with dense consolidations of both lower lobes and the lingua. The inflammatory markers continued to rise and gentamicin was added for three days. Her clinical condition progressively improved and she was discharged after nine days to the outpatient parenteral antibiotic therapy (OPAT) service, to complete a total of four week course of intravenous ceftriaxone. The patient made a full recovery with complete resolution of her respiratory symptoms and chest x-ray changes. Close contact screening did not identify the source of infection.

Learning Points/Discussion

Salmonella typhi disease can cause disseminated focal infections and the risk of translocation is often determined by the virulence of the isolate and host immunity. Despite the fact that *Salmonella spp.* are not a typical respiratory pathogen in immunocompetent hosts, chest complications can occur. Awareness of the clinical features of this disease is pivotal in prompt diagnosis and early detection of the complications.

ESPID19-0432
Science and Educational Track

Independent E-Poster Presentations 09 - Global Health - Station 03

Cat-scratch disease: different manifestations, same disease

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Background

Cat-scratch disease (CSD) is an emerging zoonotic disease caused by the bacterium *Bartonella henselae* and may present with a broad spectrum of clinical pictures.
We describe four clinical cases with different manifestations; they were previously healthy and had contact with cats. All of them had positive serology for Bartonela IgG 1/1024 and excluded tuberculosis.

Case Presentation Summary

Case 1 - An 11-year-old girl with 3-month inguinal lymphadenopathy. She underwent lymph node biopsy with chronic granulomatous lymphadenitis with necrotic areas. The ganglion evolved with spontaneous resolution without need for a specific treatment.
Case 2 - A 7-year-old girl with fever of unknown origin for 33 days and inguinal lymphadenopathy for 5 days. She received clarithromycin for 10 days with resolution of the symptons.
Case 3 - A 7-year-old girl with 2-day fever, abdominal pain and inguinal lymphadenopathy. The abdominal CT-scan showed hepatosplenomegaly with multiple hypodense nodules. The inguinal ganglion biopsy demonstrated granulomatous inflammatory reaction with necrotic areas. It was interpreted as systemic CSD presentation; she received clarithromycin for 9 days and rifampicin for 14 days. She evolved with clinical improvement and resolution of the hypodense imagens.
Case 4 - A 7-year old girl with fever for 15 days and loss of visual acuity for 1 week. Fundoscopic examination showed retinal effusion and vasculitis. She was diagnosed with ocular CSD presentation and received clarithromycin for 32 days with partial improvement of visual acuity.

Learning Points/Discussion

In immunocompetent individuals, *Bartonella henselae* infection presents as CSD, with a broad spectrum of clinical manifestations. Serology is used for diagnosis; IgG titers>1:256 strongly suggest active or recent infection. Lymphadenomegaly can be resolved spontaneously or after macrolide. For those with more serious infection, combination therapy is suggested (macrolide+rifampin).

ESPID19-0039
Science and Educational Track

Independent E-Poster Presentations 09 - Global Health - Station 03

Use of telemedicine to cure an unusual case of chronic parasitic infection due to taenia saginata

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Background

We report a chronic case of Taenia saginata infection in a 10 year child residing in a rural part of Maharastra State, India, which was managed successfully by telemedicine.

Case Presentation Summary

A 10 year old girl , resident of Parbhani, rural Maharashtra suffered from abdominal pain on and off since one year. She also suffered loss of appetite and weight loss. There was history of passing small bits of worm. The abdominal pain had interfered with her daily activities. Abdominal examination was unremarkable. She had history of receiving deworming medicine Albendazole several times. The worms in the stool on gross examination appeared like proglottids of Taenia saginata (beef tapeworm). This was confirmed by microscopic examination of stool. The standard regimen recommended for this worm is either Praziquantel or Niclosamide. Both these medicines being unavailable locally, help was sought by local practitioner using telecommunication with ID specialist in Navi-Mumbai city. She was advised to start Nitozoxanide for 3 days. Immediately on completion of course, she passed the worm nearly 1 metre in length and her abdominal pain completely disappeared. She was able to eat a full meal without discomfort after almost one year of suffering from abdominal symptoms.

Learning Points/Discussion

Taenia saginata is acquired by consumption of raw or undercooked beef containing larval forms of the tapeworm called cysticercus. The cysticercus gets stimulated in gastrointestinal tract, attaches to the wall of the small intestine by means of scolices and grows into a mature tapeworm.
In this case ,due to local unavailability of first line drugs like praziquantel or niclosamide, nitozoxanide was used for successful expulsion of the worm. This case illustrates the use of telemedicine in availing opinion of specialists usually located in urban areas.

ESPID19-1087
Science and Educational Track

Independent E-Poster Presentations 09 - Global Health - Station 03

Fever in a patient who returns from angola

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Background

Malaria remains a major cause of disease worldwide. Diagnosis is based on clinical suspicion and detection of parasites on blood samples. P. falciparum is the responsible for most cases of severe disease.

Case Presentation Summary

Previously healthy, 5-year-old child, with alternated residence for long periods between Portugal and Angola. Observed in the emergency department for fever for three days, vomiting, cough and rhinorrhea. CBC with Hb 14.4 g/dL, WBCs 5150U/ L, Platelets 77.000/L, AST 46U/L; ALT 27U/L, CRP 11.2 mg/dL, SR 5 mm/ hr. Normal Chest radiography.Plasmodium test revealed parasitemia (<1%), with positive microscopic observation for plasmodium spp. Due to oral intolerance, he was admitted for IV quinine, and discharged after 24 hours on atovaquone/proguanil.

Six months after another trip to Angola, he was again observed for fever and dehydration. Blood tests revealed Hb 12.8 g/dL, WBC's 6150U/L, platelets 103000/L, AST 32U/L; ALT 18U/L, CRP 7.6mg/dL, SR 10 mm/h. Thick drop test showed Plasmodium trophozoites and low parasitemia (<1%). He was admitted for IV hydration and started therapy with artenimol. PCR test identified Plasmodium *ovale* and Primaquine was aded to the prescription. He was discharged, clinically well, with no new episodes of fever.

Learning Points/Discussion

Optical microscopy and rapid diagnostic tests are useful for the diagnosis of the parasite, but more sensitive molecular biology methods should be performed, whenever needed. Overlap infections are common in malaria-endemic regions, and it has been suggested that treatment should be consolidated with an agent to eradicate the parasite and avoid recurrence, particularly in the case of P ovale co-infection.

ESPID19-0775
Science and Educational Track

Independent E-Poster Presentations 09 - Global Health - Station 03

A systematic review of post-discharge interventions for children aged 6-59 months hospitalised with severe acute malnutrition

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Background

Children requiring inpatient care for severe acute malnutrition (SAM) are known to have poor long-term outcomes. They are particularly vulnerable to infection, and infectious disease is thought to be a key driver of the high rates of mortality, morbidity and relapse.

There are no specific WHO recommendations for further interventions following inpatient management, except for the provision of ready-to-use therapeutic food (RUTF) by outpatient programmes. The objective of this review was to identify any additional interventions continued or implemented in the discharge period, which could improve outcomes.

Methods

We undertook systematic searches of Medline, EMBASE, Global Health and CENTRAL, and searches of grey literature. Studies of children aged 6-59 months, hospitalised with SAM, and subsequently discharged, were included. Variable definitions of SAM were accepted, according to the criteria used by each study at the time.

Results

14 articles (representing 9 studies) met the inclusion criteria. Populations were heterogeneous, with different age-ranges and rates of HIV infection. Interventions included prophylactic antibiotics (1 study), pancreatic enzyme supplementation (1 study), probiotics (2 studies), high dose zinc supplementation (2 studies) and psychosocial stimulation (3 studies). A variety of outcomes were reported, including mortality, duration of diarrhoea, weight gain and nutritional recovery. Results of note included a randomised placebo-controlled trial demonstrating no reduction in mortality following 6 months of co-trimoxazole prophylaxis in HIV negative children. A second randomised placebo-controlled trial found preliminary evidence of reduced outpatient mortality in children receiving probiotics with RUTF.

Conclusions

Included studies implemented a variety of interventions in different populations of children following inpatient management for SAM. These were of variable benefit in terms of infectious morbidity, mortality, anthropometric and developmental outcomes. Further work is required before any interventions enter clinical practice.

Systematic Review Registration (Please input N/A if not registered)

PROSPERO CRD42018111342

ESPID19-0112
Science and Educational Track

Independent E-Poster Presentations 09 - Global Health - Station 03

Clinical profile of scrub typhus

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Background

Scrub Typhus is emerging as an important cause of tropical fever and Acute Encephalitic syndrome in India. It's clinical profile is variable and diagnosis requires a high index of suspicion.

Case Presentation Summary

We have seen seven cases of Scrub Typhus from August to November 2018.The following is their clinical profile.

Parameter	No of patients	
Age		
0-5 yrs	1	
6-10 yrs	4	
10-15 yrs	2	
Sex		
Male	6	
Female	1	
Duration of illness		
<7 days		
7-14 days	4	
14 days	3	
Clinical symptoms		
Fever	7	
Headache	2	
Abdominal pain	5	
Nausea/vomiting	3	
Maculopapular rash	1	
Altered sensorium	2	
Cough	1	
Clinical signs		

Hepatosplenomegaly	5	
Meningeal signs	1	
Lymphadenopathy	1	
Ascites	3	
Pleural effusion	2	
Laboratory Investigations		
TLC normal count	3	
TLC <4000	0	
TLC >11000	4	
Anaemia (HB<10g/dl)	5	
Platelet count <100 000/cmm	2	
Increased creatinine	1	
Abnormal USG whole abdomen	4	
Abnormal Xray	2	
Complications of Scrub typhus		
Meningitis	1	
ITP	1	

One patient had a CSF examination which confirmed the diagnosis of Scrub Typhus meningitis. In one patient thrombocytopenia improved but persisted even after four weeks was diagnosed as Scrub Typhus induced ITP. Bone marrow confirmed the diagnosis. All patients responded to oral Doxycline.

Learning Points/Discussion

Scrub Typhus has a variable presentation. Rash and Eschar which are pathognomonic of this disease may not be present. Prompt diagnosis ensures complete recovery.

ESPID19-0976
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

Cases of perinatal measles in newborns

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Background

Congenital and perinatal measles is a rare disease, sometimes ranges from mild symptoms to ultimately death. Due to the fact that cases of congenital and perinatal measles are rare - international treatment recommendations and practical experience are often controversial.

Case Presentation Summary

Two newborns have been under observation. The girl was born as an uncomplicated vaginal delivery at a gestational age of 38 weeks by mother suffering from 6-day measles rash. On the third day of life, a non-intense maculose rash appeared on the face, trunk and limbs, anti-measles IgM was doubtful. On the 8th day of life anti-measles IgM was positive, PCR of urine was also positive. The general condition was normal, she did not get any treatment; on the 11th day of life girl was discharged as being recovered. A boy was born at a gestational age of 40 weeks by a mother in the measles catarrhal period, 3 days before the rash appearance. On the 5th day of the boy's life a maculopapular rash, fever, cough, and coryza developed. On the 3rd day of newborn's life rash developed in his mother. The rash developed in newborn 2 days after the mother's rash appearance. Anti-measles IgM of infant (8th day old) and his mother were positive. The child was breastfed, got Human Immunoglobulin intravenous, vitamin A orally, paracetamol rectally. The boy was discharged on 13th day of life as being recovered.

Learning Points/Discussion

The observation tactics of an infant born by mother suffering from measles with possibility of Human Immunoglobulin intravenous is justified for asymptomatic cases. For symptomatic cases we recommend Human Immunoglobulin intravenous with vitamin A.

ESPID19-0681
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

Congenital rubella syndrome in indonesia: a two years hospital surveillance results

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Background and Aims:

Congenital Rubella Syndrome (CRS) is a congenital disease that can be prevented by rubella vaccination. In Indonesia, a nation-wide Measles Rubella vaccination campaign introduced in 2017 in Java Island and 2018 in other area of the country, followed by routine immunization programme. To understand the burden of CRS, hospital based surveillance were performed in 10 tertiary hospital across Indonesia, including Soetomo Hospital, a tertiary referral hospital for eastern part of Indonesia. We report on CRS surveillance results in Soetomo Hospital Surabaya, Indonesia during 2017-2018.

Methods:

Infants < 1 year old with the diagnosis of clinical and confirmed CRS treated in Soetomo Hospital, Surabaya, Indonesia during January 2017 to December 2018 were recruited in the surveillance. Their perinatal data, congenital defect and rubella serology data were collected. The final diagnosis of clinical and confirmed CRS were made based on WHO criteria of CRS

Results:

We found 75 infants with CRS (46 clinical and 29 confirmed CRS), 41 infants were male. Mean age at diagnosis was 4.8 months. Among CRS infants, 46 (61%), 30 (40%) and 57 (76%) had congenital heart disease, congenital eye anomaly and hearing problem, respectively. Multiple congenital anomaly were found in 53 (73.6%) cinfants. Most (45/75, 60%) were born low birth weight, but only 38 (50.7%) infants were born preterm.

Conclusions:

Congenital Rubella syndrome were still common and may cause multiple congenital anomaly. Hearing problems followed by congenital heart diseases were the most common manifestation among CRS infants.

Systematic Review Registration:

None

ESPID19-0544
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

The efficacy and safety of long-term systemic acyclovir therapy of neonatal herpes in immunocompetent infants

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Background

Neonatal herpes (NH) is a rare disease, which develops prenatally or during the first 4-6 weeks of life. Unless antiviral chemotherapy is used, disseminated form of NH leads to a mortality level of about 80% and high rate of residual disabling damage to the nervous system, eyes and skin in survivors. In newborns who develop NH, administration of extended long-term suppressive antiviral therapy should be considered to reduce the rate of recurrence, and tolerability of such therapies is an issue of special concern.

Case Presentation Summary

We observed two male infants born naturally, in term, who developed *Herpes simplex virus* type 2(HSV-2) infection immediately after the birth, which was first diagnosed clinically and later confirmed by PCR detection of HSV-2 DNA in skin vesicle exudates. Mothers of both infants presented with signs of vesicular rash in the anogenital area at the time of parturitions. In both cases the presented HSV-2 infection had intranatal transmission route. Clinical course of infection was notable for recurrent vesicular rash with no signs of fever or systemic disorders. Both infants were prescribed continuous systemic acyclovir therapy from the early age for over a year. In both cases long-term course of acyclovir was well tolerated and led to long-lasting control of the infection, confirmed by symptom-free 3 months follow-up period after completion of the therapeutic course.

Learning Points/Discussion

Long-term therapeutic regimen with acyclovir might be preferable to the intermittent short-term courses for exacerbations of HSV-1 and HSV-2 infections in infants. Assessment of efficacy and optimal duration of the treatment should be mainly determined by clinical indications. It is generally advised to continue the acyclovir course unless 90 days of symptom-free period without any recurrence of herpetic exanthema is reached.

ESPID19-0388
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

Congenital cmv and autoimmune neutropaenia of infancy: cause or coincidence?

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Background

Congenital CMV (CCMV) accounts for high rates of infant morbidity and mortality. Neutropaenia is a common finding in CCMV infection, of which the age of presentation overlaps with autoimmune neutropaenia (AIN). AIN represents one of the most common forms of chronic neutropaenia in childhood. A literature search exploring biological associations between congenital CMV and AIN was conducted: PubMed (MEDLINE), Ovid, Web of Science. We further describe 2 cases of concurrent congenital CMV and AIN. Both cases were confirmed with the indirect granulocyte immunofluorescence test (GIFT) and alternative aetiologies for neutropaenia excluded.

Case Presentation Summary

Our 2 patients represent confirmed cases of AIN in infants with congenital CMV. One patient demonstrated neutropenia whilst undergoing treatment with Valganciclovir whilst the other was never treated. With interruption of Valganciclovir in Infant A, neutrophil counts did not improve and upon resumption of treatment ANC remained static.

Learning Points/Discussion

Further studies examining a possible biological link between CCMV and AIN are advocated for. We encourage clinicians to actively consider AIN in the differential diagnosis of all infants with CCMV presenting with neutropaenia.

ESPID19-0308
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

Acquired cytomegalovirus as possible cause of severe acute anemia

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Background

Congenital Cytomegalovirus (CMV) is defined by the fetal infection during pregnancy, and diagnosed through specific viral DNA test in newborn saliva or urine in the first two weeks of life. Late acquired infection could be difficult to differentiate from congenital if the diagnosis is done in the first months of life.

Case Presentation Summary

Male, born preterm at 35 WGA with adequate birth weight and mother immune to CMV. No problems reported during pregnancy and in the post-natal admission. A blood cells count done the first day of life showed an high hemoglobin level (20.5 gr/dL). At 21 days of life he referred to our A&E department to vomit and rhinitis. Blood tests showed severe anemia (hemoglobin 7.3 gr/dL) with no signs of hemolysis. An immediate blood transfusion was necessary, considering the sudden Hb decrease (13.2 gr/dL in 20 days). Serum CMV IgM antibodies and CMV DNA dosed on urine came positive. No other cause of acute anemia were found. The patient undergo a specific follow-up, but no other localizations of CMV were found (eye examination, abdominal and brain ultrasound, magnetic resonance, ear test, neurologic specific consultation). CMV DNA was also dosed on Guthrie card, with negative result, and suggesting a post-natal acquisition of the viral infection. No specific anti-viral treatment was started.

Learning Points/Discussion

Acquired CMV is a common infection: 40-80% of adults in industrialized countries and almost all of people living in developing countries acquire CMV during their life. When acquired after birth, this infection is more dangerous with an earlier acquisition. In congenital and early acquired CMV infection a specific follow-up is necessary to evaluate possible neurologic, oculistic and auditive damages. Hematologic alterations, in particular severe thrombocytopenia, can occur during acute infection.

ESPID19-0137
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

Fatal congenital echovirus 11 infection in a neonate

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Background

Neonatal Enterovirus infections are relatively common and lead to a variety of manifestations, from asymptomatic to fatal.
Enteroviruses are transmitted to neonates vertically from infected mothers during delivery or via the contact with families postnatally. Transplacental transmission has also been reported.
We report a case of fatal congenital echovirus 11 infection in a neonate who presented with hepatic necrosis and hemophagocytosis.

Case Presentation Summary

A male infant was delivered by spontaneous labor at 39 weeks of gestation. The mother had acute onset of fever and abdominal pain two weeks before delivery.
At birth, the infant had hepatomegaly, hyperferritinemia, and fulminant hepatic dysfunction with coagulopathy.
Disseminated intravascular coagulopathy with irreversible hepatic failure developed, and the infant died at nine days of age.
The autopsy revealed hemorrhagic hepatic necrosis and hemophagocytosis.
Echovirus 11 was isolated from viral cultures of stool and throat aspirate obtained at birth.
Maternal antibody against echovirus 11 was elevated in the postpartum period.

Learning Points/Discussion

Neonatal enterovirus infections sometimes become fatal, but specific treatments for severe enterovirus infections have not been identified.
The diagnosis of congenital enterovirus infections is very difficult, because other diseases, such as neonatal hemochromatosis, bacterial or other viral infections, congenital metabolic disease, and mitochondrial disease, must be ruled out.
The risk factors of severe enterovirus infections include maternal history of illness within two weeks before delivery, lack of maternal serotype specific antibody, and serotype of enterovirus such as coxsackie B virus and echovirus.

ESPID19-0109
Science and Educational Track

Independent E-Poster Presentations 10 - Viral Neonatal & Congenital Infections - Station 05

Early gross motor development among brazilian children with congenital microcephaly born right after the zika virus infection outbreak

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Background and Aims:

BACKGROUND

In 2015, when widespread epidemics of Zika virus (ZIKV) across the Americas resulted in unexpected neurological diseases and congenital malformations,as well as the prevalence of microcephaly. The cerebral palsy (CP) have been linked among children with congenital ZIKV infection with severe impairment of the gross motor development.

OBJECTIVE

To assess the gross motor development of children at risk for ZIKV infection during gestation, over the first 2 years of their lives.

Methods:

METHODS

Seventy-seven children were assessed at the median ages of 11, 18 and 24 months, using the evaluative instrument Gross Motor Function Measure (GMFM-66). At the third assessment, the children with diagnoses of CP were classified by severity through the Gross Motor Function Classification System (GMFCS) and the motor development potential was estimated based on GMFM-66 scores.

Results:

RESULTS

At 2 years of age, all children had the diagnosis of CP. Seventy-four (96.1%) presented gross motor skills similar to those of children aged 4 months or less according to the World Health Organization's standard. They were classified in GMFCS level V according to the median GMFM-66 score. The majority of children

was quadriplegic and GMFM-66 showed significant change scores between 11 and 18 months (P=0.001) and between 11 and 24 months (P<0.001). No significant difference (P=0.076) was found between 18 and 24 months.

Conclusions:

CONCLUSIONS

Despite showing some gross motor development during the initial 18 months of life, children at risk of ZIKV infection during gestation and with diagnosis of CP experienced severe motor skill impairment and presented low GMFM-66 scores at 2 years of age. We observed a tendency of children with lower motor development potential to reach their limit more quickly than children with higher potential.

Systematic Review Registration:

NO

ESPID19-0778
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

Prevalence of syphilis in adolescents and young adults vertically hiv-infected

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Background and Aims:

The acquired syphilis detection rate in Brazil has soared and prevalence of syphilis is up to 8-times higher in HIV patients.
Nevertheless, few studies analysed coinfection among vertically HIV infected patients.
This survey is aimed to evaluate prevalence of syphilis in sexually active vertically infected HIV adolescents and young adults and possible associated factors.

Methods:

A cross-sectional clinical study was performed from Set.2017 to Set.2018.
Medical record data were collected about clinical and behavioural characteristics and a rapid treponemal test and syphilis serology were conducted. The data were analysed descriptively. An HIV-infected group with syphilis was compared with an HIV-infected group without syphilis to detect factors associated with this coinfection. Approved by local IRB (n. 72885517.7.0000.5505)

Results:

Fifty-two vertically HIV-infected subjects were included, median age 21 years (16-26y), 34female (65,4%), 25with undetectable viral load (48%).
Five of them (9.6%) tested reagent for syphilis, using non-treponeme test (VDRL). The rapid test for syphilis was positive in 3 of these participants. Only one subject had genital ulcers, the remainder were asymptomatic.
Twelve out of fifty-two (23%) had already been diagnosed with a sexually transmitted infection but only one with syphilis. Only 13% had been screened for syphilis in the past year (all negative). Ninety-two percent wear condoms, but 2 out of 5 syphilis-infected (40%), reported never wearing it for anal or vaginal sex.
No statistical differences were detected in the evaluation of risk behavioural factors associated with coinfection.

Conclusions:

This study demonstrated that 9.6% of our patients had syphilis and, although there were no statistical differences associated with coinfection, screening sexually transmitted infections is an opportunity to identify which HIV-infected patients present risk behaviours and to prioritize preventative interventions in this group.

Systematic Review Registration:

N/A

ESPID19-0558
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

Recurrent skin infections: it isn't always an immunodeficiency

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Background

In the differential diagnosis of recurrent skin infections, primary immunodeficiencies must be always considered. However, we shouldn't forget that recurrent skin infections may have an infectious etiology. Colonization by community-associated methicillin resistant *S. aureus* (MRSA) is one of such causes.

Case Presentation Summary

Three cases were referred to the Pediatric Infectious Diseases Unit for recurrent skin infections, two adolescents of 12 and 13 years old and a 3 year old children. Both teenagers had a history of recurrent cutaneous abscesses, immunodeficiencies were ruled out and colonization by MRSA was demonstrated in microbiological tests. After an eradication treatment with topic mupirocin was administered and decolonization measures were put in place, recurrent skin infections disappeared. The 3 year old children also had a history of recurrent skin infections, including a MRSA cellulitis that required hospital admission. She wasn't colonized but his father (who suffered from severe atopic dermatitis) was. After the eradication treatment was given to the whole family, she hasn't had any more skin infections.

Learning Points/Discussion

Community-associated MRSA is an emerging cause of recurrent skin infections and this possibility it should be included in the differential diagnosis. The colonized individual might be asymptomatic but serve as a carrier for other members of the family so the whole household must undergo eradication treatment. Current treatments include both topic mupirocin and decolonization measures.

ESPID19-0104
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

A new way of mapping malaria transmission intensity in nigeria and beyond

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Background

There have been several attempts at mapping malaria prevalence, particularly in areas where there is the highest burden of the disease. Unfortunately, the least information exists in these areas. Most of these maps aim to bridge these gaps by estimating the prevalence, based on mathematical models, utilising geographic information of locations. prominent among these is the Malaria Atlas Project (MAPs). We propose a new way of mapping Malaria transmission globally, particularly in areas where there is some information of malaria transmission.

Methods

We use Geographic Information Systems to make these maps. Using a base map of Nigeria, we geo-locate the sites of previous malaria surveys, particularly the Nigerian Malaria Indicator Survey of 2010. The prevalence in each of the sites is transformed to the estimated prevalence among children 2 to 10 years of age and extend the prevalence in each case to 10km of the index site, based on the average flight distance of the predominant vector in this region. It is also extended a further 5Km, based on the maximum flight distance of the vector. The product is a multi-pixel map.

Results

The map shows a representation of the prevalence of malaria across the sites. This is compared with the corresponding timepoint of MAP representation. It shows significant differences from MAPs. However this is more accurate than MAPs, where data is available, but it doesn't cover the entire landscape, leaving areas of limited information.

Conclusions

Using GIS, data on malaria transmission intensity can be extended beyond the actual sites of malariometric surveys, with a greater accuracy and can be the gold standard for mapping disease-transmission-intensity. The challenge lies in ensuring that these surveys are conducted uniformly and with universal spread.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1115
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

When fever is not an infection

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Background

The most common cause of fever of unknown origin is an infection, but other possibilities must be excluded, including autoimmune diseases.

Case Presentation Summary

A 14 year-old girl, with Raynaud phenomenon for several years, presented to the emergency department with a two month history of daily fever, fatigue, weight loss (11%), arthralgias and myalgias. There was an episode of puffy hand and puffy feet at the onset of the disease. On physical exam the patient was malnourished, had decreased muscular strength, arthritis of the shoulders, elbows, wrists and knees and enlarged lymph nodes. It was detected anemia (7.2g/dL), lymphopenia (610/mcL), an elevated ESR (84mm/h), CK (548 UI/L), AST (120 U/L), LDH (773 U/L) and ferritin (1485ng/mL). The abdominal ultrasound showed hepatosplenomegaly, ascites and pleural effusion. A pericardial effusion was detected on the echocardiogram. All cultures and serologies were negative. The Coombs direct test was positive. Antinuclear antibodies, anti-DNAds, anti-Sm and anti-RNP antibodies were detected. The sCD25 (7020pg/mL) was elevated. The bone aspirate was normal, and the patient was started on methylprednisone. The patient fulfilled the SLICC criteria for systemic lupus erythematosus (SLE) and the Khan criteria for mixed connective tissue disease. Furthermore, the patient fulfilled the PRES criteria for macrophage activation syndrome in SLE patients. There was immediate clinical response to the first dose of methylprednisone. Afterwards, the patient developed myocarditis, without heart insufficiency. The patient was discharged after 3 weeks in hospital. Currently, the patient is being treated with methotrexate, prednisolone and hydroxychloroquine and is asymptomatic.

Learning Points/Discussion

This case demonstrates how similar can the presentation of an autoimmune disease be to an infection and how important it is to distinguish them, in order not to delay diagnosis and treatment.

ESPID19-0787
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

A population based observational study of childhood encephalitis in children admitted to paediatric intensive care units in england and wales

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Background and Aims:

Encephalitis is a serious neurologic condition which can result in admission to intensive care. Yet, there are no studies on paediatric intensive care unit (PICU) admission rates and usage of intensive care resources by children with encephalitis in England and Wales.
The objectives of this study were to (i) define the PICU incidence and mortality rates for childhood encephalitis, (ii) describe usage of intensive care resources by children with encephalitis admitted to PICU, and (iii) explore the associated cost from PICU encephalitis admissions.

Methods:

Retrospective analysis of anonymised data for 1031 children (0-17 years) with encephalitis admitted (January 2003 to December 2013) to PICU in England and Wales.

Results:

The PICU encephalitis incidence was 0.79/100,000 population/year (95%CI 0.74-0.84), which gives an annual total of 214 bed days of intensive care occupancy for children admitted with encephalitis and an estimated annual PICU bed cost of £414,230 (IQR 198,111-882,495) for this cohort. PICU encephalitis admissions increased during the study period (annual percentage change = 4.5%, 95%CI 2.43%-6.50%, p=<0.0001). In total, 808/1024 (78.9%) received invasive ventilation while 216/983 (22.0%) and 50/890 (5.6%) cases received vasoactive treatment and renal support, respectively. There were 87 deaths (8.4%), giving a PICU encephalitis mortality rate of 0.07 /100,000 population (0-17 years)/year (95%CI 0.05-0.08).

Conclusions:

These data suggest that encephalitis places a significant burden to the healthcare service. More work is needed to improve outcomes for children with encephalitis.

Systematic Review Registration:

N/A

ESPID19-0359
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

Benign acute childhood myositis

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Background

Acute viral myositis is one of the possible complications of infection by the Influenza virus and also by other viruses. It constitutes a little recognized clinical entity that appears as a very characteristic picture.It is very important to carry out an adequate clinical examination to avoid performing diagnostic tests and unnecessary treatments

Case Presentation Summary

Ten-year-old girl who came to the emergency department due to low-grade fever, malaise and pain in the calves of five days of evolution with limited walking.

During the examination, pain in the calf palpation without skin lesions associated, difficulty walking and antialgic walking on tiptoe, was observed. Rest of exploration and neurological examination were normal.

Blood test was performed in which leukopenia (2800 total leukocytes) and lymphopenia (900 total lymphocytes) were observed, with normal general biochemistry, except for CK 591 IU / L, CPR <0.6 mg / dl. Urine test was normal. Acute bening myositis was the diagnosis in the admission.

During admission, CK elevation was observed up to 1223IU/L, multiple PCR of respiratory viruses was performed, being positive for Parainfluenza type 2. The evolution was good, receiving fluid therapy and anti-inflammatory treatment, resolving the analytical and clinical parameters prior to discharge.

Learning Points/Discussion

Acute benign postviral myositis usually occurs at the age of 3-7 years. In most cases it is associated with infection by Influenza B (62%) and Influenza A (25%), although associations have also been described with Cosackie, Parainfluenza, HSV, CMV, Epstein-Barr virus, adenovirus, virus of rubella, parvovirus B19, arbovirus, retrovirus (HIV), mumps virus, hepatitis C and Campylobacter.

The availability of new diagnostic techniques such as multiple PCR of respiratory viruses allow us to reach an etiological diagnosis of previously unrelated cases.

ESPID19-0275
Science and Educational Track

Independent E-Poster Presentations 11 - Population Studies & Interesting Cases - Station 07

Paracetamol and antibiotic use for high fever in children admitted at the children's clinic hospital

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Background and Aims:

Introduction: Fever represents one of the most frequent causes of hospital admissions, especially in infants and young toddlers.

Aim of the study: primary objective was to unfold patterns of high fever in children.

Secondary objectives were: a.) to evaluate Paracetamol usage in patients before and during hospital admission and its association with ALT, AST elevated levels, b.) to review the rate of antibiotic prescription in those children.

Methods:

Patients and methods: A retrospective study was conducted and included all the children with body temperature>39*C at admission or during hospitalization who were admitted to the Children's Clinic Hospital Brasov, Romania.

Results:

Results: Girls outnumbered boys, 58% were less than 2 years of age, 28% were Romas. Most high fever cases occured with peaks in November-December. 93% of the patients were febrile at home, 44.72% at admission. The majority of the patients presented high fever for one day during hospitalization(43.9%).

Paracetamol use prior to hospitalization was 60%. The usage of Paracetamol did not determine higher levels of liver enzymes. (p=0.15 and p=0.75).

In 26% of the cases, antibiotics were prescribed before admission and in 66.26% after admission, from which 15.04% received 2 antibiotics.

The usage of antibiotics before hospital admission reduced the febrile period (p= 0.00034) but did not shorten the hospitalisation time. Patients with higher WBC (mean WBC=13.99 $x10^3$) were longer febrile (p=0.0013), received more antibiotics ($p=5.49X10^{-5}$), had a longer hospitalization time (p=0.00027). Patients with elevated CRP (mean CRP=5.14 mg/dl) levels were likelier to get antibiotic treatment (P=0.015) and received prolonged antibioterapy (p=0.019).

Conclusions:

Conclusions: Admission for high fever in children is more common in children with higher socioeconomic status. The usage of Paracetamol did not affect higher levels of liver enzymes

Systematic Review Registration:

Not applicable

ESPID19-0745
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

Non-aspergillus fumigatus species in children with cystic fibrosis

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Background

Patients with cystic fibrosis (CF) are at high risk of colonization of the airways by specific bacterial pathogens such as *Staphylococcus aureus*, *Haemophilus influenzae* and *Pseudomonas aeruginosa*. Recently, an increasing recognition of fungal isolates has emerged such as *Candida* and *Aspergillus* species. Among *Aspergillus* species, *Aspergillus fumigatus* is the most common filamentous agent of chronic colonization of the airways. However, other non-*Aspergillus fumigatus* (NAF) species such as *Aspergillus terreus*, *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus nidulan*s, may also be responsible for transient or chronic colonization. Our aim was to detect CF patients who were colonized by NAF species in their respiratory system during childhood.

Methods

Medical records of 208 children frequently followed at the CF center were retrospectively reviewed in order to identify those who had a history of positive respiratory cultures for NAF species.

Results

Three NAF species were detected: *A. terreus*, *A. flavus* and *A. niger* in 10 CF patients. The median age of isolation was 13.1 years. All patients had exocrine pancreatic dysfunction and 8 of them had at least one F508del mutation. The median BMI was 19.37 kg/m^2, while the median FEV_1 %predicted was 79.72%. During the last 12 months prior to NAF isolation, 6 children were receiving oral or inhaled corticosteroids and all patients were receiving oral or inhaled antibiotics. Five patients had a history of *Staphylococcus aureus* isolation, 6 patients had a history of other fungal isolation and 6 patients were chronically or intermittent colonized with *Pseudomonas aeruginosa*.

Conclusions

NAF species are not commonly detected in our patients and little is known about their epidemiology yet. Additional studies are needed to shed light on their clinical significance, risk factors and possible prophylactic measures.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1152
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

Acute viral infection as a cause of protein-losing gastropathy in children

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Background

Protein-losing gastroenteropathies result in an excessive loss of serum proteins in the gastrointestinal tract, leading to edema. This diagnosis should be considered whenever there is hypoproteinemia with an adequate supply, a normal synthesis in the liver and an exclusion of proteinuria. Acute viral infections, the most frequent infections in children, can cause this, by increasing mucosal permeability and protein leakage into the lumen.

Case Presentation Summary

2-year-old male, with a background of recurrent bronchiolitis, was admitted for sporadic, but daily, vomiting episodes evolving over 1 week and bilateral palpebral edema that started 2 days before admission. He also refered diffuse abdominal pain in the day of the admission. Upon examination he had a moderate palpebral bilateral edema. Laboratory investigation revealed hypoproteinemia, hypoalbuminemia and low serum levels of immunoglobulin G, with normal coagulation tests and without proteinuria. Culture and search for parasites in stools was negative. Cytomegalovirus (CMV) serology was IgG+ (weak)/IgM+. The endoscopy revealed inflammation of the gastric fund with superficial ulcerations of the body. Biopsies showed intense activity gastritis. Immunocytochemistry was negative for helicobacter pylori and positive for CMV. Diagnosis of CMV protein-losing gastropathy was assumed, starting a protein enriched diet (3g/Kg) and esomeprazol, with progressive regression of the edemas and normalization of total protein and albumin serum levels.

Learning Points/Discussion

This case report points to a possible complication of a common viral infection in children that can result in a significant hypoproteinemia and hypoalbuminemia potentially compromising the well being and growth of a child.

ESPID19-0715
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

First results of burkholderia infection control in russian cystic fibrosis population

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Background

The most dangerous infection for the Cystic Fibrosis (CF) patients is Burkholderia spp. The most prevalent CF species in Russia, as in Europe and North America, is B. cenocepacia. Highly transmissible strain B. cenocepacia sequence type (ST) 709 is epidemic strain for Russian CF patients. Cohort segregation of Bcc positive patients was not enough to decrease the prevalence of ST709. Individual boxes introduced in 2015 for the hospitalization and enhanced infection control during outpatient admissions helped to preclude further spread of epidemic strain. The aim of this work was the analysis of the epidemic situation after strong epidemic measures implementation.

Methods

Sputum and tracheal aspirates of 670 CF patients 1949-2018 year of birth with middle age 18 years (children were 50%) were analyzed by molecular-genetic methods including Multi Locus Sequence Typing (MLST). Strains of new ST were isolated, characterized, collected, and deposited in the PubMLST database.

Results

152 patients were infected by Burkholderia in analyzed cohort. 5 genotypes were common in adult (AG) and children group (CG). The prevalence of B. cenocepacia ST709 cases decreased from 80% in AG to 55% in CG. However the prevalence of ST208 increased to 16% in CG. The cases of B. multivorans infection were absent in CG, but new acquisitions in CG being caused by different genotypes of B. gladioli (965, 629, 903), B. stabilis ST627, B. contaminans ST482 and new B. cenocepacia ST. Transient infection was frequent in CG. Only 1 case of Burkholderia eradication was documented in AG, but there were 3 cases in CG

Conclusions

Strong epidemic measures resulted in increasing the diversity of species and genotypes of Burkholderia detected in CF patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0577
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

A case of severe meningoencephalitis caused by varicella-zoster virus and borrelia burgdorferi mixed infection

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Background

Lyme disease caused by Borrelia burgdorferi infection is one of the most common vector-borne diseases in Ukraine. Varicella - a typical form of primary Varicella-zoster virus (VZV) herpetic infection – is also extremely widespread in Ukraine due to low public immunization rate. Both pathogens may present as a neuroinfection causing immune mediated cerebral vasculitis. Due to the high prevalence of the pathogens mentioned there is a high probability of co-infection, which can lead to clinical pathomorphosis and uncertainty in assessing the possible outcome.

Case Presentation Summary

We observed a case of severe coma in a 7 year old boy which developed a week after a varicella infection episode diagnosed clinically. Acute varicella zoster encephalitis was identified, which provided a basis for acyclovir IV therapy initiation. Due to severity and progression of neurological disorders we performed additional CSF testing by PCR for Herpes simplex viruses type 1 and 2, Epstein-Barr virus, Borrelia burgdorferi, Mycobacterium tuberculosis and enteroviruses. B. burgdorferi DNA was detected. It is notable that the patient had no relevant history of tick bite or erythema migrans. Combination of ceftriaxone and acyclovir IV therapy had positive effect. Glasgow coma scale score improved from 5 to 12 points and spontaneous respiration restored on the 4th day.

Learning Points/Discussion

The mixed infection of VZV and B. burgdorferi is a potential life threatening co-infection which may have a permissive CNS damaging effect with unclear mechanisms. Testing for molecular biological and/or serological markers of Lyme disease should be a standard procedure in patients with any signs of severe neuroinfection in Ukraine, regardless of history data. Administration of the 3rd generation cephalosporines infusion in combination with acyclovir is effective first choice treatment which provides a basis for a favorable prognosis.

ESPID19-0479
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

Bocaviruses as respiratory viral pathogens in children under 5 years old in bulgaria

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Background

Acute respiratory tract infections (ARTI) are associated with high morbidity, huge number of doctors' visits and hospital admissions among young children. A wide range of viruses cause respiratory infections with varying severity. This study aims to determine the viral aetiology of paediatrc ARTI, contribution and clinical impact of bocaviruses (BoVs) during three successive epidemic seasons in Bulgaria.

Case Presentation Summary

Methods: Clinical, epidemiological data and nasopharyngeal swabs were prospectively collected from children under 5 years old presenting with ARTI during the 2016/2017, 2017/2018 and 2018/2019 seasons. Viral aetiology was determined by Singleplex Real Time PCR against 11 respiratory viruses - influenza viruses, respiratory-syncytial virus (RSV), human metapneumovirus, parainfluenza viruses 1/2/3, rhinoviruses (RV), adenoviruses (AdV) and BoV.

Results: Of the 1043 children examined, 860 (82%) were positive for at least one respiratory virus. Respiratory-syncytial virus was most frequently identified virus. BoVs were detected in 83 (8%) specimens and were the fourth in frequency after RSV, RV and influenza viruses. Co-infections including BoV were found in 37 (4.3%) of infected children and they accounted for 44% of all BoV infections. BoVs were identified in 19.5%, 11%, and 6% of children with laryngitis/laryngotracheitis, bronchiolitis and pneumonia, respectively. BoV infections were more prevalent in the autumn and the spring.

Learning Points/Discussion

BoVs are committed to the development of ARTI in children younger than 5 years of age. Our study confirms the characteristic feature of BoV- the high rate of co-infections with other respiratory viruses.

ESPID19-0169
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

Impact of down syndrome, cystic fibrosis and immunodeficiency on respiratory syncytial virus hospitalisations (rsvh) in the first two years of life

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Background and Aims:

Down Syndrome (DS), cystic fibrosis (CF) and immunodeficiency (ID) are associated with an increased risk of RSVH in young children, although data remain limited. This study assessed RSVHs in these conditions using national data over a 12-year period.

Methods:

Datasets covering National Health Service hospital care within Scotland were used to identify, using ICD-10 codes, all children with DS, CF and ID (including HIV, transplant, leukaemia) born 2000-2011. RSVHs were assessed over the first 2 years of life and compared to those in the overall population (OP).

Results:

The incidence of RSVH was 14.7% (86/587) for DS, 12.4% (30/241) for CF, and 9.5% (61/644) for ID vs. 2.1% (13,362/623,770) in the OP (all p<0.0001). The corresponding RSVH rates were 165.2/1,000, 141.1/1,000, 114.9/1,000, and 27.2/1,000, respectively (all p<0.0001 vs. OP). Median age at first RSVH was higher for DS (282 days; p<0.0001), ID (230 days; p<0.0001) and CF (206 days; p=0.15) vs. the OP (137 days). Intensive care unit (ICU)/high dependency unit (HDU) admission rates were 17.5% (17/97; p<0.0001) for DS, 12.2% (9/74; p=0.0009) for ID, and 2.9% (1/34; p=0.6981) for CF compared to 4.3% (727/16,946) in the OP. Children with CF (median 26 days; p=not calculable), DS (16 days; p<0.0001), and ID (14 days; p<0.0001) spent longer in ICU/HDU than the OP (5 days). Median length of total stay was also longer (CF: 7 days, p=0.045; DS: 6 days, p<0.0001; ID: 4 days, p<0.0001) compared to the OP (2 days).

		DS	CF	ID	OP
Number of children		587	241	644	623,770
≥1 RSVH	n (%)	86 (14.7%)	30 (12.4%)	61 (9.5%)	13,362 (2.1%)
	p-value vs. OP	<0.0001	<0.0001	<0.0001	-
Admission rate	Rate *per* 1,000 (number of admissions)	165.2 (97)	141.1 (34)	114.9 (74)	27.2 (16,946)
	p-value vs. OP	<0.0001	<0.0001	<0.0001	-
>1 admission	n (%)	9 (1.5%)	3 (1.2%)	11 (1.7%)	2,547 (0.4%)
	p-value vs. OP	<0.0001	0.0418	<0.0001	-
Age at first admission	Median [IQR]	282 [128-401]	206 [119-352]	230 [75-409]	137 [62-264]
	Mean (SD)	286 (184)	225 (141)	261 (203)	185 (156)
HDU/ICU usage	p-value vs. OP	<0.0001	0.1523	<0.0001	-
	n (% of admissions)	17 (17.5%)	1 (2.9%)	9 (12.2%)	727 (4.3%)
	p-value vs. OP	<0.0001	0.6981	0.0009	-
HDU/ICU LOS	Median [IQR]	16 [10-21]	26 [NA]	14 [6-29]	5 [2-8]
	Mean (SD)	24.12 (25.70)	26 (NA)	29.67 (46.70)	7.05 (10.02)
	p-value vs. OP	<0.0001	NC	<0.0001	-
Inpatient LOS	Median [IQR]	6 [3-12]	7 [2-12.5]	4 [2-7.75]	2 [1-4]
	Mean (SD)	10.60 (14.50)	8.32 (8.83)	22.47 (12.10)	3.80 (13.14)
	p-value vs. OP	<0.0001	0.0450	<0.0001	-

CF: cystic fibrosis; DS: Down syndrome; HDU: high dependency unit; ICU: intensive care unit; ID: immunodeficiency; IQR: interquartile range; NC: not calculable; OP: overall population; RSVH: respiratory syncytial virus hospitalisation; SD: standard deviation.

Conclusions:

This study provides further evidence that DS, CF and ID are significant risk factors for RSVH, with the results suggesting an extended period of risk and greater healthcare resource utilisation.

Acknowledgements
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Systematic Review Registration:

N/A

ESPID19-0154
Science and Educational Track

Independent E-Poster Presentations 12 - LRTI & Cystic Fibrosis & Interesting Cases - Station 09

Outcomes of respiratory viral infection in young children hospitalized with acute wheezing

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Background

Viral infection is one of the important causes of wheezing in young children. This may result in subsequent wheeze and asthma in later life. This study aimed to determine incidences of persistent wheeze and sensitization to dust mites at 24 months of follow-up among young children who were hospitalized with acute wheezing.

Methods

This was a prospective cohort study of 100 children, aged 3-48 months, who were hospitalized at Thammasat University hospital with acute wheezing and followed for 24 months. Nasopharyngeal aspiration at the admission were identified for influenza, respiratory syncytial virus (RSV), rhinovirus and enterovirus68 using polymerase chain reaction (PCR). Sensitization to dust mites was evaluated at the completion of follow-up by skin prick test with a positive result of a wheal ≥3 mm diameter.

Results

Seventy-four cases with 54 boys (73%) were completely followed for 24 months. There were 42 cases (56.8%) positive for viral PCR including rhinovirus (n=30), RSV (n=8) and enterovirus68 (n=4). The incidences of persistent wheeze (recurrent wheeze needing emergency visits in the last 4 months of follow-up) were 26.2% (95% confidence interval: 13.9%-42.0%) and 13.6% (95% confidence interval: 3.5%-29.0%) among cases with and without viral causes respectively. Sensitizations to dust mites were 28.6% and 15.6 % among cases with and without viral causes respectively. Cases with positive rhinovirus had the highest incidences of persistent wheeze (30.0%) and sensitization to dust mites (33.3%).

Conclusions

Respiratory viral infection, especially for rhinovirus, is the prognostic factor of persistent wheeze and sensitization to dust mites in young children with wheezing.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0766
Science and Educational Track

Independent E-Poster Presentations 13 - Antimicrobials - Station 11

Pandrug resistant acinetobacter baumannii ventriculitis: first experience of intrathecal colistin treatment in soetomo hospital

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Background

Healthcare-associated ventriculitis is one of the complication that will develop in neurosurgical patients with external ventricular drainage. In recent years, *Acinetobacter baumannii* has emerged as healthcare-associated infection (HAI) pathogen. It easily causes severe infection in critical and prolonged hospital stay patients and contributes to multidrug resisitant (MDR) and pandrug resistant (PDR) antibiotics. Colisitin is used as salvage therapy for infection caused by PDR. We here report the first experience use of intrathecal colistin in healthcare associated ventriculitis caused by pandrug resistant Acinetobacter baumannii.

Case Presentation Summary

A one-month-old boy suffers from fever and recurrent seizure. Three weeks ago he had undergone cranio-surgery to evacuate intraventricular and subdural hemorrhage which unknown caused of bleeding. Cerebrospinal fluid (CSF) analysis showed a bacterial infection. Tigecyclin antibiotics was given intrathecally for initial treatment based on CSF culture yielded *Cronobacter sakazakii complex* but the condition persists. The evaluation of CSF culture yielded *A. baumannii* which is resistant to all antibiotics. Colisitin is administered intrathecal every 8 hours for 21 days. During colisitin therapy, patients showed clinical improvement, and the evaluation of CSF culture yielded sterile. We didn't find any side effect during therapy and he was discharged in good condition.

Learning Points/Discussion

Our first experience suggests that intrathecal colistin is a potentially effective and safe therapy for the treatment of pan-drug-resistant *A. baumannii* healthcare-associated ventriculitis.

ESPID19-0688
Science and Educational Track

Independent E-Poster Presentations 13 - Antimicrobials - Station 11

Current antimicrobial susceptibility testing overlooks azithromycin activity against achromobacter xylosoxidans

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Background

Müeller-Hinton Broth (MHB) has been the standard media utilized in performing antimicrobial susceptibility testing across the globe, serving as the foundation for clinical antibiotic management, health care epidemiology, and drug discovery. In the current era where serious infections are often “resistant” to most, if not all, safe and reliable antibiotics in standard MHB susceptibility testing, we have been exploring a key question: can useful insight be gained if antibiotic susceptibility testing is performed in a media designed to better recapitulate the *in vivo* environment? Here we probe differential activity of the familiar antibiotic azithromycin (AZM) vs. multidrug-resistant (MDR) Gram-negative bacillus *Achromobacter xylosoxidans* (AX) in eukaryotic tissue culture media vs. MHB.

Methods

Eleven clinical strains from refractory AX infections in which AZM treatment was used in salvage therapy were included. AZM MIC testing, time-kill assays, biofilm assays and fluorescence microscopy were performed in MHB or mammalian tissue culture media. AZM sensitization of AX to innate immune clearance was tested in human serum and neutrophil killing assays.

Results

We observed potent bactericidal activity of AZM against AX in mammalian tissue culture medium that was absent in bacteriological medium. Human serum strongly potentiated AZM killing of AX. Additionally, AZM monotherapy inhibited preformed biofilm growth in a dose-dependent manner together with a reduction in viability of AX at physiological attainable AZM doses.

Conclusions

Despite lack of activity in standard MIC testing utilizing MHB, AZM kills AX in medium mimicking tissue fluid conditions, paralleling its successful use as salvage therapy in difficult AX cases. AZM merits further exploration in the treatment of drug-resistant AX infections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0119
Science and Educational Track

Independent E-Poster Presentations 13 - Antimicrobials - Station 11

The impact and cost-effectiveness analysis of multiplex pcr respiratory panel for pediatric respiratory infection in japan.

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Background and Aims:

Rapid molecular diagnosis has been contributed to timely treatments and antimicrobial stewardship. However, its benefit and cost-effectiveness vary in each country or community because they have different standard practice and health care system. Japan frequently uses rapid antigen tests (RATs) for pediatric respiratory infections. We investigated the impact and cost-effectiveness of multiplex PCR (mPCR) respiratory panel for pediatric respiratory infection in Japan.

Methods:

We replaced rapid antigen tests to mPCR (FilmArray® respiratory panel) for all admitted pediatric respiratory infections at the end of March 2018. We compared days of antimicrobial therapy (DOT) and length of stay during mPCR period (April 2018 to August 2018) with those of RAT period (March 2012 to March 2018).

Results:

During the RAT and mPCR periods, 1,179 and 52 patients were analyzed. Microbiological diagnosis rates were 29.6% vs 88.5% ($p<0.001$). DOTs/patient were 12.7 vs 6.8 ($p<0.001$), and lengths of stay were 8.2 vs 7.1 days ($p=0.371$) in RAT and mPCR periods. The medical and social costs during admissions were \182,102 vs \161,683 JPY and \109,290 vs \94,378 JPY, respectively. Considering the cost for one mPCR test is approximately \20,000 JPY, the mPCR in the study setting was cost-saving and dominant.

Conclusions:

The mPCR has contributed to a significant antimicrobial reduction in a Japanese community hospital for admission-requiring pediatric respiratory infections compared to conventional RAT. Further studies are warranted to evaluate the overall impact and cost-effectiveness in the nation.

Systematic Review Registration:

N/A

ESPID19-0042
Science and Educational Track

Independent E-Poster Presentations 13 - Antimicrobials - Station 11

The use of antibacterial drugs for treatment of acute diarrheal diseases in ''nork'' ich, armenia

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Background and Aims:

Armenia is located in the South of Caucasus and diarrheal diseases are actual problem of healthcare system. The most common causes of diarrheal diseases are Rotavirus and other viruses, Shigella, non-typhoid Salmonellas, E. coli (including EHEC), Campylobacter, Giardia etc. The last outbreak of cholera was in 1998. Our goal is to describe the use of antibacterial therapy in acute diarrheal diseases of hospitalized patients.

Methods:

We used the medical charts of patients(up to 7 years) with acute diarrheal diseases admitted to “Nork” hospital during the period of 01.04-15.05 in 2018.

Results:

During the above mentioned period 156 patients were admitted from which 125(80.1%) had watery and 31(19.9%) bloody diarrhea. The most common pathogens were Salmonella(13), Shigella(4), Clostridium difficile(2), EHEC(2). Double culturing of stool was done for all of the patients. Stool culture was positive in 12(9.6%) cases suffering from watery diarrhea and 10(32.3%) cases from bloody diarrhea. Overall, 90 patients were managed with antibacterial drugs. All 10 culture-positive (including 2 patients with diagnosed EHEC) and 14(66.67%) of 21 culture-negative patients with bloody diarrhea had taken antibacterial treatment. Antibacterial treatment was also given to 7(58.3%) of 12 culture-positive and 49(41.5%) of 118 culture-negative patients with watery diarrhea. Widely used antibacterials were nifuroxazide50(55.6%), azithromycin4 (4.4%), amoxicillin1 (1.1%), metronidazole3 (3.3%), ciprofloxacin12 (13.3%), TMP-SMX6(6.7%), cefotaxime1(1.1%), ceftriaxone13(14.5%). It was found out, that antibacterials were not indicated to 81(90%) of 90 patients according to the guidelines.

Conclusions:

The vast majority of patients with watery diarrhea were treated with antibacterials which is not in agreement with international and national guidelines. To prevent overuse of antibacterials we recommend to implement guidelines actively into clinical practice by supplying the information with seminars for primary and secondary care physicians.

Systematic Review Registration:

N/A

ESPID19-0034
Science and Educational Track

Independent E-Poster Presentations 13 - Antimicrobials - Station 11

Voiding cystourethrography-related urinary tract infection in patients with previous uropathy

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Background and Aims:

Pediatric population subjected to voiding cystourethrography (VCUG) is a risk group for the development of VCUG-related urinary tract infection (UTI). Several studies about the incidence of urinary tract infection after VCUG showed variable data. The objective of this study is to determine the incidence of UTI after performing the VCUG, describe prophylaxis guidelines and risk factors.

Methods:

Retrospective, observational, descriptive and unicenter study. All consecutive immunocompetent patients below 18 years of age, with previous uropathy, who underwent VCUG from January to December 2016, were included. VCUG-related UTI was defined as the presence of compatible symptoms and urine growth of $\geq 10^5$ colony-forming units (CFU) of a single microorganism for samples of midstream urine or $\geq 10^4$ CFU in samples taken by catheterization, in the following 7 days after the test.

Results:

One-hundred and one patients were included. Median age was 1.2 years (IQR=6.3) and 58% (n=59) were male. The most prevalent uropathies were pelvicalyceal dilatation in 78% (n=79) and vesico-ureteral reflux (VUR) in 26% (n=26), respectively. Forty four percent of all patients (n=45) had a history of recurrent UTI. The most commonly prescribed prophylactic antibiotics were trimethoprim (42%) and trimethoprim-sulfamethoxazole (35%). High-grade VUR was found in 28%. The incidence of VCUG-related UTI was 5% (n=5). In 4 cases high-grade VUR (grade≥III) was found, with a statistically significant risk ratio (OR=12, 95% CI 1.2-112.6; $p < 0.05$).

Conclusions:

The incidence of VCUG-related UTI is significative and may be related to the exclusive inclusion of patients with uropathies. Its implementation should be limited to cases with a clear clinical indication and preventive measures should be optimized.

Systematic Review Registration:

NA

ESPID19-1197
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

10 years of hpv vaccination in slovenia, what can we do better?

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Background

The vaccination schedule programs in Slovenia were all mandatory. In 2009 the new **HPV** vaccine was approved from the Ministry of Health. It was the first recommended vaccine in Slovenia free of charge and payed from the government. This was a new challenge for school doctors of our country to implement it to school girls at contemporary rate of developed countries. Due to the European references and guidelines we vaccinate girls in the 6 grade of primary school with 9-valent vaccine. Our main goal in the last years is to achieve high vaccination rate for girls in all regions. In addition, we intend to convince the Ministry of Health for implementation of the general neutral vaccine (GNV) also for boys.

Methods

The acceptance of the HPV recommended vaccine was a great challenge. On professional level we tried to build a communication bridge between medical experts and school doctors on annual meetings. On public level, school doctors have possibility for communication with parents on annual school meetings.

Results

The vaccination coverage for girls in different regions still varies from 30 to 80%. The highest rate is achieved in regions where school doctors have good communication with school administration and parents.

Conclusions

Acceptance of a HPV vaccine depends on education, information, communication and confidence between medical experts, school doctors, parents and health providers. In the last years school doctors in some regions gained the confidence with local authorities and managed to vaccinate boys, free of charge. Due to the guidelines, implementation of the general neutral vaccine (GNV) should be spread also in Slovenia.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESPID19-0212
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

Post-marketing surveillance of hexyon vaccine administered in preterm infants in the apulia region (italy) in 2017

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Background and Aims:

While clinical trials and surveillance data of hexavalent vaccines have demonstrated good tolerability in term-born infants, data about preterms are limited. After more than two years' use, we conducted a post-marketing surveillance of Hexyon (Hexaxim) safety in preterms born in the Apulia Region in 2017.

Methods:

To identify preterms, we extracted the hospital discharge records of infants born between January-June 2017, using DRG and ICD-9-CM codes; then we linked this list with the immunization records. To investigate adverse events (AEs) after the first dose, we interviewed via phone the parents of preterms vaccinated with at least one dose of Hexyon. AEs frequencies were calculated and compared to those reported for term-born infants in the Summary of Product Characteristics.

Results:

In Apulia, a total of 866 preterms out of 936 (92.5%) received the first dose of hexavalent vaccine and 57.6% were vaccinated by the 3rd month of age as recommended. Out of 866, 80.8% received Hexyon. We interviewed the parents of 339 preterms vaccinated with Hexyon, 97.8% of whom received co-administration with PCV13 and 72.5% also with anti-rotavirus. The most common local reactions were: pain (35.7%), redness (27.1%) and swelling (26.5%). As for systemic AEs: irritability (27.4%), fever (22.4%) and somnolence (16.2%). No serious AEs were reported.
Compared to the expected frequency of AEs in term-born infants, in our preterm population the injection site induration, nodule and the rash were more frequent, while loss of appetite, vomiting and persistent crying were less frequent (Table).

Conclusions:

This surveillance study showed that over 40% of preterms received delayed hexavalent vaccination. The AEs to Hexyon were mainly local or mild. These preliminary results confirm the safety of this hexavalent vaccine also in preterm population.

Systematic Review Registration:

ESPID19-1146
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

Tick-borne encephalitis vaccination in patient with cryopyrin-associated periodic syndrome treated with il-1 receptor antagonist

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Background

Cryopyrin-associated periodic syndromes (CAPS), caused by gain-of-function mutations in NLRP3, are characterized by IL-1β-mediated systemic inflammation. Neonatal onset multi-system inflammatory disease (NOMID) is the most severe form of CAPS with involvement of CNS.

In Slovenia incidence of tick-borne encephalitis (TBE) is among highest in Europe. The most effective method of preventing TBE is vaccination.

We report a case of patient with NOMID that went through TBE vaccination.

Case Presentation Summary

Female patient, first child in family, was diagnosed at the age of 2 years with NOMID due to episodes of periodic fevers, skin rash and raised inflammatory markers since birth. Mutation in NLRP3 confirmed the disease. At the evaluation, there were already signs of CNS involvement on brain MRI, which partially resolved together with other signs of the disease on IL-1 receptor antagonist (anakinra) treatment.

At the age of 3.5 years risks of possible TBE infection in NOMID patient were evaluated.

Patient received three doses of FSME Immune Junior vaccine (0-2-10 months interval) with continuation of anakinra treatment. Before receiving each dose, patient was thoroughly examined and vaccinated only if no clinical or laboratory markers of inflammation were present. After first dose, reappearance of fever with rash together with increase of multiple inflammatory markers were observed. Episode was self-limiting, fever and rash resolved within 3 days, inflammatory markers normalized within a week. Second dose was uneventful, reaction after third dose was less intense and lasted only 48 hours.

Specific antibodies on TBE after third dose are pending.

Learning Points/Discussion

To our knowledge there is no specific data on safety and efficacy of TBE vaccination in CAPS patients receiving IL-1 receptor antagonist. Our patient received TBE vaccine without major adverse events.

ESPID19-0899
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

Mathematical modelling on the impact of changing from a 2+1 to a 1+1 pcv13 schedule on invasive pneumococcal disease in england and wales

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Background

The Joint Committee on Vaccination and Immunisation in the United Kingdom has recommended In October 2017 removal of one primary dose of the 13-valent pneumococcal conjugate vaccine (PCV13) currently given as a 2+1 schedule (2, 4 and 12 months) based on a mathematical modelling study and a 1+1 immunogenicity study.

Methods

We developed age-structured, dynamic, deterministic models of pneumococcal transmission in England and Wales to describe the impact on IPD cases of 7-valent PCV (introduced in 2006) and PCV13 (introduced in 2010). We considered various models to investigate potential reasons for the rapid increase in non-PCV13 (NVT) IPD cases since 2014.

Results

Our findings did not implicate the introduction of live attenuated influenza vaccine for children in 2014 and indicated that emergence of individual NVT serotypes with higher virulence as a result of ongoing replacement was likely responsible and that the NVT increase would level off from 2020. Long-term simulation results suggest that changing to a 1+1 schedule would have little overall impact as any increase in vaccine-type IPD would be offset by a reduction in NVT IPD. Under the base case scenario, a change to a 1+1 schedule in 2018 was predicted to produce 24 (5, 51) additional IPD cases over five years and 56 additional pneumococcal-CAP cases, with 5 (0, 13) additional deaths, none of which were in children under 15 years.

Conclusions

Our study found that, with the current mature status of the PCV programme in England and Wales, removing one of the primary doses in the first year of life would have little impact on IPD or pneumococcal CAP cases or associated deaths at any age.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0640
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

The current status of immunisation against multi-drug resistant gram negative bacteria: review of the literature

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Background and Objective

The burden of sepsis caused by enteric Gram-negative bacteria continues to rise globally and is becoming increasingly difficult to treat because of resistance to multiple antibiotics. In many parts of the world, multi-drug resistant Gram-negative bacterial (MDR-GNB) infections are now a major threat to achieving the Sustainable Development Goal of reducing neonatal mortality. With limited options for new antibiotics in the pipeline , prevention through immunisation must be considered an equally important strategy to pursue.

Methods

A review of the literature was performed along with a structured internet search including pharmaceutical agency websites, was performed to identify the most prevalent MDR-GNB responsible for neonatal sepsis and the immunisation pipelines against these pathogens

Learning Points Discussion

Escherichia coli, *Klebsiella* sp., *Enterobacter* sp., *Pseudomonas aeruginosa*., and *Acinetobacter* sp. were the five major MDR-GNB identified. E coli is a common cause of neonatal sepsis, and there are several vaccines in late-phase clinical trials, mainly for adults.. Passive-antibody immunisation strategies are licensed for *Pseudomonas* sp. and several phase 1-3 vaccine trials are in progress, although current experimental vaccines only have limited coverage against infecting strains. *Klebsiella* and *Enterobacter* sp. cause sepsis in the immunocompromised host; few trials effective beyond phase 1-2 have been reported. Acinetobacter is a common cause of hospital-acquired and ventilator-associated sepsis, with experimental vaccines currently in phase 1-2 research.

The current immunisation pipelines for the most prevalent MDR-GNB are years away from licensure. Similar to incentives for development of new antibiotics, global efforts are urgently warranted to expedite the development, evaluation and licensure of effective vaccines against MDR-GNB.

ESPID19-0513
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

Immunogenicity and persistence of trivalent measles, mumps and rubella vaccines: a systematic review and meta-analysis

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Background

Despite the universal use of the two-dose trivalent measles-mumps and rubella (MMR) vaccine in recent decades, outbreaks of these pathogens still occur in countries with high vaccination coverages. This raises concerns about primary and secondary vaccine failure as potentially important contributing factors to the re-emergence of these vaccine-preventable diseases. We aimed to determine primary and secondary vaccine failure estimates for MMR vaccines through systematic review and meta-analysis to estimate seroconversion and waning rates for each of the three antigens.

Methods

A systematic search was performed in PubMed (incl. MEDLINE), Web of Science (WOS) and Embase using search terms related to the immunogenicity and the persistence of MMR vaccines. Articles in English from the earliest dates to September 2018 were considered eligible. We extracted information about the study design, patient characteristics, and vaccine information. The estimated seroconversion and waning rates were combined per component of the MMR vaccine to obtain overall estimates through meta-analysis with a random effects model using the DerSimonian-Laird estimator for the between-study variability.

Results

We identified 56 eligible studies through database search and 4 from their references. The estimated overall seroconversion rates for measles, mumps and rubella are 0.963 [0.945, 0.978], 0.939 [0.910,0.963] and 0.976 [0.963,0.988] respectively. The overall exponential waning rates for measles, mumps and rubella are 0.008 [0.004, 0.020], 0.021 [0.014, 0.030] and 0.016 [0.013, 0.018], respectively.

Conclusions

There is evidence that primary and secondary vaccine failures exist for different MMR vaccines and their components. Our meta-analysis provides important information to improve the accuracy of models that can help understand and predict the occurrence of measles, mumps and rubella outbreaks in countries with high vaccine uptake, with the ultimate aim to control and prevent such outbreaks.

Systematic Review Registration (Please input N/A if not registered)

CRD42019116705

ESPID19-0293
Science and Educational Track

Independent E-Poster Presentations 14 - Vaccines - Station 13

Health and economic burden associated with 15-valent pneumococcal conjugate vaccine (pcv15) serotypes in children in 8 european countries

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Background and Aims:

A 15-valent PCV containing the 13 serotypes in PCV13 and 2 additional serotypes, 22F and 33F is under development. This study quantifies the health and economic burden of pediatric invasive pneumococcal disease (IPD) associated with PCV15 serotypes in UK, Germany, France, Italy, Spain, Norway, Switzerland, and Denmark.

Methods:

A Markov model estimated PCV15-type IPD cases and deaths in hypothetical unvaccinated birth cohorts over 20 years. Inputs, including base-case pre-PCV era epidemiological inputs, were obtained from the published literature. In scenario analysis, pre-PCV era inputs were applied to PCV7 serotypes only whereas pre-PCV13 and current-day epidemiological inputs were used to estimate PCV13 not PCV7 type (PCV13-PCV7), and 22F/33F disease, respectively. Costs were estimated from a societal perspective (2017 Euros) and discounted at 3%.

Results:

In the base case, 5,122 PCV15-type IPD cases would occur in all 8 countries' birth cohorts over 20 years. 3,638 (71%) attributable to PCV7 serotypes, 1,381 (27%) to PCV13-PCV7 serotypes, and 103 (2%) to 22F/33FF. PCV15 serotypes would cause 222 IPD deaths. Total direct and indirect costs due to PCV15-type IPD was estimated at €135 million.

In scenario analysis, PCV15-type IPD increased to 6,663 cases of which 2,756 (41%) were PCV13-PCV7 types. The additional 1,375 PCV13-PCV7 cases were serotypes 1 (577 cases, 38%), 3 (95 cases, 6%), 7F (442 cases, 29%) and 19A (324 cases, 21%). 268 cases (4%) were 22F/33F. Total costs associated with PCV15-type IPD increased to €163 million.

Results from deterministic sensitivity analyses will be presented.

Conclusions:

PCV7 serotypes cause the majority of pneumococcal-related morbidity and costs and should be retained in investigational PCVs. Specific PCV13 serotypes also contribute significantly to the disease burden. Expanding coverage to non-vaccine serotypes can prevent additional morbidity and costs.

Systematic Review Registration:

N/A

ESPID19-0898
Science and Educational Track

Oral presentation session 01 - Global paediatric health

Clinical presentations and aetiologies of fever of children in Nepal

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Background and Aims:

There are few data on clinical presentations and aetiologies of febrile illness among children attending hospital and community clinics in Nepal. A high burden of enteric fever has been documented locally and is thought to be an important cause of fever. In this study, we aimed to describe the spectrum of causes of fever and clinical outcomes among children presenting with fever as part of an ongoing typhoid vaccine trial, TyVAC-Nepal.

Methods:

In 20 urban clinics in Nepal, children under 16 years who were vaccinated as part of TyVAC-Nepal, and presented with a documented fever or a reported fever ≥2 days, from January to December 2018 were included in this analysis. Recruitment occurred through passive surveillance, whereby children were brought to medical attention by caregivers. Among children presenting with fever, a blood culture, along with data on clinical presentation, diagnosis, antibiotic treatment, and treatment outcome, were collected.

Results:

Since January 2018, 7552 children were enrolled into TyVAC-Nepal surveillance. 1941 children presented with fever; among them, 1394 blood cultures were collected. 31 (2.2%) blood cultures were positive for *Salmonella* Typhi, and 3 (0.2%) for *Salmonella* Paratyphi. We will present complete data on clinical presentation, blood culture results, antibiotic treatment, and treatment outcome, along with a preliminary analysis on differences across age groups and locations.

Conclusions:

This study will provide helpful insight into the clinical presentations and aetiologies of fever, including the prevalence of *Salmonella* Typhi and Paratyphi, and other pathogens, among Nepali children. Results could influence guidance on management of febrile children in Nepal.

Systematic Review Registration:

N/A

ESPID19-1053
Science and Educational Track

Oral presentation session 01 - Global paediatric health

Pediatric chagas disease in the community of madrid: from latin america to Spain (2004-2018)

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Background and Aims:

Chagas disease (CD), a parasitic infection caused by *Trypanosoma cruzi (T. cruzi)*, is endemic in Latin-America and emergent in Europe due to immigration (being Spain the country with the highest number of cases). The vertical transmission rate is around 5%. However, systematic screening is not performed in all the regions. There is little public health attention and frequent lack of clinician´s awareness. Our aim was to describe the clinical and epidemiological situation of children with CD in the community of Madrid from 2004 to 2018.

Methods:

Retrospective multicenter study. We reviewed the medical files of all children (<18 y.o.) with the diagnosis of CD in 10 hospitals in Madrid.

Results:

Fifty-one cases were identified. All mothers came from Latin America (Bolivia 94%). Screening during pregnancy was performed in 24%; 10% had been diagnosed before pregnancy without receiving specific treatment. Twenty-six children (51%) were born in Spain. Children at diagnosis were aged from < 1 month to 17 years (median: 103 months). Only a child was symptomatic (hydrops fetalis). Treatment was completed in 90% of the cases, but in 2 (3.9%) it had to be definitely stopped, due to drug intolerance. Benznidazole caused adverse reactions (mainly cutaneous) in 29% of the treated patients.

Conclusions:

An important number of children were diagnosed under the 1st year of age (31%) following the screening recommendation. In most cases, treatment was well tolerated. It is important to highlight the high percentage of patients lost to follow up (up to 37%) probably in relationship with psychosocial adversity, and the lost opportunities of planning treatment before pregnancy in mothers who were diagnosed previously. Clinicians in non-endemic regions must be aware of the potential for childhood *T. cruzi* infections

Systematic Review Registration:

N/A

ESPID19-0973
Science and Educational Track

Oral presentation session 01 - Global paediatric health

Clinical characteristics and risk factors for sapovirus gastroenteritis in early childhood: a population-based study in Nicaragua

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Background

Sapovirus, sharing the Caliciviridae family with norovirus, is increasingly recognized as a major cause of acute gastroenteritis (AGE). In the MAL-ED Study, sapovirus was the second most important cause of diarrhea in children <2 years. Despite this high disease burden, little known about its clinical characteristics and risk factors.

Methods

We conducted a nested case-control study within a population-based birth cohort of 444 children in León, Nicaragua. Fieldworkers visited households weekly to identify AGE and collect risk factor information. AGE stools and stools from household contacts were tested for sapovirus using quantitative RT-PCR. We selected two age-matched controls (± 3 months of the case) from the risk set at the first sapovirus episode. We used conditional logistic regression to identify sapovirus predictors.

Results

Between June 2017 and November 2018, we identified 34 sapovirus cases and 68 controls. All cases experienced diarrhea, lasting on average 7 days with a maximum 6 stools daily. Ten cases experienced fever, 9 experienced vomiting, and 7 were attended in the emergency department. Seven cases were co-infected with another enteric virus.

Bivariate sapovirus predictors included having a household member testing positive for sapovirus ($p=0.02$), any prior AGE ($p<0.0001$), vaginal delivery ($p=0.001$), lower mean WAZ ($p=0.03$) and LAZ ($p=0.02$), and having soap at all sinks ($p=0.03$). Eating food outside the home was protective ($p=0.04$). Adjusting for other predictors, vaginal delivery remained a significant predictor of sapovirus AGE

(Table).

Table. Risk factors for sapovirus AGE (n=102)[1]

	Crude OR (95% CI)	Adjusted OR (95% CI)[3]
Household member testing positive for sapovirus	10.00 (1.12, 472.98)[2]	-
Vaginal delivery vs. Cesarean delivery	5.52 (1.83, 16.73)	3.62 (1.09, 12.00)
Prior AGE episode vs. no history of AGE[4]	24.58 (5.21, ∞)[2]	-
Mean WAZ (continuous)	0.65 (0.43, 0.98)	-
Mean LAZ (continuous)	0.72 (0.54, 0.97)	0.76 (0.53, 1.07)
Water source interruption vs. continuous water supply in the past week	7.20 (0.74, 354.57)[2]	-
Indoor toilet in the household vs. latrine or none	0.52 (0.22, 1.23)	0.58 (0.12, 2.82)
Dirt floor in the household vs. other building material	1.90 (0.84, 4.30)	1.16 (0.26, 5.24)
Pig in the household vs. no pig	6.00 (0.48, 314.98)[2]	-
Presence of soap at all sinks in home vs. some or none	0.24 (0.03, 1.04)	-
Ate food outside the home vs. no food outside the home in the past week[5]	0.33 (0.09, 0.96)[2]	-

Abbreviations: AGE=acute gastroenteritis WAZ=weight-for-age Z score; LAZ=length-for-age Z score.
[1]Includes statistically significant bivariate predictors at α=0.1.
[2]Exact logistic regression used for variables with cell sizes ≤5.
[3]Model adjusted for vaginal delivery, LAZ, indoor toilet, dirt floor, and mean age difference between matched controls and cases to adjust for residual confounding by age matching. Variables with cell sizes ≤5 and collinear variables were excluded from the multivariable model.
[4]AGE due to bacteria, parasites, or viruses other than sapovirus.
[5]1 observation missing.

Conclusions

The associations of sapovirus with vaginal delivery, prior AGE, and nutritional status are novel findings. Gut microbiome composition and its effects on AGE risk and growth may mediate the relationship between vaginal delivery and sapovirus, or vaginal delivery may be a proxy for other risk factors. Further investigation is warranted.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0581
Science and Educational Track

Oral presentation session 01 - Global paediatric health

Tularemia in children during last outbreak in Kosovo

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Background and Aims:

Tularemia is a zoonosis caused by Francisella Tularensis. Kosovo faces the first outbreak of Tularemia with 247 cases following the war in Kosovo (1999 – 2000). Several outbreaks of Tularemia were reported since then in Kosovo, with the last one during years 2014 -2015 involving around 500 cases with the annual incidence 11.35 cases per 100.000 population.

The aim of this study was to analyze epidemiological, clinical and diagnostic features of tularemia in children in last outbreak during years 2014 – 2015.

Methods:

This retrospective study enrolled 36 children until 15 years of age treated for Tularemia at our department.

Results:

Children manifested glandular form of Tularemia in 34 cases (94%). All children came from rural places, 26 patients (72%) used unsafe water supply from wells. Male gender predominated (58%), while mean age of patients was 9.4 years (range 2 –15 years). Duration of symptoms prior to hospitalization was 14 days (range 3 – 60 days). Clinical manifestations were: temperature (97%) and cervical lymphadenopathy (94%). From laboratory findings, 35 patients (97%) had elevated erythrocyte sedimentation rate and 15 (41%) had leukocytosis. Tularemia in children was confirmed by serology in all cases; by agglutination test in 89% (32), by ELISA testing in 22% (8) and by PCR in 25% of cases (9). Most of children were treated with gentamycin in 35 cases (97%), and single case with erythromycin and streptomycin. Due to abscess formation and suppuration, incision and drainage of lymph nodes as accessory therapy underwent 18 patients (50%). Relapse had 3 patients (8%) and were treated with streptomycin.

Conclusions:

Tularemia continues to be a health problem for children in Kosovo. Cervical glandular form dominated and gentamycin remains first drug of choice.

Systematic Review Registration:

N/A

ESPID19-0383
Science and Educational Track

Oral presentation session 01 - Global paediatric health

Persistent giardiasis in children: prevalence and management

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Background and Aims:

Giardia intestinalis (GI) is the most prevalent protozoan parasite worldwide. Metronidazole is the first line treatment in children, with variable treatment success rate. The aim of this study was to estimate the prevalence of refractory GI infection among pediatric patients and to evaluate the safety and efficacy of second line therapy.

Methods:

Children below 18 years old, diagnosed with GI in a Spanish Tropical Pediatric Reference Unit were included. Epidemiological and clinical data were collected retrospectively from January 2014 to December 2017. Diagnosis was done based on microscopy and immunochromatographic test for the detection of GI antigens in three stool samples collected on alternate days.

Results:

Seventy-five children were included; median age 3.65years (2.1-7.3), 53.3% males. Origin; 48% Africa, 28% Asia, 17.3% Europe, 6.6% South-America. A total of 74.6% were internationally adopted children. Only 58.6% were symptomatic. Microscopy was positive in 96% and immunochromatography in 50.6%. We found concomitant parasites in 28%. First line therapy was Metronidazole in all cases (15 mg/Kg/day/7days), with a GI persistence of 17.3%. High dose Metronidazole (40 mg/Kg/d/10days) was second-line therapy with a success rate of 54%. Six (8%) non-responders received Quinacrine with 100% eradication. Persistent giardiasis was not related to concomitant intestinal parasites (p 0.68).

Conclusions:

GI infection resistant to first line treatment is common, with a rate up to 17% in our series. High-dose metronidazole was safe and well tolerated but is commonly unsuccessful. Quinacrine has to be considered the drug of choice in refractory cases.

Systematic Review Registration:

ESPID19-0045
Science and Educational Track

Oral presentation session 01 - Global paediatric health

Evidence of plasmodium falciparum kelch 13 polymorphisms among sumatran plasmodium falciparum parasites

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Background

Plasmodium falciparum parasite has a long history of resistance to the previous used antimalarials. Currently, the WHO recommends artemisinin-combination therapies for the treatment of uncomplicated *P.falciparum* infection. However, reduced sensitivity of *P.falciparum* to artemisinin and its partner drugs have been reported in the Greater Mekong subregion. Polymorphisms in several genes namely *pfcrt*, *pfmdr1* and *pf*k13 have been associated to the development of resistance to these combinations. Of great concern that resistance might spread or emerge in the neighbouring Indonesia, we evaluated the polymorphisms in *P.falciparum* parasites from North Sumatra province, Indonesia.

Methods

Genotyping and direct sequencing on the *pfcrt* gene, *pfmdr1* gene and *pf*k13 propeller domain were done on 404 *P.falciparum* isolates according to the established methods.

Results

Successful analysis in the *pfcrt* gene on 183 samples revealed majority of samples (91.8%) carried mutant 76T with haplotype SVMNT of *pfcrt* gene codons 72-76 as the most dominant (76.5%), followed by wild-type CVMNK (34.9%) and mutant-CVIET (20.2%). Genotyping of *pfmdr1* gene at codons 86 was successful in 267 samples showing prevalences of wild-type and mutant N86Y at 63.7% and 33.3%, respectively. Prevalences of wild-type and mutant Y186F of *pfmdr1* in 262 samples were 85.1% and 14.1%, respectively. Meanwhile, majority of the 232 samples genotyped for the *pf*k13 propeller domain had wild-type parasites suggesting parasites sensitive to artemisinin. Only 4.3% of samples had mutations, however only 1 sample harboured the known C580Y artemisinin-resistant parasite. Mutant T474A was the most common mutation found in the *pf*k13.

Conclusions

Our study revealed that the majority of Sumateran *P.falciparum* parasites carried *pfcrt*-SVMNT and *pfmdr1* N86 and 184Y suggesting parasites resistance to chloroquine and amodiaquine, but sensitive to artemisinin as shown by dominant wild-type *pf*k13 parasites.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0673
Science and Educational Track

Oral presentation session 02 - Immunology and the host pathogen interaction

Activation of antibacterial autophagy promotes group b streptococcal clearance in neonatal macrophages

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Background

Group B Streptococcus (GBS) has the ability to persist inside neonatal phagocytes and resist to phagocyte killing, facilitating its dissemination in neonatal hosts. Classical activation of macrophages (M1 macrophages) results in enhanced autophagy and bactericidal capacity however the effect of this macrophage phenotype against GBS infection has not been investigated. Aim of the study was to delineate the mechanism of GBS persistence in macrophages and evaluate the role of neonatal M1 phagocyte activation in GBS elimination

Methods

WT primary macrophages from newborn mice were infected with GBS *ex vivo* and compared with GBS - infected *Akt1* deficient macrophages; a model of M1 activated neonatal macrophages

Results

Akt1 deficient, neonatal macrophages (M1 macrophages) had significantly enhanced ability to eliminate intracellular GBS *ex vivo* compared to WT ones (30% to 5% reduction 2hours post-infection, $p<0.001$). GBS elimination was delayed in WT neonatal macrophages compared to *Akt1* deficient neonatal macrophages (12hours vs 6hours). Phagosome examination by electron microscopy revealed that 41.56% of GBS–containing phagosomes were damaged in WT macrophages compared to 4.46% in *Akt1*$^{-/-}$ neonatal macrophages ($p<0.01$). Both oxidative stress and autophagy markers (ATG5, LC3II) were increased >2 fold in *Akt1*$^{-/-}$ neonatal macrophages compared to WT ($p<0.05$). In WT macrophages LC3II protein failed to colocalize with GBS-containing phagosomes while all GBS-containing phagosomes in *Akt1*$^{-/-}$ neonatal macrophages were LC3II positive ($p<0.001$). Inhibition of antibacterial autophagy via *ATG5* mRNA silencing, abrogated GBS clearance in *Akt1*$^{-/-}$ neonatal macrophages only ($p<0.01$).

Conclusions

Classical activation of neonatal macrophages, via suppression of *Akt1* kinase, blocks GBS phagosome evasion and promotes rapid GBS clearance, via induction of oxidative stress and the antibacterial autophagy pathways. *(This work was funded by two ESPID Small Grant Awards. The authors gratefully acknowledge the support of ESPID).*

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0271
Science and Educational Track

Oral presentation session 02 - Immunology and the host pathogen interaction

Quantitative proteomic analysis for identification of surrogate markers for prediction of dengue fever severity in admitted children

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Background

Mechanisms triggering progression of dengue fever (DF) into severe forms are still not well understood resulting in delayed disease management. Biomarkers that predict and explain its progression to more severe hemorrhagic form are much needed. The current study provides a comprehensive understanding of disease severity by proteomic analysis of various proteins differentiation in all stages of DF i.e. dengue with no warning signs (DNWS), dengue with warning signs (DWS) and severe dengue (SD).

Methods

This case control study enrolled 168 admitted children of DF [DNWS(n=58); DWS(n=92), SD(n=18)] from January 2016 to December 2018. The primary diagnosis was based on clinical examination and by kit-based immuno-chromatographic assay. Further confirmation was done with ELISA based IgM analusis (titre≥1:400) and PCR. Comparative proteomic analysis was done by using gel-free Isobaric tags for relative and absolute quantification (iTRAQ) based quantitative proteomics methodology.

Results

A statistical analysis of the differentially regulated proteins using Mann–Whitney U test revealed 14 significantly altered proteins ($p<0.05$). In Children suffering from DNWS, 5 proteins (Complement factor H, Hemopexin, Serotransferrin, Transthyretin and Zinc-alpha-2-glycoprotein) showing significant under-expression were identified ($p<0.001$) with fold changes (FC) <0.75. In children suffering from DWS and SD, 4 proteins (alpha-1 antitrypsin, Apolipoprotein A-I, Plasma protease C1 inhibitor and Vitamin D-binding protein) showed significant up-regulation ($p<0.001$) with FC >1.90. Five proteins (alpha-2 macroglobulin, angiotensinogen, apolipoprotein B-100, serotransferrin, and ceruloplasmin) showed differential expression and opposite regulation in DNWS and DWS/SD. They were upregulated (FC >1.2) in all DWS/SD cases and downregulated in DNWS (FC <0.83) and may facilitate in predicting the progression of DNWS to DWS/SD.

Conclusions

These new observations identify several putative molecular leads for future biomarker development and precision medicine in relation to forecasting dengue disease severity.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-1077
Science and Educational Track

Oral presentation session 02 - Immunology and the host pathogen interaction

The impact of immune cells phenotype, cytomegalovirus-specific response and sex on immunity following vaccination with bacillus calmette-guérin (bcg)

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Background

Understanding factors associated with varying efficacy of Bacillus Calmette-Guérin (BCG) would aid the development of improved vaccines against tuberculosis (TB). In addition, investigation of individual-level factors affecting mycobacterial-specific immune responses could provide insight into confounders of vaccine efficacy in clinical trials. Mycobacterial growth inhibition assays (MGIA) have been developed to assess vaccine immunogenicity *ex vivo* and provide a measure of immune function against live mycobacteria.

Methods

In this study, we assessed the impact of immune cell phenotype, cytomegalovirus (CMV)-specific response and sex on *ex vivo* growth inhibition following historical BCG vaccination in a cohort of healthy individuals (n=100). Peripheral blood mononuclear cells (PBMC) were incubated with live BCG and inhibition of growth was determined. Immune mechanism was investigated using ELISpot and ELISA, as well as flow cytometry to characterise cell phenotype along with mycobacterial antigen-specific and CMV-specific response.

Results

A higher frequency of cytokine-producing NK cells in peripheral blood was associated with enhanced *ex vivo* mycobacterial growth inhibition following historical BCG vaccination. We confirmed findings from previous studies regarding the role of T-cell activation associated with a CMV-specific response as a risk factor for TB disease and our study is the first to show the association with *ex vivo* mycobacterial growth. Interestingly, BCG-vaccinated females in our cohort controlled mycobacterial growth better than males, which may provide an explanation to the higher number of TB cases in males worldwide.

Conclusions

In summary, our present study has implemented the MGIA to assess changes in the innate immune compartment as well as adaptive immunity following BCG vaccination. Individual-level factors influence capacity to control mycobacterial growth and the MGIA could be used as a tool to assess how vaccine candidates may perform in different populations.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1060
Science and Educational Track

Oral presentation session 02 - Immunology and the host pathogen interaction

Determinants of long- term growth in HIV-infected children in Spain

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Background

Previous studies have described impaired growth in HIV-infected children. Most series include children from resource limited settings in which malnutrition is frequent and treatment is not fully available. We aim to characterize long-term growth in a cohort of HIV-infected children and to identify determinant factors.

Methods

HIV-infected children born between January 2000 and December 2017 participating in the Spanish Cohort of HIV-infected Children (CoRISpe) with available anthropometric data were included. Clinical and immunovirological variables and anthropometrics were collected yearly during the study period.

Results

A total of 124 infant were included, 60.5% female, all vertically HIV-infected and on treatment, 34% born abroad. A 55% of cases were diagnosed immediately after birth, and 53% achieved viral suppression within one year of treatment. Median CD4 cell counts at diagnosis: 1400 cell/mL []. Seven patients (5%) were late diagnosis (<200 CD4). At baseline, median Z-score for weight, height and BMI were -1,19 [-1.7 to -0.29], -1.1 [-1.93 to -0.03] , and -0,72 [-1.31 to -0.04] respectively. We observed an increase in weight gain and linear growth rate after one year (median z -score for weight, height and BMI: - 0.65 [-1.13 to 0.02], - 0.36 [- 1.46 to 0.20] and - 0.67 [-1.07 to 0.42]. No differences were found at other time points. Viremic patients and those diagnosed late or at an older age showed a tendency towards delayed growth.

Conclusions

In our study in an European cohort, prompt ART initiation improved growth status of HIV-infected children. The effect of the immunological status seems to impact growth in early stages of life. Larger studies are warranted to evaluate the role of treatment / viral suppression on long- term growth in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0503
Science and Educational Track

Oral presentation session 02 - Immunology and the host pathogen interaction

Discriminating acute kawasaki disease from infections in childhood: the search for laboratory markers

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Background

Kawasaki disease (KD) is a systemic vasculitis of early childhood, mimicking various infectious diseases. Differentiation between KD and infectious diseases is essential as KD's most important complication - the development of coronary artery aneurysms - can largely be avoided by timely treatment with intravenous immunoglobulins. Currently, KD is diagnosed based only on clinical criteria. The aim of this study was to evaluate whether MRP8/14, CRP and/or Elastase (elastase-a1 anti-trypsin [HNE-α1AT complexes]) are possible biomarkers to distinguish KD from infectious diseases.

Methods

Children with acute KD (<14 days after disease onset) and children with proven viral- or bacterial infections were recruited. MRP8/14, CRP and HNE-α1AT complexes were measured by ELISA and assessed for their discriminatory ability.

Results

A total of 48 KD patients, 65 patients with bacterial infections and 40 patients with viral infections were included. MRP8/14 appeared to be the strongest marker to discriminate KD from an infection (ROC AUC 0.86 (0.78-0.93)). CRP showed an AUC of 0.76 (0.68-0.85). HNE-α1AT complexes were noncontributing. For incomplete KD, MRP8/14 is the only predictor. When the chance of having KD turns out to be low, a combination of MRP8/14, CRP and HNE-α1AT complexes gives the strongest discriminatory power between bacterial and viral infections with an AUC of 0.95 (0.89-0.998). The robustness of the abovementioned model was confirmed by a multinomial regression analysis and by internal bootstrapping.

Conclusions

MRP8/14 is a strong marker to discriminate between KD and an infection. When the chance of having KD is low and a physician should discriminate between a bacterial of viral infection, a combination of MRP8/14, CRP and HNE-α1AT complexes has the strongest discriminatory power.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0183
Science and Educational Track

Oral presentation session 02 - Immunology and the host pathogen interaction

Diminished immune responses in malaria-exposed individuals

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Background

Malaria still remains a major health burden with children under the age of 5 in sub-Saharan Africa being the most vulnerable population affected. Infections with the malaria causing parasite *Plasmodium* fail to induce sterile immunity and “clinical immunity” is only acquired after years of exposure. With no highly effective vaccine available to date, analyzing mechanisms of naturally acquired immunity is crucial to inform future vaccine strategies. In light of recent evidence that malaria vaccine candidates work well in the US or Europe but fail to induce sterile immunity in endemic settings, we analyzed immune responses in individuals with a lifelong exposure to intense seasonal malaria transmission in Mali.

Methods

Dendritic cell (DC) responses were compared longitudinally by enriching DCs from peripheral blood of asymptomatic Malians (n=48) before the transmission season and then again during peak malaria transmission. DCs were incubated for 24 h with parasite lysate and activation was analyzed by quantifying surface marker expression and secretion of cytokines and chemokines in the culture supernatants by flow cytometry. To address T cell responsiveness, CD4 T cells and antigen presenting cells were enriched and incubated together with parasite lysates. T cell proliferation and cytokine secretion were then analyzed.

Results

When comparing DCs from the same individual when uninfected and during asymptomatic infection, DC responses to the parasite were impaired characterized by lower chemokine secretion and marker up-regulation. CD4 T cell responses to the parasite were found to be significantly lower in Malian compared to naïve US individuals.

Conclusions

Our findings suggest that even asymptomatic infections can alter the function of innate cells like DCs and repeated infections can lead to a diminished T cell response instead of functional memory in the case of malaria.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-1004
Science and Educational Track

Oral presentation session 03 - Neonatal infections

Using disease-based registries to compare trends in antiviral treatment of congenital cmv infection: the european congenital cytomegalovirus initiative (ecci)

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Background

Congenital CMV (cCMV) treatment remains controversial. Treatment has been influenced by a RCT presented in 2014 that found treating symptomatic cCMV-affected children aged ≤30 days with valgancyclovir for 6 months, compared to 6 weeks, improved hearing and developmental outcomes at age 24 months; we aimed to review current practice using data from the ECCI cCMV registry.

Case Presentation Summary

Relevant information on cCMV-infected children is entered onto a study-specific electronic database. Treated cases from the UK were entered into V1.0 and since 2017 both treated and untreated cases from Greece, Italy and the UK have been entered into V2.0 of the ECCI registry.

72 cases born before 31/12/13 and 84 cases born 01/01/14 onwards had data entered.

Of 61 cases known pre-2014, 13 (21%) received valgancyclovir alone, 26 (43%) received gancyclovir alone and 22 (36%) a combination of both. Of 24 cases known post-2014, 12 (50%) received valgancyclovir alone, 1/24 (4%) received gancyclovir alone and 11/24 (46%) a combination of both. Most (88%) were started on treatment at age ≤30 days (similar proportion in both eras).

Of 58 cases with data pre-2014, 53 (91%) received a 6-week course and 5 (9%) received a 6-month course. Of 21 cases post-2014, 11 (52%) received a 6-week course and 10 (48%) received a 6-month course.

Of 78 treated cases, 69 (89%) were symptomatic at diagnosis. Of 50 untreated cases, 12 (24%) were symptomatic (most (83%) with isolated CMV-related abnormalities on neuroimaging).

Learning Points/Discussion

Over recent years, there is a trend towards longer duration of treatment with valgancyclovir alone, however there is also an apparent trend not to treat cases with CMV-related abnormalities on neuroimaging. On-going follow-up will allow us to better appreciate the potential impact of treatment in different circumstances.

ESPID19-0272
Science and Educational Track

Oral presentation session 03 - Neonatal infections

Congenital plasmodium vivax malaria: a eight year prospective observational analysis from bikaner, northwestern india

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Background

Congenital malaria is defined as malaria parasitaemia in the first week of life. Although having few recent reports of congenital *P.vivax* malaria, its non classical clinical presentations in neonatal period made it to be difficult to diagnose even in endemic areas. This study describes the occurrence and clinical spectrum of congenital *vivax* malaria in Indian perspective.

Methods

This prospective study was conducted on admitted neonates from January 2011 to December 2018. The species diagnosis was done by peripheral blood smear examination, rapid diagnostic test and polymerase chain reaction analysis. The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results

A total of 3896 neonates admitted in first week of life were screened. Out of them 148 (3.8%) neonates had evidence of parasitaemia (*P.vivax,*125 and *P.falciparum,*23). The criteria for admission were septicemia (48.15%), prematurity (36.46%), jaundice (23.15%), perinatal asphyxia (17.38%), and seizures (8.54%). The clinical malaria was seen in 139 (93.9%) neonates in which spectrum was anemia (82.77%), thrombocytopenia (86.92%), poor feeding (75%), fever (71.54%) and hepatosplenomegaly (61.92%). Although the presence of parasitaemia didn't differ the proportion of neonates having fever (χ^2=0.238; p=0.52) and hypoglycemia (χ^2=0.117; p=0.63) from those without parasitaemia, but it was significantly associated with anemia (χ^2=14.676; p=0.001) and thrombocytopenia (χ^2=12.768; p=0.001). The mean Hb level was 8.9±2.7 gm/dl; mean platelet count was 106744.32±32465.56/µl; mean reticulocyte count was 4.2±1.2%; and mean parasite density was 14788.38±2739.21/mm^3. All these neonates were treated according to WHO guidelines and none of them expired.

Conclusions

This study strongly emphasizes the occurrence of *P.vivax* congenital malaria with non classical malaria manifestations. Routine screening should be essential for all neonates in endemic areas for awareness about this preventable and treatable disease.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0170
Science and Educational Track

Oral presentation session 03 - Neonatal infections

Gentamicin levels in low birthweight infants

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Background and Aims:

Gentamicin is important in the treatment of suspected neonatal sepsis, but is also potentially oto- and nephrotoxic. Therapeutic drug monitoring of gentamicin levels helps prevent this. An audit done in 2013-2015 suggested that while 90% of trough gentamicin levels taken at the Neonatal and Paediatric Intensive Care Unit (NPICU) were safe, low-birthweight infants may be at higher risk of toxicity.

Methods:

We enrolled 185 neonates admitted to NPICU from 2013-2017 who needed intravenous gentamicin treatment. The dosing regimen, dose of gentamicin, gentamicin concentration, and demographic details including gestation and birthweight, were recorded for each neonate. Trough gentamicin concentrations ≥2mg/L before the 2nd dose were taken as indicative of unsafe levels.

Results:

A total of 169 neonatal gentamicin results were included. Nineteen (11.2%) of these were higher than recommended. Stratifying the results according to weight showed significantly higher mean gentamicin levels in neonates weighing <1.5kg (1.34mg/L; 95% CI: 1.16-1.53) and 1.5-3kg (1.33mg/L; 95% CI: 1.13-1.52), compared to those weighing >3kg (0.71mg/L; 95% CI 0.57-0.85). However, no significant differences in gentamicin levels were found between small-for-gestational age, appropriate-for-gestational age, or large-for-gestational age neonates. On the other hand, premature neonates born at 28 weeks' gestation or less had significantly higher mean gentamicin levels (1.69mg/L; 95% CI: 1.33-2.04) than those born at term (0.84mg/L; 95% CI: 0.68-0.99mg/L).

Conclusions:

Our study confirms that the current gentamicin dosing guidelines are safe, while showing premature neonates born under 28 weeks to be at higher risk for gentamicin toxicity.

Systematic Review Registration:

N/A

ESPID19-1161
Science and Educational Track

Oral presentation session 03 - Neonatal infections

Population pharmacokinetics of intraventricular vancomycin in neonatal ventriculitis

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Background

Intraventricular vancomycin (IVV) is an effective treatment for neonatal ventriculitis, as the cerebrospinal fluid (CSF) vancomycin levels reach adequate concentrations, to achieve microbiological cure. There is limited data on pharmacokinetics, influencing covariates and optimal dosing of IVV. Our study aimed to examine the pharmacokinetic behaviour of IVV in the preterm population of < 28 weeks gestation and the impact of covariates on the CSF vancomycin levels.

Methods

7 preterm infants with neonatal ventriculitis (median gestation age 25.6 weeks ; range 23.9 - 27.7)were included in this study. All available data on intravenous and intraventricular vancomycin dosing and associated plasma/CSF levels were collected. Population pharmacokinetics (non-linear mixed effects modelling) were described with one- and two-compartment models to fit plasma concentrations of vancomycin. A CSF compartment was added to the plasma modelling and mass transfer examined. We tested 3 covariates (serum creatinine, ventricular index and CSF protein) on the final model. Area under the curve (AUC) and average CSF concentration predictions(defined as AUC(0-t)/t; t=time)were generated from the final model and compared with time to microbiological cure.

Results

A one-compartment model provided the best fit to the data. Goodness of fit plots (Figure 1) and visual predictive checks demonstrated stability and good predictive properties of the proposed population model.There was no appreciable transfer between plasma and CSF. None of the covariates provided a significant reduction in the objective function value (OFV). There was a trend of shorter time to sterilisation with higher CSF AUC (0-24) and C average.

Conclusions

This population pharmacokinetic analysis provides important information to support optimisation of dosing and management of IVV treatment in the preterm population.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0312
Science and Educational Track

Oral presentation session 03 - Neonatal infections

Pharmacokinetics and safety of trimethoprim-sulfamethoxazole in hiv-exposed low birth weight infants

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Background

Limited pharmacokinetic (PK) and safety data exist for low birth weight (LBW ;<2500g) infants receiving trimethoprim-sulfamethoxazole (TMP-SMX) to prevent opportunistic infections.

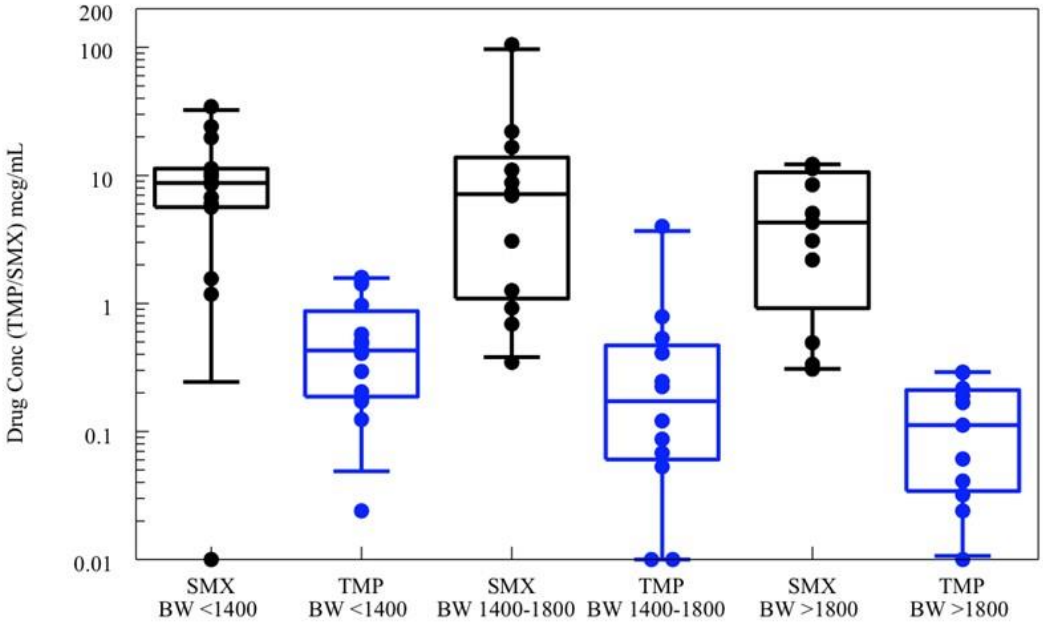
Methods

IMPAACT P1106, a Phase IV study assessing PK and safety of antiretrovirals and related medicines including TMP-SMX in South African LBW infants. Analysis included HIV-exposed infants receiving TMP-SMX (20/100mg) from age 6 weeks. PK and safety evaluations were performed from enrollment (7-14 days of life) to week 24. Adverse events (AE) classification included expected (associated with prematurity) or unexpected. Plasma samples were assayed by LC MS/MS methods.

Results

As of October 2018, 39 infants were included with median (range) birthweight 1650g (880-2424) and gestational age (GA) 32 (28-38) weeks. TMP-SMX was started at 5.5 (4.1 – 8.5) mg/kg/day at 39 (35-49) weeks corrected GA, and continued for 16 (3-21) weeks. Twenty-nine infants contributed 138 TMP-SMX concentrations; 38 (28%) observations below quantifiable levels for both TMP and SMX suggesting non-adherence were excluded. Median trough levels were TMP (0.22 mcg/ml) and SMX (7.35mcg/ml). Higher TMP troughs (0.62 vs 0.14 mcg/ml; p = 0.01 from t-test) were observed in infants born <1800g compared to >1800g (Figure 1). Seventeen (44%) had grade 3/4 expected AEs, with sepsis (n=5, 13%) the most common, only rare cases of anemia (n=2, 5%) and thrombocytopenia (n=1, 3%) and no neutropenia. Nine (23.1%) had grade 3/4 unexpected AEs, with pneumonia (n=5, 13%) the most common. Two infants died of SIDS.

Figure 1. Trough TMP-SMX concentrations by birthweight.



Conclusions

TMP-SMX prophylaxis was well tolerated; grade 3/4 AEs were assessed as unrelated to TMP-SMX. Higher TMP troughs in infants with the lowest birth weight suggests immature clearance. Standard infant TMP-SMX prophylaxis was safely used in LBW infants from 35 weeks corrected GA.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0049
Science and Educational Track

Oral presentation session 03 - Neonatal infections

Risk factors and clinical features of neonatal listeriosis: a hospital-based study

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Background and Aims:

Listeriosis has a high fatality rate in newborns; however, due to a lack of national surveillance or mandatory notification system for *Listeria monocytogenes* infection in Taiwan, its incidence in the population is not available. The aim of our study was to define the clinical features and outcomes of neonatal listeriosis and identify the neonatal and maternal risk factors to seek strategies for improvement.

Methods:

We retrospectively collected data on the clinical characteristics, laboratory test results and outcomes in neonatal patients and pregnant women who tested positive for *Listeria monocytogenes* in a tertiary-care hospital in northern Taiwan and in a regional hospital in eastern Taiwan during July 2001 to June 2018. The medical records in the neonates and mothers were reviewed and the clinical presentation and laboratory data were evaluated.

Results:

A total of 18 neonates and 19 pregnant patients were analyzed. The incidence of neonatal listeriosis increased during 2001-2018 (R^2=0.30, P=0.02) with neonatal and fetal death rates reaching 24%. The mortality was higher in cases of birth at less than 28 weeks of gestation (P=0.03), with Apgar score < 5 at the fifth minute after birth, or with extreme acidosis. Majority of the clinical presentation in neonates included respiratory distress, leukocytosis or leukopenia, bandemia, thrombocytopenia, hypocalcemia and elevated C-reactive protein (CRP). All maternal cases with elevated CRP levels were identified, but only 25% of the patients completed the antepartum antibiotic course.

Conclusions:

Neonatal listeriosis has emerged to be a great threat in Taiwan, especially for preterm neonates. Maternal listeriosis should be treated adequately with appropriate empirical antibiotics.

Systematic Review Registration:

NA

ESPID19-1069
Science and Educational Track

Oral presentation session 04 - Diagnostics

Performance of serum β-d glucan assay (fungitell®) for the diagnosis of invasive candidiasis in neonates: a prospective study in a neonatal intensive care unit

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Background and Aims:

Diagnostic performance of β-D-glucan (BDG) to detect invasive candidiasis (IC) in neonates are variable with a sensitivity ranging from 63 to 100% and specificity from 64 to 100%. Our objective was to assess the diagnostic performance of BDG in a population of neonates with clinical suspicion of IC.

Methods:

We prospectively included all infants less than 28 days old, hospitalized in the neonatal intensive care unit of the Nantes University Hospital, with clinical suspicion of IC and for whom serum BDG was determined. Clinical suspicion of IC was defined as a clinical deterioration associated with risk factors already described in the literature or the absence of improvement after appropriate antibiotic therapy. BDG serum level were assessed with the Fungitell® assay kit (positive threshold = > 80 pg/mL). Proven/probable IC were defined as followed.

IC	Risk factors of IC	Clinical deterioration	*Candida* colonization (superficial sites)	Positive Candida culture(s) from blood and/or cerebrospinal fluid
Proven	Yes	Yes	+/-	Yes
Probable	Yes	Yes	Yes	No

Results:

61 BDG serum assays were determined in 55 infants with a median gestational age of 27.6 weeks (IQR 26–33.9) and a median age of 11 days (IQR 7-23). Two infants had proven IC, 5 had probable ICs. Sensitivity, specificity, positive and negative likelihood ratios of the test to detect proven/probable IC were 86% (95% CI 49-97), 52% (95% CI 39-65), 1.78 (95% CI 1.18-2.68) and 0.276 (95%CI 0.04-1.72), respectively.

Conclusions:

The BDG assay showed good sensitivity in this pre-selected population of infants. Regarding the low prevalence of IC, meta-analysis of existing data may now help to evaluate more accurately its diagnostic performance before setting up a study to assess the potential impact on antifungal use.

Systematic Review Registration:

N/A

ESPID19-1019
Science and Educational Track

Oral presentation session 04 - Diagnostics

Viral loads in nasopharyngeal swabs of children with respiratory tract infections or fever without a source correlate with immunoxpert™ scores and trail levels

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Background

Viral and bacterial infections are often clinically indistinguishable, which poses the main clinical challenge. ImmunoXpertä(IX), a novel host-response proteomic signature consisting of CRP, TRAIL, and IP-10, helps to improve clarifying etiology. Previous studies have shown that low IX scores and high TRAIL levels are indicative of viral infection. The role of viral loads in respiratory specimens especially in respiratory tract infections (RTI) is under debate.

Methods

Nasopharyngeal swabs were taken from patients recruited within the multinational prospective AutoPilot-Dx-Study (NCT03052088), designed to validate the IX in children with febrile RTI and fever without a source. Viral loads were measured via qPCR in the four most prevalent mono-virus detections, i.e. influenza virus, respiratory syncytial virus, human rhinovirus, and adenovirus, and assessed whether these findings correlated with the IX score and TRAIL levels.

Results

In a preliminary subcohort analysis we identified 219 children with a viral mono-infection. Children with TRAIL levels of ³50 pg/mL had significantly higher viral loads than those with TRAIL levels of <50 pg/mL ($p<0.01$). Moreover, viral loads were significantly higher in children with a low IX score indicative of viral etiology than in those with a high IX score indicative of a bacterial etiology. These differences were also detectable for each virus subgroup, albeit no statistical significance was reached.

Conclusions

Higher viral load correlated significantly with higher TRAIL levels and lower IX scores, indicating a potential complimentary role of viral load measurement in infectious disease diagnostics.

Acknowledgments:

This work was kindly supported by the ESPID Small Grant Award (C.P.).

Clinical Trial Registration (Please input N/A if not registered)

NCT03052088

ESPID19-0425
Science and Educational Track

Oral presentation session 04 - Diagnostics

A QPCR assay of 1-transcript expression signature in host differentiates viral from bacterial infections in febrile children

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Background

The diagnosis of viral and bacterial infections in hospital settings is currently performed using *ad hoc* pathogen-based routine tests, but they are lengthy and have limited pathogen spectrum coverage, usually leading to a misuse of antibiotics as preventive tool. Transcriptomic biomarkers are becoming promising tools for diagnosis with potential applicability in clinical routine.

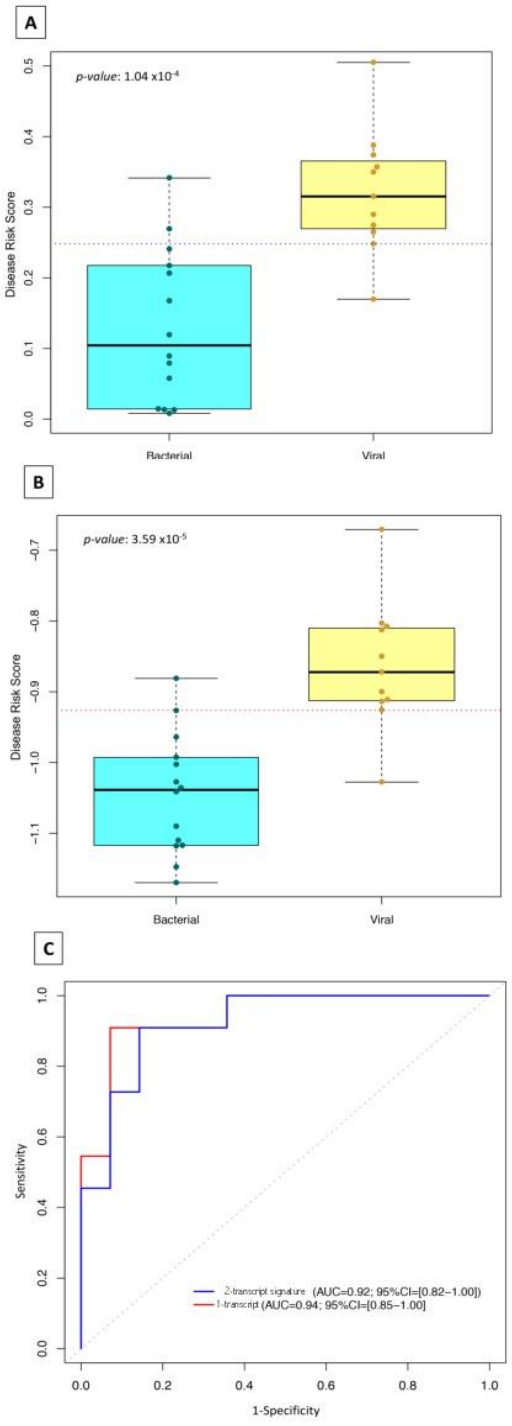
Methods

We evaluated a RT-qPCR assay for a 2-transcript host expression signature previously inferred from microarray data that allow to differentiate between viral and bacterial infection in febrile children. PAXgene^{TM} tubes were used to collect blood samples from 25 febrile children admitted to hospital with confirmed bacterial (n = 14) and confirmed viral infections (n = 11). Additionally, we collected healthy control samples (n = 10) for comparisons.

Results

This assay was able to efficiently discriminate viral from bacterial infections (P-value = 1.04×10^{-4}; AUC = 92.2%; sensitivity = 90.9%; specificity = 85.7%) and showed very high reproducibility regardless of the reference gene(s) used to normalize the data.

Unexpectedly, when testing the discrimination power of these genes expression individually, the monogenic expression signature yielded better results than those obtained from the joined 2-transcript signature (P-value = 3.59×10^{-5}; AUC = 94.1%; sensitivity = 90.9%; specificity = 92.8%). We validated this host monogenic expression signature in RNA-seq data from patients affected by diarrhea of viral and bacterial etiology, confirming that this gene alone differentiates between both groups, thus saving time, effort, and costs.



Conclusions

We demonstrate that host expression microarray data can be successfully translated into a fast, highly accurate and relatively inexpensive *in vitro* assay that can be implemented in clinical routine.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0387
Science and Educational Track

Oral presentation session 04 - Diagnostics

Detection of group b streptococcus colonisation in pregnant women: comparison of two different culture methods

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Background

Group B streptococcus (GBS) is a leading cause of sepsis and meningitis in infants globally. In addition, the incidence in the UK has increased in recent years. To detect GBS colonisation in pregnant women most UK microbiology laboratories use direct plating onto selective agar. However, the sensitivity might be poor in the presence of light GBS colonisation, since it may be masked by the overgrowth of Enterobacteriaceae.

Methods

A total of 597 double-head rectovaginal swabs were analysed from pregnant women from 35 weeks of gestation onwards. Each swab was plated on Chromagar with and without being previously incubated in Lim broth for 6 to 24 hours. The positive cultures were then serotyped with a rapid latex agglutination test and PCR if non-typable by latex. We used McNemar's test to assess the difference in positive predictive values for each method.

Results

Overall, the GBS colonization rate was 20% (119/597). The cultures which used two-step Lim broth-Chromagar identified 97% (115/119) of the positive swabs whereas only 75% (89/119) were identified by direct plating. The difference between the two culture methods is statistically significant ($p<0.001$). The serotype distribution found in the cohort of colonised women was: 25% Ia, 14% Ib, 16% II, 30% III, 1% IV and 14% V.

Conclusions

In conclusion, using a selective broth medium, such as Lim, followed by plating on selective agar, such as Chromagar, is more sensitive than direct plating onto selective agar. This finding suggest that the culture method for GBS detection used routinely in most UK laboratories should be reconsidered.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0116
Science and Educational Track

Oral presentation session 04 - Diagnostics

Characterization of bacterial community structures in neonatal, per-puberty and adolescent stages in the lipopolysaccharide-induced maternal immune activation offspring

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Background

During pregnancy, mother exposure to lipopolysaccharides (LPS) of gram-negative bacteria, called maternal immune activation (MIA), provides a long-term risk to induce social behavior deficits at adolescent offspring. We establish a murine MIA offspring model to longitudinally investigate the changes of intestinal bacterial community that potentially affects brain development *via* gut-to-brain axis activities.

Methods

The pregnant C57BL/6 mice were (SC) injected with LPS (50 μg/Kg) at prenatal GD16. At adolescence, home-cage and 3-chambered behavioral tests were conducted. Total cecum DNAs were extracted at neonatal (4 d), prepuberty (4 weeks old) and adolescent (5 weeks old) offspring. Bacterial community structures derived from V3-V4 16S rDNA amplicons were measured by MiSeq platform (Illumina protocols).

Results

At 5 weeks old, the MIA offspring displayed 38.93±1.54 times of active behaviors (nose-to-nose or nose-to-body) times than did the PBS-treated controls (27.09±1.58 times; $t(90) = 5.3737$, $P<0.01$) on home-cage behavioral test. The proportion of time the mice spent exploring object areas relative to the total time spent to exploration in the MIA offspring was 38.58%±1.63%, which was higher than the 29.63%±1.79% observed in the PBS-treated controls for the 3-chambered behavioral test ($t(66) = 3.6924$, $P<0.01$). In terms of bacterial community, total OTUs were increased in cecum following as the growth of offspring. However, *Clostridium cocleatum* uniquely appeared in MIA neonatal and persisted until adolescent stages.

Conclusions

Social behavioral deficits were induced in MIA offspring. The plasticity of cecal bacterial community was increased during the growth. *C. cocleatum* was a potential target that specific appeared in MIA offspring during the growth. The interplay of intestinal bacterial community may play a role in developing social behavioral deficits in murine MIA model.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0241
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Changes in invasive pneumococcal disease spectrum after 13 valent pneumococcal conjugate vaccine implementation

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Background and Aims:

Pneumococcal conjugate vaccines (PCV) implementation has led to a sharp decrease in invasive pneumococcal disease (IPD) due to the reduction of those due to PCV serotypes (VTs). We aimed to describe the changes in the clinical spectrum of IPD after PCV13 implementation.

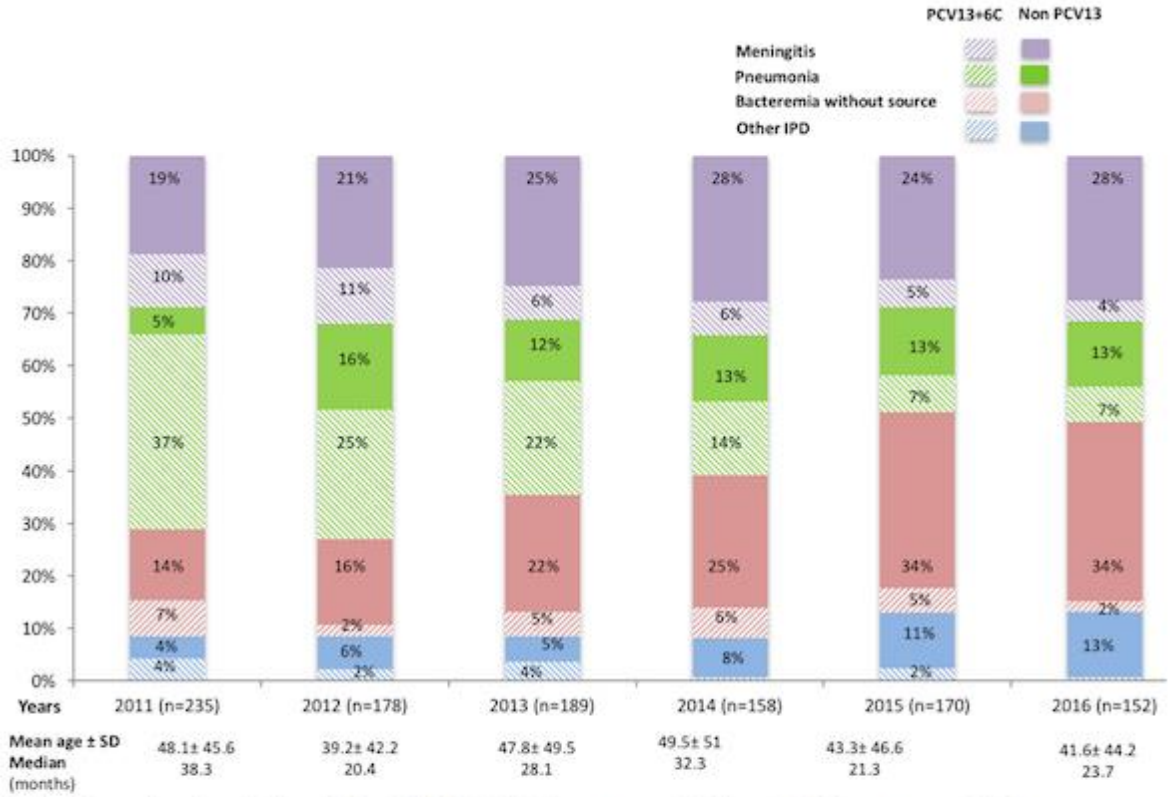
Methods:

This prospective hospital-based active surveillance involved 130 pediatric wards and microbiology departments throughout France. We analyzed IPD cases from 2011 to 2016 for which a pneumococcal isolate was sent to the National Reference Center for Pneumococci for serotyping. Clinical data recorded were history, vaccination status, type of IPD, clinical features and short-term evolution.

Results:

Among 1082 IPD cases collected, the IPD cases decreased from 2011 to 2016 by 35.3% (95%CI [29.2;41.8]) and the median age shifted from 38.3 to 23.7 months ($p = 0.007$). The change in IPD type was mostly due to a reduction of bacteremic pneumonia (from 42.1% to 19.1%, $p<0.001$). The proportion of VTs decreased (from 58.3% to 13.2% from 2011 to 2016) and that of NVTs increased (from 41.7% to 86.8%). Among the emerging non-PCV13 types (NVTs), those known to have the highest disease potential (8, 12F, 24F, and 33F) were isolated more frequently in patients without underlying conditions and induce all IPD entities including bacteremic pneumonia. Conversely, serotypes with lower disease potential (15A, 15BC, 16F and 23B) were rarely isolated from bacteremic pneumonia cases and were more involved in IPD in patients with underlying conditions (35.8%).

Figure. Distribution of invasive pneumococcal disease (IPD) cases by serotypes over time



Meningitis, trend tests from 2011 to 2016, p=0.742, PCV13+6C serotypes, p=0.177, non-PCV13 serotypes, p=0.026
Pneumonia, trend tests from 2011 to 2016, **p<0.001**, PCV13+6C serotypes, **p=0.01**, non-PCV13 serotypes, p=0.350
Bacteremia without a source, trend tests from 2011 to 2016, **p<0.001**, PCV13+6C serotypes, **p=0.041**, non-PCV13 serotypes, p=0.039
Other IPD, trend tests from 2011 to 2016, p=0.05, PCV13+6C serotypes, p=0.918, non-PCV13 serotypes, p=0.162
- Age comparison, **p=0.007**
bold: p significant

Conclusions:

Besides the decrease in IPD incidence after PCV7 then PCV13 implementation, the spectrum of the remaining IPD cases showed significant changes, with substantial discrepancies across NVTs implicated in terms of clinical features and underlying conditions.

Systematic Review Registration:

N/A

ESPID19-1130
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Invasive pneumococcal disease caused by rapidly replacing serotypes in children (less than 15 years) after PCV13 introduction in england; prospective observational cohort study, 2014-18

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Background and Aims:

Four years after the introduction of PCV13 in England, a sudden and rapid increase in invasive pneumococcal disease (IPD) due to non-PCV13 serotypes was observed, with three serotypes – 8, 12F and 9N – being responsible for almost 40% of all laboratory-confirmed IPD cases. We describe the trends in IPD caused by serotypes 8, 12F and 9N among <15 year olds, clinical characteristics, and outcomes compared to PCV13 serotypes and the remaining non-PCV13 serotypes.

Methods:

Public Health England conducts enhanced national IPD surveillance in England and provides a national reference service for serotyping of pneumococcal isolates.

Results:

Between 1 July 2014 and 30 June 2018, there were 1,275 confirmed IPD cases. 326 (26%) were infected by one of the three emerging serotypes (8, 12F, 9N). Serotypes 8 and 9N were more common among younger children (<1 year old) causing IPD in over half of all children (51% and 56%, respectively), while serotype 12F was more common among 1-4 year olds (52%). Cases were significantly more likely to present with pneumonia if infected by any of the emerging serotypes compared with remaining non-PCV13 serotypes, notably for 9N (aOR 2.44, 95% CI 1.29-4.61). While meningitis was significantly more common among those infected by serotype 8 compared to PCV13 serotypes, after adjusting for age and comorbidity status (aOR 2.25, 95% CI 1.27-3.98). Fifty-four cases died within 30 days of their IPD episode, of which 19% were due to an emerging serotype (serotype 8, n=1; serotype 12F, n=9).

Conclusions:

In England, pneumococcal conjugate vaccines have led to large and sustained declines in overall and vaccine-type IPD. Ongoing enhanced surveillance is important to understanding disease severity and outcomes of IPD due to emerging serotypes.

Systematic Review Registration:

N/A

ESPID19-1009
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Impact of 10 and 13-valent pneumococcal conjugate vaccines on invasive pneumococcal disease in children under five years of age: results of a european multicentre study

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Background and Aims:

We estimated the impact of 10 and 13-valent pneumococcal conjugate vaccines (PCV10/13) on invasive pneumococcal disease (IPD) in children <5 years of age from 10 European countries (12 SpIDnet sites and Finland). Nine sites used PCV13, two PCV10 and two both vaccines in their childhood vaccination programmes

Methods:

We calculated IPD incidence rate ratios (IRR) in children <5 years, by site, comparing the incidence in the last PCV10/13 year (2017) with the average incidence during the PCV7 period. We computed pooled IRRs and 95% confidence intervals using random-effects meta-analysis for sites using only PCV13 and for sites using PCV10 (PCV10 only or both PCV10 and PCV13). We measured impact as (1-IRR)*100.

Results:

Compared with the PCV7 period, IPD incidence caused by any, PCV7 and PCV10non7 serotypes declined by 42% (28; 53), 87% (70; 94) and 96% (93; 98) respectively in PCV13 sites, and by 60% (42; 72), 97% (90; 99) and 90% (55; 98) in sites using PCV10. The incidence of PCV13non10 serotypes decreased by 63% (49; 73) in PCV13 sites and remained stable in sites using PCV10 (-6% (-282; 71)). Serotype 19A IPD incidence decreased by 78% (62; 87) in PCV13 sites. The incidence of IPD caused by non-PCV13 serotypes increased by 93% (45; 156) in PCV13 sites and by 85% (17; 194) in sites using PCV10.

Conclusions:

Childhood PCV10/13 vaccination programmes resulted in substantial declines in any and vaccine serotype IPD incidence. The decrease in PCV13non10 IPD incidence in PCV13 sites was related to the impact on 19A IPD incidence. The increase in the incidence of IPD caused by non-PCV13 serotypes in both groups suggests serotype replacement which requires close monitoring.

Acknowledgments: SpIDnet is funded by participating institutes and ECDC.

Systematic Review Registration:

NA

ESPID19-0741
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Serotype distributions in childhood pneumococcal diseases in finland before and after pneumocccal vaccinations

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Background and Aims:

Most data on pneumococcal (Pnc) serotype distributions are limited to invasive pneumococcal disease (IPD) and nasopharyngeal carriage. We evaluated the serotype distributions in IPD, bacteremic pneumonia and otitis media in unvaccinated and PCV-vaccinated children aged <2 years.

Methods:

PCV10 was introduced into the Finnish National Vaccination Programme (NVP) for 3-month-old children (2+1 schedule) in 2010. To identify bacteremic pneumonia (BP) episodes, serotyped cases of IPD with blood isolates (bacteremia) were collected from the National Infectious Disease Register (NIDR) for children aged <2 years in 2004-2009 and 2012-2016 and linked with hospital in- and outpatient discharge notifications with diagnoses compatible with pneumonia (ICD-10 codes J10.0/J11.0/J12-J18/J85.1/J86) from national Care Register by using national identifier. Hospital-treated primary pneumonia (HTPP) was defined as primary pneumonia diagnosis after inpatient hospitalization. Serotypes for otitis media (OM) episodes among PCV7-vaccinated and non-vaccinated children were obtained from the Finnish Otitis Media (FinOM) vaccine trial conducted in 1995-1999. Cases and episodes (duration of 30 or 90 days for OM and BP, respectively) were categorized into vaccine serotype groups.

Results:

Among unvaccinated children, the proportion of vaccine-type disease was higher or similar in IPD compared to BP or OM, and the PCV7/10-associated decrease was greatest in IPD (Table 1). The proportion of the 3 extra PCV13 serotypes was high in BP both before and after PCV10 vaccination, while the proportion of non-vaccine serotypes was highest in otitis.

Table. Number and proportion (%) of bacteremia cases and episodes of bacteremic pneumonia and otitis media among PCV10-eligible or PCV7-vaccinated and control children <2 years of age.

	Pre-PCV10 period 2004-2009		FinOM trial control arm 1995-1999
	All bacteremia	Bacteremic pneumonia	Otitis
All cases/episodes	401 (100)	53 (100)	414 (100)
PCV7 serotypes	282 (70.3)	28 (52.8)	250 (60.4)
PCV10 serotypes	294 (73.3)	29 (54.7)	254 (61.3)
PCV13-PCV10 serotypes	69 (17.2)	20 (37.7)	84 (20.3)
3	5 (1.2)	4 (7.5)	26 (6.3)
6A	16 (4.0)	3 (5.7)	13 (3.1)
19A	48 (12.0)	13 (24.5)	45 (10.9)
PCV13 serotypes	363 (90.5)	49 (92.5)	334 (80.7)
Non-vaccine serotypes	22 (5.5)	1 (1.9)	80 (19.3)
Undefined	16 (4.0)	3 (5.7)	0 (0)
	PCV10 period 2012-2016		FinOM trial PCV7 arm 1995-1999
	All bacteremia	Bacteremic pneumonia	Otitis
All cases/episodes	63 (100)	17 (100)	271 (100)
PCV7 serotypes	0 (0)	0 (0)	107 (39.5)
PCV10 serotypes	16 (25.4)	3 (17.6)	111 (41.0)
PCV13-PCV10 serotypes	30 (47.6)	12 (70.6)	49 (18.1)
3	12 (19.0)	5 (29.4)	17 (6.3)
6A	0 (0)	0 (0)	13 (4.8)
19A	18 (28.6)	7 (41.2)	19 (7)
PCV13 serotypes	46 (73.0)	15 (88.2)	156 (57.6)
Non-vaccine serotypes	17 (27.0)	2 (11.8)	115 (42.4)
Undefined	0 (0)	0 (0)	0 (0)

Conclusions:

After PCV vaccinations, the vaccine-type disease reduced remarkably, but remained high in otitis. The incomplete direct effect against otitis requires development of the indirect effect to eradicate vaccine-type disease, yet the replacement by non-vaccine types remains to cause pneumococcal otitis.

Systematic Review Registration:

ESPID19-0733
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Impact of ten-valent pneumococcal conjugate vaccine (PCV10) on lower respiratory tract infections among vaccine-eligible children in Finland

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Background and Aims:

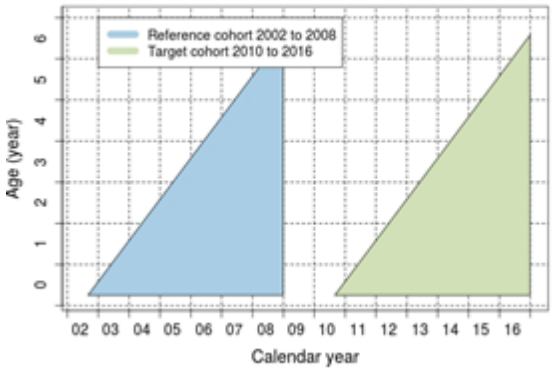
PCV10 was introduced into the Finnish National Vaccination Programme (NVP) in September 2010 using the Nordic schedule with vaccinations at 3, 5 and 12 months of age. In the National Vaccine Register, uptake was estimated at ~93%. Universal influenza vaccine was introduced to children 6-35 months of age in 2007 with annual uptake ranging 13-40%. We evaluated the impact of PCV10 on lower respiratory tract infections (LRTI) among vaccine-eligible children.

Methods:

LRTI episodes (excluding pneumonia and influenza) in vaccinated target cohort eligible for NVP (children born 06/2010-09/2016) were compared with a season and age-matched (3-78 months) reference cohort before introduction (Figure). In- and outpatient hospital discharge notifications with diagnoses compatible with any LRTI (ICD-10 codes J20-22) were collected from national Care Register to calculate rates of LRTI and hospital-treated primary LRTI (HTP-LRTI, LRTI as the first diagnosis after in-patient hospitalization) before and after introduction. LRTI and HTP-LRTI were further stratified by ICD-10 code to undefined (or streptococcal) LRTI (J20.2/J20.9/J22), and to non-pneumococcal (other LRTI, J20.0-1/J20.3-8/J21). Episode duration was 90 days.

Results:

The rate of any LRTI was 5.4 in the reference cohort and 6.2/1000 person-years in the target cohort. Compared with the reference cohort, the rate of other LRTIs was 19.3% higher (95% CI 15.1 to 23.7%; 0.9/1000 person-years) in the vaccine-eligible cohort. However, the rate of undefined LRTI decreased by 9.3% (2-16.1%) or 0.1/1000 person-years. The relative and absolute reductions of undefined HTP-LRTI were 31.3% (20.5-40.7%) or 0.11/1000 person-years, respectively.



Conclusions:

This nation-wide study suggests a reduction in the undefined LRTI in routine vaccination program setting whereas other LRTIs increased. Further investigation is needed to better understand the impact of the viral epidemics and possible changes in diagnostics.

Systematic Review Registration:

ESPID19-0560
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Increase of ST19A invasive pneumococcal disease in young children after switch from PCV13 to PCV10

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Background and Aims:

In July 2015 (Flanders (northern region of Belgium)) and May 2016 (Wallonia (southern region of Belgium) and Brussels), the 13-valent pneumococcal conjugate vaccine (PCV13) (2+1) was replaced by PCV10 (2+1) in the childhood vaccination program. We evaluated the serotypes causing invasive pneumococcal disease (IPD) in children less than 2 years old before and after this switch in conjugate vaccine.

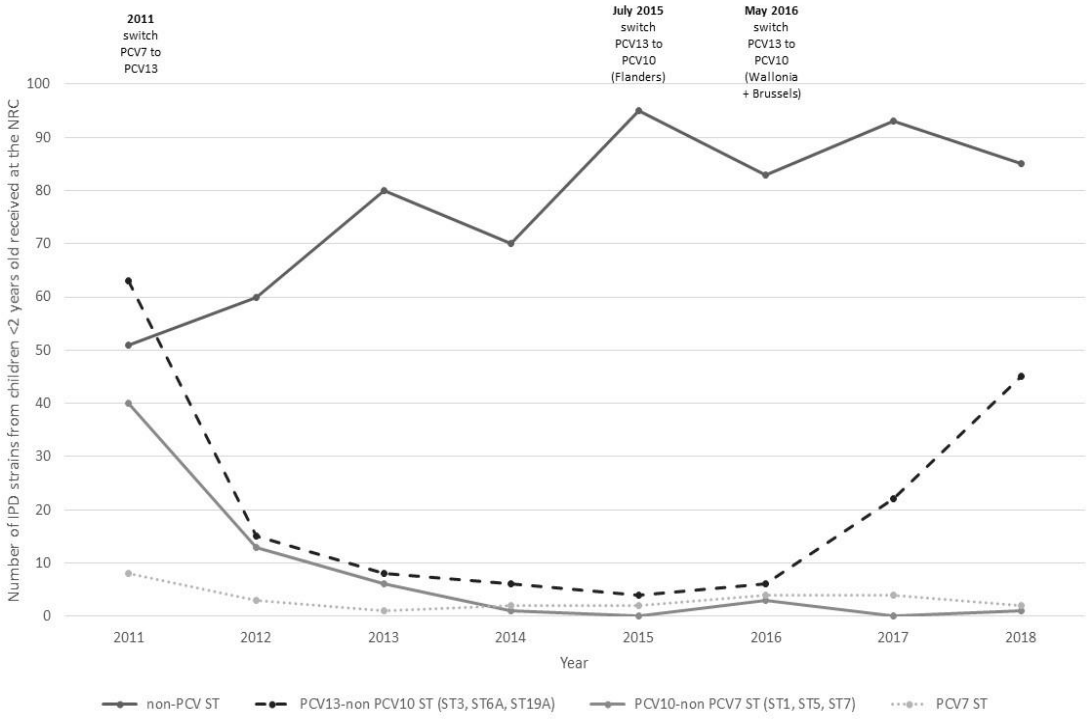
Methods:

Surveillance of IPD in Belgium is based on a stable laboratory-based system involving a yearly mean of 101 laboratories, evenly spread over the country, sending their IPD strains to the National Reference Centre for capsular typing and antibiotic susceptibility testing.

Results:

In 2014, before the switch from PCV13 to PCV10, the most important serotypes (STs) in children <2 years old were ST12F (23%), ST10A (13%), ST33F (9%), ST22F (8%) and ST15B (6%). Only 11% of all 79 cases were caused by PCV13 serotypes (5.1% ST19A, 2.5% ST3, 3.9% other STs).

Since 2017 we detect an increase in the proportion of IPD caused by PCV13 STs (Figure). In 2018, ST19A (27%) has become the most important ST, followed by ST12F (9%), ST24F (9%), ST3 (7%). 37 ST19A of a total of 136 IPD cases were detected in 25 different hospitals. Most of the cases were detected in Flanders (n=30), but also cases were detected in Wallonia (n=3) and Brussels (n=4). ST19A IPD were detected in children aged <6 months (n=5), 6-11 months (n=21) and 12-23 months (n=11).



Conclusions:

Two to three years after the switch from PCV13 to PCV10, we detect an emergence of ST19A IPD in children <2 years old. Deep characterization of ST19A strains by means of whole genome sequencing is ongoing to help to clarify this evolution.

Systematic Review Registration:

N/A

ESPID19-0428
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Invasive pneumococcal disease after a vaccine switch in the pneumococcal conjugate vaccination program in belgium: data in perspective

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Background and Objective

Recent systematic reviews have found no consistent evidence of a difference between 13-valent pneumococcal conjugate vaccine (PCV13) and pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine (PHiD-CV) in their impact on overall pneumococcal disease. Several countries/regions have switched from PCV13 to PHiD-CV in their infant immunization programs. In Belgium, increases in the number of overall and 19A invasive pneumococcal disease (IPD) isolates were reported in <2-year-olds in 2017, 1-2 years after the PCV13-to-PHiD-CV switch (Figure). We explored whether these increases may be related to the switch.

Methods

We reviewed IPD surveillance reports from the Belgian National Reference Center (NRC) and surveillance data/published literature from other countries.

Learning Points Discussion

The available Belgian surveillance data could be considered preliminary:

- Only numbers/percentages of IPD isolates and no incidences over time are available, preventing confirmation of conclusions on increases in the overall/19A IPD incidence.
- The increase is driven by bacteremia/pleuritis while the number of meningitis isolates remained stable, suggesting possible changes in non-meningitis case report patterns.
- Publicly available NRC data show that increases are mainly confined to one winter season (Figure). However, preliminary data for Jan-Sep 2018 indicate an ongoing trend.
- Vaccination status for 19A IPD cases was heterogenous (Figure).
- Increases were also present in ≥2-year-olds who probably received PCV13 (vaccinated pre-switch).
- Longer follow-up is needed to confirm/understand this signal.

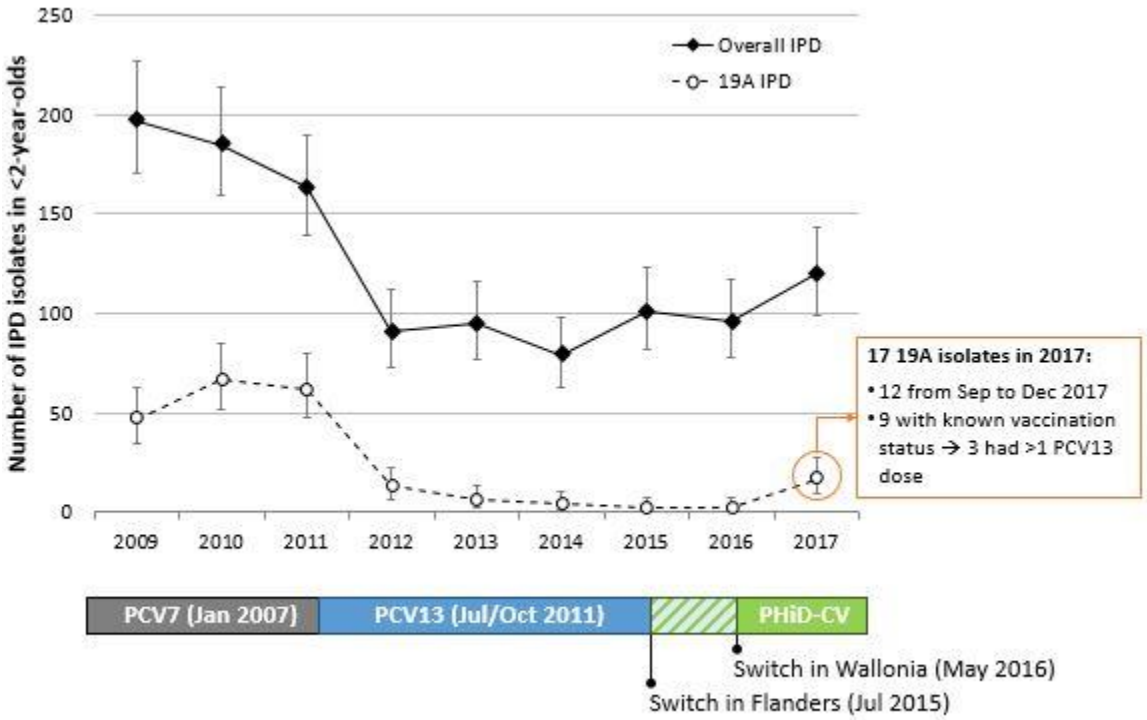
In other PHiD-CV- or PCV13-using countries:

- 19A is still circulating, although incidence is low compared to the pre-PCV13/PHiD-CV incidence and the remaining overall IPD incidence.
- Despite decreases in 19A IPD following PCV13 use, fluctuations have been observed in some countries.

Data from other countries switching from PCV13 to PHiD-CV are scarce. However, available data show no increases in overall/19A IPD incidence following the switch.

Funding: GlaxoSmithKline Biologicals SA

Figure. Overall and 19A IPD isolates in children <2 years old in Belgium



Error bars depict 95% confidence intervals, calculated using Poisson regression.
Preliminary data for Jan–Sep 2018: 95 overall IPD isolates, 23 19A IPD isolates in children <2 years old.

ESPID19-0252
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Circulating clonal complexes and sequence types of streptococcus pneumoniae serotype 19a worldwide: the importance of multidrug resistance

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Background and Objective

Multidrug-resistant (MDR) isolates of serotype 19A pneumococci have appeared worldwide in the last decades, raising concern over the effectiveness of antimicrobial therapies and vaccination programs. Pneumococci of the same serotype may differ genetically, based on which they are assigned to a sequence type (ST) and grouped into clonal complexes (CCs), which can display different antimicrobial susceptibility. We reviewed data on genetic characteristics of serotype 19A isolates collected from patients with pneumococcal disease reported from different geographic regions to have an overview on CCs and STs worldwide.

Methods

Available surveillance data from 1986 to 2018 were analysed to conduct a descriptive analysis of serotype 19A pneumococci circulating worldwide. These were grouped into CCs and/or STs based on multilocus sequence typing or whole genome sequencing. Isolates were included regardless of patient age and whether collected pre-/post-introduction of a pneumococcal conjugate vaccine (PCV) in the national immunisation program.

Learning Points Discussion

− Our analysis included datasets from 11 countries of which all reported MDR clones of serotype 19A. The percentage distribution for the most frequent CCs/STs circulating worldwide and reported in the analysed countries is shown in the figure.

− The increased resistance of serotype 19A pneumococci circulating worldwide was shown to be related to an increase in occurrence of MDR clones. CC320, known to be MDR, was prevalent in most of the evaluated countries (ranges: 2.9%–45.2% of isolates), irrespective of population age, pre-/post-PCV introduction and PCV used. In addition, CC199 was within the 3 most prevalent in 5 out of 11 countries analysed.

− Further surveillance of pneumococcal CCs and STs is advised to assess the impact of PCV use, serotype 19A epidemiology, and antibiotic resistance.

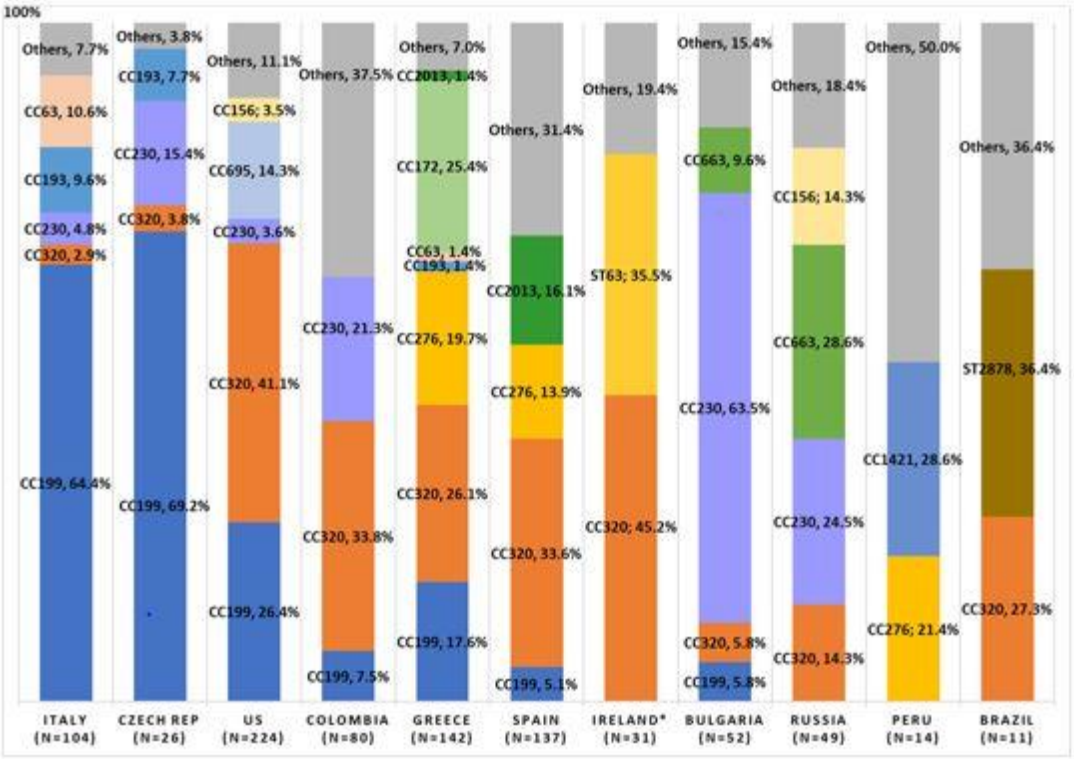

Figure. Percentage distribution of CCs and STs in 19A isolates per country, regardless of age groups, pre-/post-PCV introduction, and PCV used. We reported percentage of STs only when data on the corresponding CCs were not available.

Notes: Countries (period of time, population age) included in the analysis were: Italy (2001–2003 and 2006–2009, age not available); Czech Republic (2014, 0–79 YOA); US (2009, 2012–2013, <5 YOA); Colombia (1994–2012, 0–87 YOA); Greece (1986–2015, ≤14 YOA); Spain (2010–2013, all ages); Ireland (2009–2014, 0–16 YOA); Bulgaria (1992–2013, 0–84 YOA); Russia (2002–2013, age not available); Peru (2006–2011, all ages); Brazil (2007–2012, 0–94 YOA). The 'Others' category includes CCs and STs labelled as such in the published papers, identified in only 1 country while the percentage distribution was <15% (except for US, where CCs with percentage distribution <10% were included because of the large US territory), identified in ≤2 countries while each had a percentage distribution <10%, or that had a percentage distribution ≤1%. *CCs were analysed on MDR serotype 19A isolates.

Funding: GlaxoSmithKline Biologicals SA

ESPID19-0354
Science and Educational Track

Oral presentation session 05 - Pneumococcal disease

Post PCV13 dynamics of new non-PCV13 pneumococcal vaccine serotype candidates: differences between carriage and invasive pneumococcal disease in young children

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Background and Aims:

PCV13 implementation in children resulted in a substantial decline in carriage, invasive pneumococcal disease (IPD) and overall disease caused by vaccine serotypes (VT13). However, disease caused by non-PCV13 serotypes (NVT) is still relatively prevalent and even increasing, especially in compromised populations, leading to an effort to develop higher-valency PCVs (e.g. PCV15, PCV20).

We assessed VT13 and NVT dynamics in nasopharyngeal (NP) carriage and IPD in children <2 years following PCV implementation. We specifically assessed NVT candidates to be included in PCV15/PCV20 (Add-VT20; 8, 10A, 11A, 12F, 15B/C, 22F, 33F) *vs*. other-NVT.

Methods:

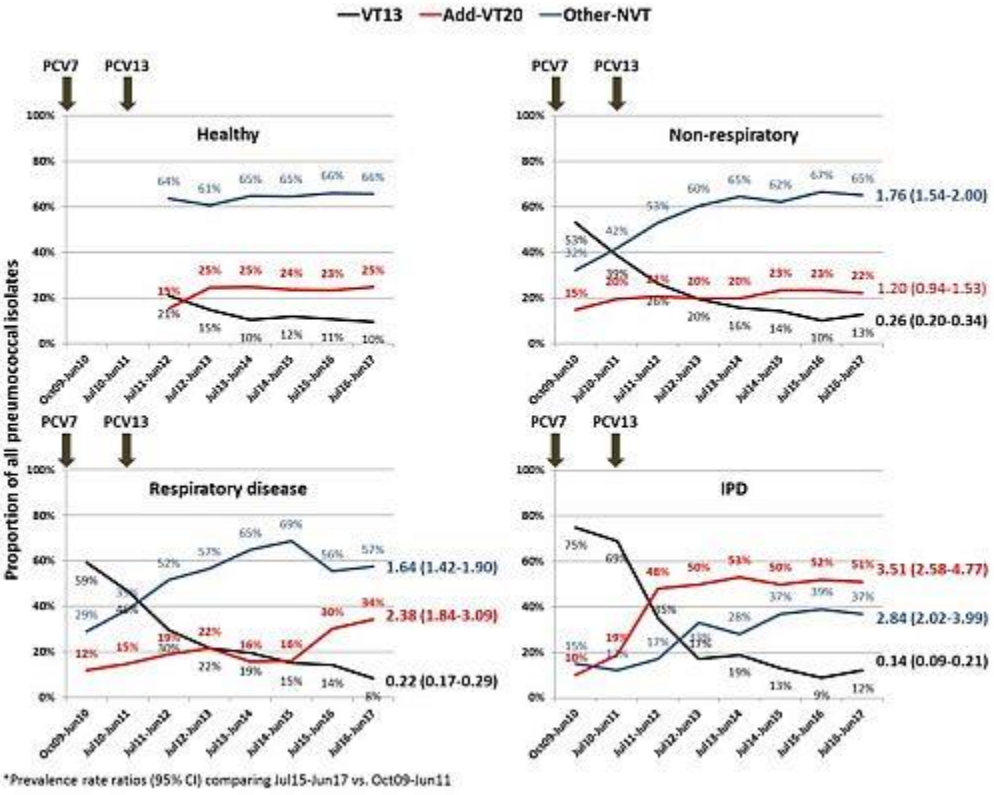
An ongoing prospective, population-based surveillance, conducted between Oct-2009 and Jun-2017, in Israel. We studied 4 groups: IPD, and carriage in healthy children, respiratory disease and non-respiratory disease (Surveillance for healthy children started only from 2011).

Rate ratios (RRs) with 95% CIs were calculated, comparing VT13, Add-VT20 and other-NVT proportions of all pneumococcal isolates during early-PCV (2009-2011) and late-PCV13 (2015-2017) periods.

Results:

Overall, 14,695 NP cultures and 974 IPD episodes were recorded. VT13 declined significantly in all 4 groups by 74-84% (**Figure**). Overall-NVT proportions substantially increased by 58%, 85% and 220% in non-respiratory disease, respiratory disease and IPD, respectively. Proportions of Add-VT20 significantly increased in respiratory disease carriage and IPD (51% of IPD in 2015-2017), but not in non-respiratory disease carriage. In contrast, other-NVT increased in all 4 groups. Add-VT20 rapidly became the leading fraction in IPD but not in carriage.

Figure. Dynamics of pneumococcal carriage and IPD rates (proportion of VT13, add-VT20 and other-NVT of all pneumococcal isolates) in children <24 months, Israel, October 2009 through June 2017



*Prevalence rate ratios (95% CI) comparing Jul15-Jun17 vs. Oct09-Jun11

Conclusions:

PCV13 implementation resulted in a substantial increase in proportions of NVT carriage and IPD. These trends were more marked for Add-VT20 in respiratory diseases and IPD, suggesting a higher disease potential of Add-VT20 vs. other-NVT for these endpoints.

Systematic Review Registration:

N/A

ESPID19-1198
Science and Educational Track

Oral presentation session 06 - Vaccines

Associations between enteropathogens and rotavirus vaccine immunogenicity among rural zimbabwean infants

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[5]Cincinnati Children's Hospital, Department of Pediatrics, Ohio, USA
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Background

Oral rotavirus vaccines (RV) are less efficacious among infants in low-income compared to high-income settings. The reasons for this remain unclear but intestinal factors may be important, including infection with enteropathogens, which are prevalent from early infancy in low-income settings. We hypothesised that enteropathogen infection would reduce RV immunogenicity.

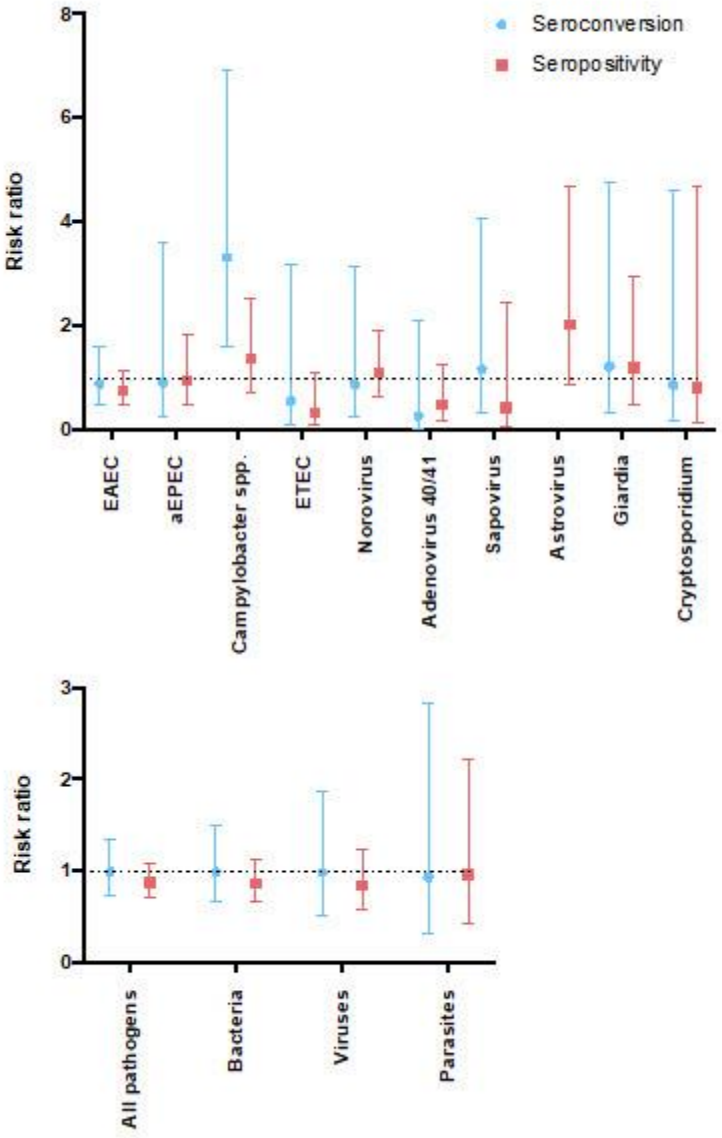
Methods

We used quantitative molecular methods to measure enteropathogens in stool specimens collected from a subset of infants enrolled in the SHINE trial, a cluster-randomised 2x2 factorial trial of improved water, sanitation and hygiene (WASH) and improved infant feeding in rural Zimbabwe. Using multivariable regression analyses, we explored associations between individual and grouped pathogens and RV seroconversion (primary outcome) and RV seropositivity and geometric mean titre (GMT) (secondary outcomes).

Results

440 infants had stool specimens with valid stool qPCR results and available RV immunogenicity data. Median age at stool collection was 74 days (IQR 39-108). 231/440 (52.5%) infants had >1 detectable pathogen and 101/440 (23.0%) had >2 pathogens detected. Enteroaggregative *E. coli* was the most prevalent pathogen detected in stools (32.0%) followed by norovirus (9.1%). Seroconversion to RV was low overall (21.8%). There were no significant associations between individual pathogens and RV seroconversion, seropositivity or GMT in unadjusted analyses. After adjusting for pre-specified variables including age, birth-weight, breastfeeding and season, detection of *Campylobacter* species was positively associated with RV seroconversion (RR 3.31 (95%CI 1.59, 6.90), P=0.054). In both unadjusted and adjusted analyses, there were no significant associations between pathogen groups (bacteria, viruses,

parasites or all pathogens) and any measure of RV immunogenicity.



Conclusions

Enteropathogens were commonly detected around the time of RV receipt in rural Zimbabwean infants. However, we found no consistent associations between enteropathogens and immune responses to RV.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0555
Science and Educational Track

Oral presentation session 06 - Vaccines

Hpv vaccination and a reduction in cervical intraepithelial neoplasia in british columbia, canada: results from an ecological analysis

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Background

Since 2008, girls in British Columbia (BC), Canada, have been offered the HPV vaccine through a school-based vaccination program. The oldest birth cohort eligible for the vaccination program is 1994 and uptake is on average 63%. To evaluate the impact of the HPV vaccine in BC, ecological trends in cervical intraepithelial neoplasia (CIN) rates were assessed in young women before and after the implementation of the HPV vaccination program.

Methods

Information on all Pap smears and histopathological abnormalities, in calendar years 2004-2017 in women under age 28 for BC were obtained from the population-based cervix cancer screening program database. Rates of cervical intraepithelial neoplasia (CIN) were calculated as the number of cases divided by the number of cytology specimens for that period. Incidence rate ratios (IRR) were calculated by piece-wise Poisson regression analysis. IRR were adjusted for age and screening year. We performed a sensitivity analysis including only women eligible for routine screening.

Results

Incidence rates of CIN, adjusted for age and year of screening, in BC declined significantly by comparing birth cohorts ineligible and eligible for the the HPV vaccination program. The total number of screens in the unvaccinated cohort was 1,417,512 and in the vaccinated cohort 73,343. The adjusted IRR for CIN1, 2 and 3 were respectively 0.60 (95%CI 0.53-0.67), 0.49 (95%CI 0.41-0.57) and 0.39 (95%CI 0.32-0.47). Sensitivity analysis confirmed these findings, also indicating a significant decline in CIN rates in birth cohorts eligible for the HPV vaccination program.

Conclusions

The observed decline in rates of CIN since the introduction of the school-based HPV vaccine program, illustrates the population impact of the BC provincial school-based HPV vaccination program.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0772
Science and Educational Track

Oral presentation session 06 - Vaccines

Safety and tolerability of human rotavirus vaccine in extremely preterm infants

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Background

Preterm infants are at increased risk of severe acute gastroenteritis (AGE) and rotavirus (RV) is the most common pathogen. Human RV vaccine (HRV) is currently licensed for infants with a gestational age (GA) of at least 27 weeks, leaving preterm infants of younger GA at risk. We assessed the safety and tolerability of HRV among extremely preterm infants, born at GA < 27 weeks.

Methods

Within the Risk-group Infant Vaccination Against Rotavirus [RIVAR] project, 13 Dutch hospitals implemented targeted HRV vaccination as standard of care for infants with medical risk conditions, including prematurity. Four out 13 hospitals decided to include extremely preterm infants for off-label use of HRV. Among them, we evaluated serious adverse reactions (SAR) following HRV administration as reported in medical records up to 5 months of age. Within a subset of extremely premature infants, we compared the tolerability of the first dose of NIP vaccines + HRV versus a control group of NIP without NIP. We used parent reported symptoms in the 7 days following administration of either combination of vaccines.

Results

Within the four hospitals, 40 (median GA 26,0 weeks, range: 24,0-26,86) out of 50 extremely preterm infants received HRV (80%), no SARs following HRV administration were reported. There were no statistically significant differences in the number of parent-reported symptoms following administration of

NIP versus NIP+HRV in extremely preterm infants (Table

Table 1. Tolerability of first dose NIP vaccines versus NIP + HRV in extremely preterm infants

Parent reported symptoms	HRV+ NIP (N=14)	NIP only (N=21)	p-value
Fever	4 (29%)	4 (19%)	0,69
Skin rash	0	0	NA
Irritability	0	6 (29%)	0,06
Loss of appetite	2 (14%)	0	0,15
Vomiting	0	0	NA
Loose stools	2 (14%)	0	0,15
Bloody stools	0	1 (5%)	1,0
Any symptom	8 (57%)	8 (38%)	0,27
More than one symptom	0	3 (14%)	0,08

1).

Conclusions

To our knowledge, this is the first study on safety and tolerability of HRV in extremely preterm infants. We conclude that administration of HRV in this vulnerable population is not associated with SARs and is generally well tolerated.

RIVAR project is funded by UMCUtrecht, ZonMw, InnovatiefondsZorgverzekeraars and GlaxoSmithKline(StudyID:203108).

Clinical Trial Registration (Please input N/A if not registered)

(www.trialregister.nl NTR 5361)

ESPID19-0721
Science and Educational Track

Oral presentation session 06 - Vaccines

Challenges in using the newly established swedish vaccine register for surveillance and research purposes – data completeness and reporting methods

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Background and Aims:

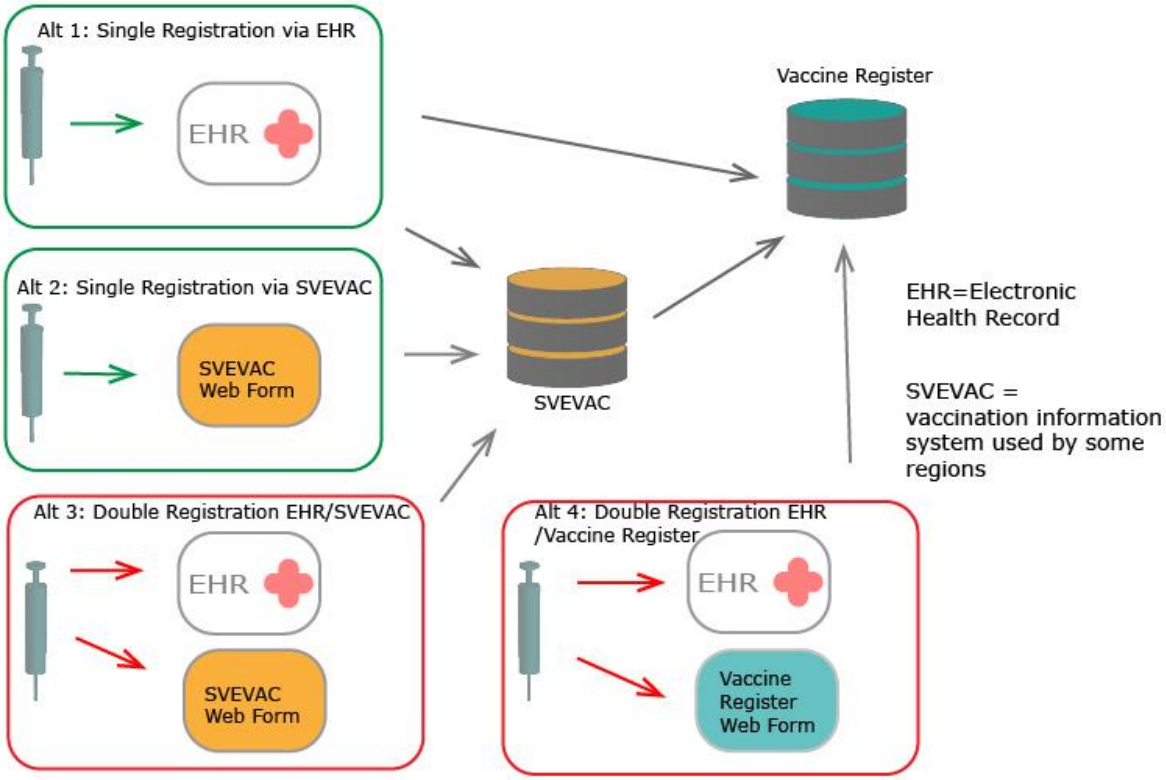
Vaccine Registers are considered important tools in both surveillance of vaccine coverage, effectiveness and safety and for research purposes. The Swedish Vaccine Register was founded in 2013 and reporting is compulsory for the care-givers by law. This is the first study using data from the Swedish Vaccine Register, with the aim of evaluating the completeness of register data.

Methods:

The study population was defined from the Swedish Total Population Register and contained all infants born in Sweden during 2014-2015 with a Swedish personal number, 226 661 individuals. Data regarding programme vaccinations until the age of 24 months was taken from the Swedish Vaccination Register. Information about reporting systems were gathered from register keepers at the Public Health Agency of Sweden (see Fig1).

Results:

Figure 1. The four alternative methods in use 2014-2017 for registration of data in the Swedish Vaccination Register



In the study population, 98% had at least one DTP-containing vaccination registered in the Vaccine Register and 85,2 % had three or more DTP-containing vaccine doses at two years of age (mostly given as hexa- or pentavalent vaccines).

During the study period, the Stockholm region changed reporting system from double registration to single registration. When switching reporting system, the proportion with three or more reported DTP doses in the Stockholm region increased from 85% to 95,2%.

Conclusions:

In the newly established Swedish Vaccination Register, the proportion of infants fully vaccinated with DTP vaccine is considerably lower than in national coverage data (3-dose DTP born 2015 97,5%). Reporting is not complete, which is expected in the start-up phase for a national register. Double registration procedures are associated with low completeness. Setting up a reliable vaccine register with single registration procedures is a challenging task considering the variety of electronic health care record systems even in a small country like Sweden.

Systematic Review Registration:

0

ESPID19-0645
Science and Educational Track

Oral presentation session 06 - Vaccines

Microrna s are potential correlates of vaccine protection and biomarkers of infection in a human challenge model of salmonella enterica serorvar typhi

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Background

Typhoid fever is a life-threatening infection caused by *Salmonella* enterica serovar Typhi. It is an important cause of childhood febrile illness in low income countries. Typhoid can be challenging to diagnose thus new diagnostic biomarkers are needed. Several *S.* Typhi vaccines exist, but none have a correlate of protection. Post transcriptional regulation of protein-coding genes by microRNAs (miRNAs) is important in immunity. We investigated whether *S.* Typhi vaccination and exposure changes miRNA expression in peripheral blood mononuclear cells (PBMCs) in man and correlated these changes with outcome post *S*. Typhi challenge.

Methods

Participants were vaccinated with a plain Vi-polysaccharide vaccine (Vi-PS) or Vi-polysaccharide conjugated to tetanus toxoid (Vi-TCV) and exposed to an oral, pathogenic dose of S. Typhi 28-days later. sRNA-sequencing was conducted on PBMCs at baseline, 7- and 10-days after vaccination, day of challenge, 1-day after challenge, at diagnosis, and 7-days after challenge in participants not developing typhoid.

Results

Samples were obtained from 53 participants. The best correlates of protection 10-days after vaccination were miR-582-3p and miR-7974 in Vi-PS and Vi-TCV vaccinees respectively. Median microRNA foldchanges were greater 1-day post challenge in participants who remained well compared with those who developed typhoid. Eighty (11%) miRNAs were differentially expressed during acute typhoid. One of the most differentially expressed microRNAs during acute typhoid was miR-21; this microRNA targets genes involved in the bacterial invasion of epithelial cells (KEGG pathway).

Conclusions

Greater perturbation of miRNA expression after *S*. Typhi exposure is associated with resistance to typhoid. We identified potential vaccine correlates of protection and infection biomarkers. In the long-term, these findings could be useful in vaccine development, diagnostics, or creating miRNA-based treatments that augment host responses to *S.* Typhi.

Funding: European Commission FP7 grant ADITEC, MRC

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov:NCT02324751

ESPID19-0520
Science and Educational Track

Oral presentation session 06 - Vaccines

Long intervals between two doses of hpv vaccines and magnitude of the immune response: a post-hoc analysis of two clinical trials

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Background

The objective of this analysis was to compare the anti-HPV antibody titers (GMTs) and their distribution after a 6- month or a 3-8 years interval between two HPV vaccine doses.

Methods

The results from two clinical trials, conducted by the same team in the same region, with serological assays performed at the same laboratory using the same ELISA methodology were compared. In the first study, 173 9-10 year-old girls and boys received two doses of nonavalent HPV vaccine (9vHPV) at a 6-month interval; in the second study, 31 girls vaccinated with one dose of quadrivalent HPV vaccine (4vHPV) at the age 9-14 years received a dose of 9vHPV 3-8 years later (mean 5.4 years). In both studies blood samples were collected before and 1 month post-second dose.

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Results

Despite large differences in the time since the first dose, all subjects (100%) were seropositive to HPV6, 11, 16 and 18, with comparable GMTs and titer distributions before the second dose. One-month post-second dose, the GMTs increased 40- to 91-fold for those with a 6-month interval between doses and 60- to 82-fold for those with 3-8 years interval. Titer distributions after the second dose were comparable in the two studies.

Conclusions

These results indicate that 2-dose HPV vaccination schedules with an interval of several years could be used for pre-adolescents. Intervals longer than 6 months may facilitate logistics for immunization programs and could be useful during periods of vaccine shortage or as a transition while the effectiveness of a one-dose schedule is being evaluated.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: 03431246 and 02567955

ESPID19-0251
Science and Educational Track

Oral presentation session 06 - Vaccines

Prolonged shedding of oral pentavalent bovine-human reassortant rotavirus vaccine g1 strain predisposes for genetic alterations of vp7

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Background

Prolonged shedding of live oral pentavalent bovine-human reassortant rotavirus (RV) vaccine RotaTeq® has been detected in immunocompetent and immunocompromised children and is commonly associated with genotype G1. We studied genetic alterations in VP7, VP4 and VP6 of RotaTeq® derived G1 vaccine strains in children with prolonged shedding.

Methods

Stool samples were obtained from 292 infants 5-10 days after the first dose at age 2 months and from 247 infants 0-7 days before the third dose of the vaccine at age 5 months. Additional samples 6 and 12 weeks later were collected if the second stool sample was positive for RV. All stools were studied with RT-PCR for RV VP7, VP4 and VP6 and further sequenced.

Results

We found RV G1 genotype from 75% (220 of 292) of the first samples, of which 17% were still positive for RV VP7 G1 prior to the 3rd vaccine dose. In 68% (26 of 38) of these samples, nucleotide changes in VP7 were detected; only in 32% (12 of 38) VP7 sequence remained identical to RotaTeq® vaccine strain. Of samples with nucleotide changes, 85% (22 of 26) resulted in amino acid changes, of which majority were located in antigenic epitope 7-2. Aspartic acid in position 145 had changed to asparagine in 19 samples. In three cases the amino acid substitution remained 12 weeks after the 3rd vaccine dose. No changes at amino acid level were detected in VP4 or VP6 sequences.

Conclusions

Prolonged vaccine shedding of G1 RotaTeq strain is common and may predispose for genetic substitutions in antigenic epitopes of VP7. The detected amino acid change in VP7 antigenic epitope may cause escape from neutralization and thus increase potential for prolonged shedding of VP7.

Clinical Trial Registration (Please input N/A if not registered)

Eudra-CT 2014-004252-60

ESPID19-0035
Science and Educational Track

Oral presentation session 06 - Vaccines

Factors influencing antibody responses to routine immunisations during the first year of life

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Background

There are substantial variations between individuals in the immune response to immunisation.In this study, we investigated the effect of maternal immunisation during pregnancy and the effect of early-life factors, namely sex, delivery mode, feeding method and antibiotic exposure, on antibody responses to routine immunisations administered during the first year of life.

Methods

A total of 471 healthy infants were included. One and seven months after the primary course of routine vaccines at 6 weeks, 4 and 6 months of age, and one month after routine vaccines at 12 months of age, antibodies against diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b, pneumococcus, meningococcusC, measles, mumps and rubella were measured. The seroprotection rate for each vaccine antigen, together with the geometric mean concentration (GMC) of antibodies (adjusted for effect modifiers) were compared between infants whose mothers did or did not receive dTpa or TIV immunisation during pregnancy and for each early-life factor.

Results

Maternal dTpa immunisation was associated with significantly reduced antibody responses to both specific (diphtheria and pertussis) and heterologous (polio and pneumococcus) vaccines. This effect was stronger for persistence of antibodies at 13 months of age than it was at 7 months of age. Maternal TIV immunisation had minimal effect on infant vaccine responses. Sex influenced antibody concentrations, but not seroprotection rates at 7 and 13 months of age. Delivery mode, feeding method and antibiotic exposure (including intrapartum antibiotics) did not have a substantial influence on antibody responses.

Conclusions

There is a difference between males and females in the humoral response to routine immunisations in the first year of life. Maternal dTpa immunisation during pregnancy reduces responses to both specific and heterologous (unrelated) vaccines.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0006
Science and Educational Track

Oral presentation session 06 - Vaccines

Retrospective multicentre matched case-control study on the risk factors for intussusception in children under one year of age, germany, 2010–2014

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Background and Aims:

In Germany, rotavirus vaccination was implemented in the vaccination schedule in 2013. Studies associate rotavirus vaccination with intussusception. In Germany, a retrospective multicentre matched case-control study was performed to identify risk factors for intussusception and to quantify the detected risks.

Methods:

Children with place of birth and residence in Germany who had been treated for intussusception from January 2010 through December 2014 in a German paediatric clinic and who had been less than one year old at the time of intussusception were recruited. Case report forms were independently validated by two paediatricians according to the criteria of intussusception defined by the Brighton Collaboration (BC). Confirmed cases of intussusception (BC level of diagnostic certainty 1) were matched with population-based controls by date of birth (±30 calendar days), gender, federal state, and place of residence. Statistical analysis included a multiple logistic regression analysis with backward elimination as variable selection method.

Results:

A total of 116 validated cases were matched with 272 controls. A significantly increased Odds Ratio for intussusception (adjusted Odds Ratio, aOR, 5.41; 95% CI: 1.26–23.24) was detected in individuals immunised with rotavirus vaccine dose 1 prior to symptoms onset as compared to non-exposed individuals whereas the ORs for intussusception after dose 2, dose 3, and any dose were not elevated. Two further risk factors for intussusception, family history of intussusception (aOR 4.19; 95% CI 1.37−12.83) and gastroenteritis in the first year of life (aOR 4.66; 95% CI 2.49−8.72) were identified. Breastfeeding had a protective effect (aOR 0.56; 95% CI 0.33−0.93).

Conclusions:

Administration of rotavirus vaccine dose 1, family history of intussusception and gastroenteritis in the first year of life were found to be independent risk factors whereas breastfeeding may protect from intussusception.

Systematic Review Registration:

N/A

ESPID19-1050
Science and Educational Track

Oral presentation session 07 - Respiratory

Mycoplasma pneumoniae vaccines should induce local antibody levels to protect against upper respiratory tract carriage

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Background

Mycoplasma pneumoniae (*Mp*) is the most common bacterial cause of community-acquired pneumonia in children. Asymptomatic carriage of *Mp* in the upper respiratory tract (URT) can precede infection and is a reservoir for transmission. A vaccine that interferes with *Mp* transmission should therefore protect against URT carriage. Whether antibodies in the URT protect against *Mp* carriage is unknown, thus we set out to study their role in URT carriage.

Methods

Nasal lavages were taken from healthy children and children with *Mp* infection, and at follow-up visits of asymptomatic *Mp*-carriers and *Mp*-infected children. Nasal lavages were analyzed for *Mp* load by qPCR and *Mp*-specific antibodies using ELISA. Effect of nasal lavage antibodies on *Mp* adherence to A549 respiratory epithelial cells was measured using an *in vitro* assay.

Results

Nasal lavages of healthy children, both *Mp*-positive or –negative, contained low levels of *Mp*-specific IgA, IgG and IgM. By contrast, *Mp*-specific IgA levels in the URT of *Mp*-infected children were significantly higher when compared with asymptomatic *Mp* carriers ($p<0.001$). High levels of *Mp*-specific IgA in URT trended towards predicting clearance of *Mp* carriage in the subsequent visit ($p=0.07$). *In vitro*, addition of nasal lavage decreased *Mp* adhesion to A549 cells, which was correlated with the amount of *Mp*-specific IgA in nasal lavage (Spearman's $r = -0.65$, $p=0.0037$).

Conclusions

Mp-infection led to (hyper)induction of *Mp*-specific IgA in the URT, whereas asymptomatic carriage of *Mp* did not. The effect of *Mp*-specific IgA on *Mp* carriage may be explained by its ability to block adhesion to the respiratory epithelium. A *Mp* vaccine that protects against *Mp* carriage should strongly induce antibodies in the URT. Whether the effects of antibodies depends on IgA or IgG warrants further investigation.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0781
Science and Educational Track

Oral presentation session 07 - Respiratory

Ventilator-associated events in three picus in greece

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Background and Aims:

Healthcare-associated infections (HAIs) are associated with increased morbidity and mortality and excess costs. Ventilator-associated events (VAEs) are HAIs associated with prolonged mechanical ventilation and hospital death. The broad objective of this study was to develop a VAE collaborative in pediatric intensive care units and to present the results.

Methods:

We conducted active surveillance for VAE in three pediatric intensive care units (PICUs) in Greece from June 2016 to June 2018, using the Centers for Disease Control and Prevention's National Healthcare Safety Network definitions from 2016. VAE definitions include ventilator-associated conditions (VAC) and subcategories for infection-related ventilator-associated complications (IVAC) and possible ventilator-associated pneumonia (PVAP). Data were collected and managed using REDCap electronic data capture tools.

Results:

A total of 7176 ventilator days (VN days) and 10864 patient days (PT days) were analyzed. Twenty-three VAE were identified, of which 11 were VAC, 9 were IVAC, and 3 were PVAP. Ventilation utilization (VUN) ratios ranged from 0.39 to 0.86, and VAE rates ranged from 0.00 to 5.93. The events occurred at a median of 15 days (IQR:9-36) after intubation and patients remained on the ventilator a median of 18.5 days (IQR:7-42) after the event. Six of the 19 patients that experienced a VAE died; 4 died within 10 days of the
event.

Table 1: Average Ventilator-Associated Event VAE rates in Three PICUs in Greece (June 2016-June 2018)

	VAEs	VAC	IVAC	PVAP	VN days	Pts Days	VUN ratio	VAE rate
PICU 1	20	11	6	3	3375	3948	0.86	5.93
PICU 2	3	0	3	0	3281	4304	0.76	0.91
PICU 3	0	0	0	0	1015	2612	0.39	0.00

PICU: Pediatric intensive care unit, **VAE:** Ventilator-associated Events, **VAC:** Ventilator-associated conditions, **IVAC:** Infection-related ventilator-associated complications, **VN Days:** Ventilator days, **Pts Days:** Patient days

Conclusions:

We established a surveillance mechanism that allows for a uniform description of VAE rates and ventilator utilization ratios in PICUs in Greece. This mechanism demonstrated considerable variability among these rates and ratios. These results will be used to inform the implementation of a care bundle.

Systematic Review Registration:

N/A

ESPID19-0348
Science and Educational Track

Oral presentation session 07 - Respiratory

Community acquired alveolar pneumonia (caap) incidences in children <24m by gestational age group before and after the introduction of pneumococcal conjugate vaccines (pcvs)

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Background and Aims:

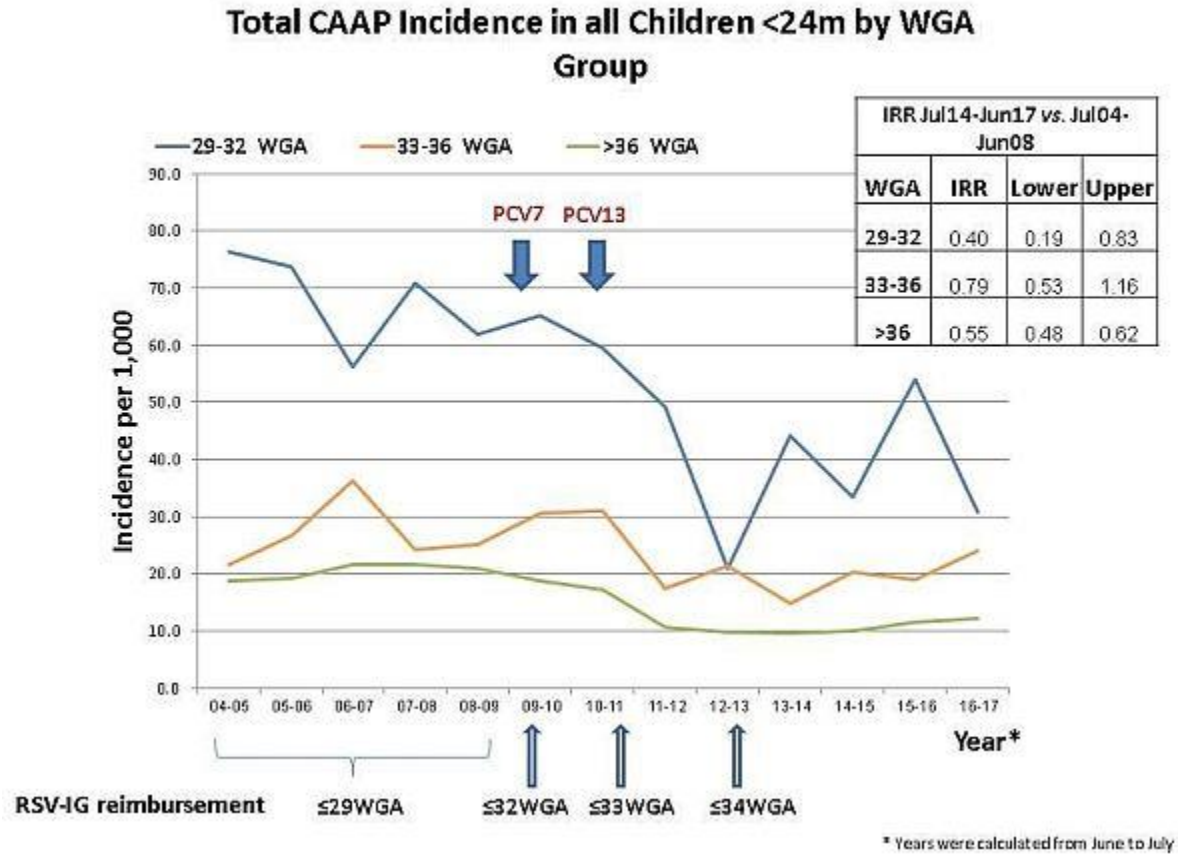
CAAP is more common in premature than in term-born infants. The aim of the current study was to determine the impact of PCV implementation on CAAP in premature *vs.* term-born infants.

Methods:

A prospective population-based study, conducted between 2004 and 2017 in southern Israel. All hospital visits of children <24m old with CAAP to the only hospital in the region were recorded. Three distinct gestational age groups were studied: 29-32, 33-36, and >36 week gestational age (WGA). PCV7 was introduced in the National Immunization Plan in Jul-2009 and gradually replaced by PCV13 in Nov-2010. All infants WGA 29-32 received RSV immunoglobulin (RSV-IG). Reimbursement indication for WGA 33-36 was expanded gradually (**Figure**). Incidences, incidence rate ratios (IRR) and 95% CI were calculated for each gestational age group separately. Continuous incidence graphs were drawn (**Figure**). Two distinct periods were compared: Pre-PCV (July 2004 throughout June 2008) and PCV13 (July 2014 – June 2017). CAAP was prospectively diagnosed as per the WHO protocol (Greenberg et al, Vaccine 33:4623-9, 2015).

Results:

During the study period, 6,670 children were enrolled: 211, 653 and 5,806 children born at 29-32, 33-36 and >36 WGA, respectively. The overall incidence of CAAP visits declined by 60%, 21% and 45%, respectively (95% CI intervals overlapping between WGA groups). The respective declines in hospitalized children were 56%, 16% and 33%; and for non-hospitalized children were 79%, 40% and 65% (95% CI overlapping between WGA groups).



IRR Jul14-Jun17 *vs.* Jul04-Jun08			
WGA	**IRR**	**Lower**	**Upper**
29-32	0.40	0.19	0.83
33-36	0.79	0.53	1.16
>36	0.55	0.48	0.62

Conclusions:

Following the sequential introduction of PCV7/PCV13, the same trends in reduction of CAAP were observed in preterm and term infants <24m. These trends were seen in both hospitalized and non-hospitalized patients. Factors such as RSV-IG possibly contributed to CAAP reduction as well.

Systematic Review Registration:

N/A

ESPID19-1196
Science and Educational Track

Oral presentation session 07 - Respiratory

Health resource utilization (hru) among infants without high risk factors (hrf-) diagnosed with respiratory syncytial virus (rsv) infection in the netherlands: a retrospective database analysis

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Background and Aims:

To compare health resource utilization (HRU) among infants without high risk factors (HRF-) with and without an RSV infection diagnosis in the Netherlands.

Methods:

The Perinatal Registry and the PHARMO Database Network including electronic records from primary and secondary healthcare settings in the Netherlands were used. Infants (<=12 months) with an RSV infection diagnosis (ICD9/10) or an RSV infection mention between 2008-2014 were identified. Infants had >= one-year of follow-up and were HRF-. RSV diagnosed infants were matched 1:1 to infants without an RSV/bronchiolitis diagnosis on age, gender, region, and HRF- status. We assessed HRU in the first year after RSV diagnosis and hospital readmissions for respiratory disease <=30 days (RAR<=30) after RSV hospital discharge. HRU for RSV infection infants and their matched controls were compared using regression analyses.

Results:

Of 725 HRF- infants (median age months: 3; IQR 1 - 5) with an RSV diagnosis, 69.1% were first diagnosed by a GP and 36.7% during a hospitalization. 97% of the RSV diagnoses occurred between October and April. 31% developed acute otitis media within 1-year of RSV diagnosis. Median length of stay (LOS) for an RSV hospitalization (N=275) was 5 days (IQR 3 - 6). 3.3% of these had an RAR<=30. The likelihood of any-cause hospitalization among RSV patients was higher compared to the matched patient group (OR=14.75, CI=10.71-20.31). Moreover, a larger number of any cause GP visits (RR=1.70, CI=1.60-1.80) and longer LOS (RR=1.66, CI=1.15-2.41) for any-cause hospitalizations was observed.

Conclusions:

RSV is associated with substantial ambulatory and hospital HRU among infants, even among those without specific high-risk factors. The development of more effective preventive strategies and antiviral treatments is essential to reduce the burden of RSV infection.

Systematic Review Registration:

N/A

ESPID19-1193
Science and Educational Track

Oral presentation session 07 - Respiratory

Cumulative incidence of asthma/wheezing (aw) among respiratory syncytial virus (rsv) infected infants without high risk factors (hrf-) in the netherlands: a retrospective database analysis

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Background and Aims:

To describe the cumulative incidence of AW following RSV infection among HRF- infants/children. The impact of RSV infection hospitalization, as a proxy for disease severity, was also assessed.

Methods:

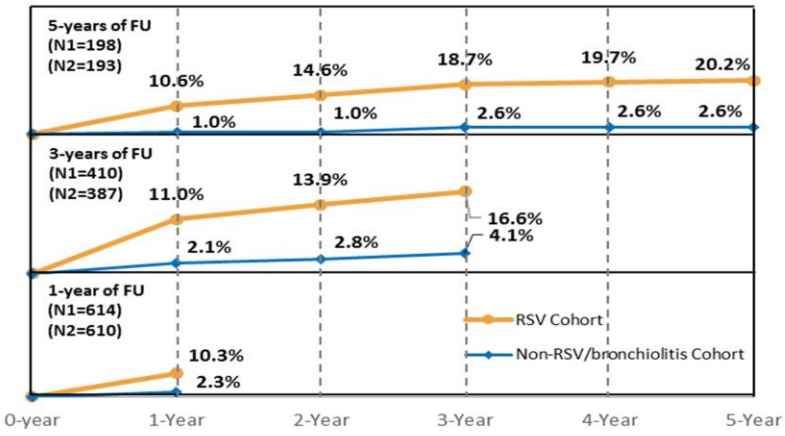
The Perinatal Registry and the PHARMO Database Network including electronic records from primary and secondary healthcare settings in the Netherlands were used. Infants/children (≤2 years) with an RSV infection diagnosis (ICD9/10) or an RSV infection mention between 2008-2014 were identified. Infants had at least 1/3/5 years of follow-up, no AW diagnosis 30 days before or after the RSV infection date and were HRF-. RSV diagnosed patients were matched 1:1 to patients without an RSV/bronchiolitis diagnosis on age, gender, region, HRF- status, and follow-up time. Comparisons in cumulative incidence of AW and the likelihood of AW are presented.

Results:

614 infants with RSV infection (mean age: 6 (SD=6) months) were included. Over 1, 3, and 5-years, the cumulative incidence of AW among RSV patients was 10.3%, 16.6% and 20.2%, respectively, versus 2.3%, 4.1% and 2.6% among no RSV/bronchiolitis patients. Annual cumulative incidence is shown in Figure 1. The likelihood of AW was higher in RSV versus no RSV /bronchiolitis patients at 1-year (OR=4.19, p=<.0001), 3-years (OR=4.12, p=<.0001) and 5-years (OR=7.32, p=<.0001). RSV patients hospitalized with RSV had a higher likelihood of AW at 5-years (OR=2.45, p= 0.0453) compared to non-

hospitalized RSV patients. Length of RSV hospitalization was not significantly associated with AW.

Figure 1. Annual cumulative incidence of asthma/wheezing for infants/children with 1,3, and 5 years of follow-up (FU) with RSV and their non-RSV matched cohort on age, gender, region and HRF- matched cohort



N1: RSV Cohort; N2: Non-RSV/bronchiolitis Cohort

Conclusions:

This study's strength is the ability to identify patients in all settings of care. HRF- infants/children with an RSV infection have a higher likelihood of developing AW compared to HRF- non-RSV/bronchiolitis infants/children. RSV hospitalization increased AW development at 5 years. However, length of RSV hospitalization seems not to impact AW.

Systematic Review Registration:

N/A

ESPID19-0997
Science and Educational Track

Oral presentation session 07 - Respiratory

Human coronavirus in hospitalized children with respiratory tract infections and healthy controls – a nine-year long prospective surveillance study

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Background

The clinical significance of HCoV is difficult to determine as previous studies have found equal detection rates of HCoV in patients and controls, and HCoV is often co-detected with other RTI-causing viruses.

Methods

From 2006 to 2015 we prospectively enrolled all children admitted with RTI to the Children's department, St. Olav University Hospital, Norway, and children admitted to elective surgery were recruited as control group. Nasopharyngeal aspirates were collected analyzed for four species of HCoV: OC43, NL63, 229E, and HKU1, and thirteen other respiratory viruses.

Results

The detection rate of HCoV among RTI-children was 9.1% (313/3458) and 10.2% (38/373) among controls. The four investigated HCoV species had different detection rates and different seasonal distributions. Co-detection rates of other viruses were equally in the two groups: 68.1% and 68.4%, respectively. HCoV-positive children with RTIs more often had a high genomic load (Ct<28) compared to asymptomatic controls (OR = 2.59, *P* = .010). There was no difference in genomic load between controls with single detections and controls with viral co-detections (OR = 1.11, *P* = .72). In a logistic regression analysis, a high HCoV genomic load was associated with RTIs (OR = 3.12, *P* = .016) adjusted for age, prematurity and chronic disease.

Conclusions

HCoV virus types HCoV: OC43, NL63, 229E, and HKU1 occur in one tenth of children with and without RTI. However, those with RTI have higher genomic loads supporting a causal contribution in to RTIs in need of hospitalization.

Clinical Trial Registration (Please input N/A if not registered)

The study was approved by the Regional Committees for Medical and Health Research Ethics Central in 2006 (No: 4.2006.2289) and 2012 (No: 2012.1042).

ESPID19-0708
Science and Educational Track

Oral presentation session 07 - Respiratory

Reduced antibiotic prescription for pneumonia in low-risk children and less therapy failure by implementation of a validated clinical prediction model

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Background

Improving targeted antibiotic prescription for respiratory tract infections (RTI) is crucial to fight antimicrobial resistance. This study aims to safely reduce antibiotic prescription in children under five suspected of a lower RTI at the emergency department (ED), by implementing a clinical decision rule.

Methods

We performed a stepped wedge, cluster randomized trial, including children aged one month to five years, presenting with fever and cough/dyspnoea at 8 EDs in the Netherlands (2016 – 2018), including a 1-week follow-up. During the intervention period antibiotics were withheld in children with a low predicted risk of bacterial pneumonia (<10%), based on a validated clinical prediction model including clinical characteristics and CRP. We calculated the effect on antibiotic prescription and therapy failure using multilevel logistic regression, clustered by hospital and adjusted for time-step, age, gender, season, ill appearance and duration of fever. Therapy failure was defined as secondary antibiotic prescription or hospitalization, persistence of fever or oxygen need up to day 7 or complications.

Results

1002 children were included (61% male, median age 17 months (IQR 9 – 30)), of whom 403 during the intervention period. Overall antibiotic prescription was not significantly reduced (30% to 25%; odds ratio 1.06 (95% CI 0.58-1.94)), but therapy failure reduced from 22% to 15% (OR 0.55 (0.34-0.89)). Subgroup analysis showed a significant reduction of antibiotics in the low-risk group (17% to 6%; OR 0.33 (0.14-0.81)) with non-significant change in prescription in the high-risk group during the intervention period (47% to 59%; OR 2.2 (0.81-5.96)).

Conclusions

Implementation of a clinical decision rule for childhood pneumonia improved targeted prescription of antibiotics, reducing unnecessary antibiotic prescription in low-risk children and resulting in less therapy failure.

Clinical Trial Registration (Please input N/A if not registered)

Netherlands Trial Registry: NTR5326

ESPID19-0704
Science and Educational Track

Oral presentation session 07 - Respiratory

Impact of nasopharyngeal carriage on immune responses to pneumococcal conjugate vaccination

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Background

Previous studies have shown that serotype-specific immune responses to pneumococcal conjugate vaccines (PCVs) are diminished in children colonized with homologous pneumococcal serotypes before/during vaccination. We assessed interactions between nasopharyngeal pneumococcal colonization (NPC) before/during the primary infant series and immune responses to PCVs.

Methods

We performed post-hoc exploratory analyses on data from studies in South Africa and The Gambia. The South African study included 484 HIV-infected and non-infected infants who received PHiD-CV. The Gambian study included 1200 infants who received PHiD-CV with/without pneumococcal proteins, or PCV13. We used mixed models to assess pneumococcal serotype-specific IgG concentrations in infants with/without pre-PCV NPC and those colonized (acquired carriage)/not colonized during the primary series. Pre-PCV IgG concentrations and NPC pre-PCV or 1 month post-priming were covariates. Analyses were restricted to frequently carried serotypes (6B/9V/14/19F/23F).

Results

High pre-PCV IgG concentrations were associated with lower post-primary IgG concentrations for a given serotype in both studies. Too few infants were colonized pre-PCV to assess the impact of pre-PCV NPC on post-primary IgG concentrations, except for serotype 19F in the Gambian study (n=35). Infants with pre-PCV 19F NPC had significantly lower 19F IgG concentrations post-priming versus non-carriers ($p<0.005$).

Infants who were not found colonized pre-PCV and acquired NPC during the primary series had lower IgG 1 month post-priming for the homologous serotypes versus infants without acquired carriage. This difference was significant for 6B/19F/23F ($p<0.0007$, both studies), 9V ($p<0.0001$, Gambian study only) and 14 ($p=0.0022$, South African study only). Modelling results were confirmed based on geometric mean concentrations/ratios in infants with/without acquired NPC (Table).

Table. Anti-pneumococcal geometric mean antibody concentrations (GMCs) and ratios (GMRs) 1 month post-primary vaccination in infants who had not been found colonized pre-PCV and acquired or did not acquire carriage during the primary series

	Acquired carriage		No acquired carriage		GMR (acquired carriage/no acquired carriage)			
Serotype	**N**	**GMC**	**N**	**GMC**	**GMR**	**LL**	**UL**	**p-value**
South African study								
6B	16	0.1440	440	0.9238	0.1559	0.0863	0.2816	**<0.0001**
9V	3	1.5721	462	3.7459	0.4197	0.1415	1.2450	0.1173
14	15	2.2208	444	5.0064	0.4436	0.2639	0.7457	**0.0022**
19F	18	4.0688	437	9.1617	0.4441	0.2783	0.7086	**0.0007**
23F	32	0.4509	424	1.4828	0.3041	0.1986	0.4656	**<0.0001**
Gambian study								
6B	23	0.1308	1121	0.8265	0.1583	0.0861	0.2910	**<0.0001**
9V	6	0.2407	1149	2.9019	0.0830	0.0381	0.1804	**<0.0001**
14	18	2.9076	1130	3.4890	0.8334	0.4876	1.4242	0.5047
19F	36	2.8127	1068	9.2272	0.3048	0.2262	0.4108	**<0.0001**
23F	36	0.3638	1087	1.2126	0.3000	0.1916	0.4698	**<0.0001**

Acquired carriage: infants who for a given serotype had not been found colonized pre-PCV but had a positive carriage swab result at the 1-month post-priming visit. **No acquired carriage**: infants who for a given serotype had not been found colonized pre-PCV and had a negative carriage swab result at the 1-month post-priming visit. **p-value** for the null-hypothesis that GMR=1 (significant if <0.05); **LL/UL**, lower/upper limit of the 95% confidence interval; **N**, number of infants in specified category.

Conclusions

These results extend on previous observations that pneumococcal colonization before/during the primary vaccination series negatively impacts immune responses to PCVs.

Funding: GlaxoSmithKline Biologicals SA/PATH

Clinical Trial Registration (Please input N/A if not registered)

NCT00829010/NCT01262872

ESPID19-0499
Science and Educational Track

Oral presentation session 07 - Respiratory

Pre-hospital antibiotic treatment of paediatric parapneumonic pleural effusion/empyema and its effects on clinical outcome and pathogen detection

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Background

We analysed the effects of empirical pre-hospital oral antibiotic therapy (PH-ABT) on pathogen detection and clinical outcomes in paediatric parapneumonic pleural effusions/empyema (PPE/PE) in Germany.

Methods

Between 2010 and 2018, the German Surveillance Unit for Rare Diseases in Childhood (ESPED) monitored patients <18 years of age hospitalised with pneumonia-associated PPE/PE (>7 days or requiring drainage). Patient and clinical data were collected by questionnaire. All bacteria detected in blood or pleural fluid by culture or PCR were considered.

Results

A total of 1724 hospitalised children with PPE/PE (median age of 4.7 years, IQR 2.9-9.5) were included. Of these, 32.4% had received PH-ABT. Antibiotics used for monotherapy were cephalosporins (39.2%), aminopenicillins (20.4%), macrolides (13.8%), aminopenicillin/beta-lactamase inhibitor combinations (4.5%) and penicillins (2.1%). For children with/without PH-ABT, median hospital length of stay (LOS) was 15 (IQR 11-22) versus 18 (IQR 14-25) days (p<0.001), median duration from onset of symptoms until hospital discharge was 25 (IQR 19-33) vs. 23 (IQR 18-30) days (p=0.002), rate of intensive care unit admission was 58.5% vs. 64.7% (p=0.013) and occurrence of complications was 52.4% vs. 59.8% (p=0.004). Bacterial detection was achieved in 34.6% of all patients. In samples tested by culture (n=1456), the detection rate in children with/without PH-ABT was 17.1% versus 29.1% (p<0.001), whereas in samples tested by PCR (n=560), the detection rate was 48.6% vs. 53.3% (p=0.300).

Conclusions

PH-ABT of children with PPE/PE was associated with shorter LOS and a lower rate of intensive care treatment and complications. PH-ABT reduced the sensitivity of bacterial culture but not of PCR. Only one fifth of children with PH-ABT received an oral aminopenicillin, despite existing recommendations for the treatment of paediatric community-acquired pneumonia in Germany.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1100
Science and Educational Track

Oral presentation session 08 - Influenza

Severity of influenza primo- and re-infection in pre-school children by influenza type and by subtype – results from a prospective surveillance study

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Background

It is unknown whether the course of the first-ever acute respiratory infection (ARI) with a specific influenza type or subtype (primo-infection, PI) is more severe than during later ARI by the same influenza type or subtype (re-infection, RI).

Methods

During January to May (2013-2015), children 1-5 years of age, presenting at paediatric practices with ARI (body temperature ≥38.0°C; respiratory symptoms; onset ≤ 48h) and unvaccinated for influenza, were enrolled. Pharyngeal specimens were tested for influenza A(H1N1)pdm09/A(H3N2)/B by PCR. For the influenza types A and B, type-specific PI/RI were defined from blood samples by negative/positive IgG antibody status (ELISAs); subtype-specific PI/RI were defined by additional hemagglutination inhibition assays (subtype-specific antibodies). Clinical data were collected from a patient diary.

Results

For 217 children (median age 3.7 years, IQR 2.1-4.8), PCR-confirmed influenza could be classified on the type level as PI/RI in 87(49%)/91(51%) of 178 influenza A cases and in 38(97%)/1(3%) of 39 influenza B cases. Comparison of influenza A PI/RI showed that RI were associated with higher age (p=0.016), and a longer duration of fever plus respiratory symptoms in multivariable analysis by 19% (median 4 vs. 3 days, p=0.03). For 140 (79%) of 178 children with influenza A, classification of PI/RI on the subtype level was possible, with 78(85%)/14(15%) PI/RI in 92 A(H3N2) patients and 44(92%)/4(8%) in 48 A(H1N1)pdm09 patients. Both subtypes showed (non-significant) trends for longer disease duration of RI.

Conclusions

In pre-school children with ARI due to influenza A treated in paediatric practices, about half of the patients had experienced an infection with influenza A before, but almost 90% experienced their first-ever infection with the specific influenza A subtype. Interestingly, disease duration was slightly longer in already primed children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0986
Science and Educational Track

Oral presentation session 08 - Influenza

Evolution of influenza immunization program in children in quebec, canada: differences from other programs in north america

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[3]Ministère de la Santé et des Services sociaux, Direction générale adjointe de la protection de la santé publique, Montreal, Canada

Background and Aims:

Children of all ages are included in influenza immunization programs in almost all jurisdictions in North America. Children with chronic conditions and all 6-23-month-old children have been included in the Quebec influenza immunization program (QIIP) up to 2018, with the goal to prevent influenza-associated hospitalizations and deaths. A revision of QIIP was requested by the Ministry of Health in December 2015.

Methods:

The Quebec Immunization Committee (QIC) reviewed the QIIP from 2016-2018 based on the Erikson-de-Wals framework including such criteria as burden of disease, economic analysis, feasibility, acceptability, safety, etc. Estimation of burden and economic analyses included five influenza seasons and were based on data from a prospective study in 4 community Quebec hospitals, from 3 tertiary-care Quebec hospitals participating in the Canadian network IMPACT, vaccine uptake surveys, and literature data. All analyses were stratified by presence or not of chronic conditions.

Results:

The burden of influenza in children consisted mainly of medically-attended influenza infections. Influenza-associated hospitalizations were at least 10-fold more frequent in children with chronic conditions compared to healthy children and were shorter. For 6-23-month-olds, the difference for hospitalization rate was >12-fold (2,492/100,000 compared to 200/100,000). Death associated with influenza was extremely rare (<1/100,000). Vaccination uptake in Quebec children was <20%. From a healthcare perspective, the program was cost-effective only in children with chronic conditions 6 months to 4 years.

Conclusions:

The QIC recommended to maintain a program targeting persons at high risk for influenza-associated hospitalization and death, prioritizing the achievement of an optimal vaccination uptake in these groups. The definition of high-risk was updated based on recent data and presence of chronic conditions. The Ministry decided to keep all children with chronic conditions in the program; healthy 6-23-month-olds were removed.

Systematic Review Registration:

ESPID19-0884
Science and Educational Track

Oral presentation session 08 - Influenza

Inactivated quadrivalent influenza vaccine reduces antibiotic use in healthy children 6-35 months in europe during a randomised controlled trial

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Background

In paediatric populations, influenza illness is associated with substantial healthcare use, including use of antibiotics which may contribute to the emergence of antibiotic resistance. We previously demonstrated vaccine efficacy of an inactivated quadrivalent influenza vaccine (IIV4) and it's overall impact on associated antibiotics use in children 6-35 months.[1] Here we present the reduction of antibiotics use following vaccination, by class, focusing on the European cohorts. We have extrapolated these results to Germany, estimating the potential reduction of annual antibiotics use due to influenza.

Methods

A phase III, observer-blind, randomised efficacy trial was conducted in five independent cohorts of healthy children 6-35 months over 5 influenza seasons (NCT01439360). This post-hoc analysis included children (n=3341) from European countries from 2 seasons (2011/12 and 2012/13). Relative risk reduction of antibiotic use associated with RT-PCR-confirmed influenza of any severity has been calculated on the total vaccinated cohort. Results have been extrapolated to Germany using local data inputs.[2-4]

Results

In the IIV4 group, fewer subjects were RT-PCR positive for influenza. Antibiotic use associated with confirmed influenza illness was reduced following IIV4 vaccination (table). According to data from Germany, in a population of children 6-35 months, we estimated that vaccination will prevent 14831

antibiotic prescriptions each year (table).

Table. Relative risk reductions for antibiotic use, by class, associated with RT-PCR-confirmed influenza of any severity (IIV4 versus control)

	IIV4 N= 1672	CONTROL N= 1669	Reduction of antibiotics use	German extrapolation
	Number of subjects	Number of subjects	Relative risk reduction % (95% CI)	Number of prevented prescriptions each year
Number of subjects having at least one RT-PCR confirmed influenza case of any severity	81	240	-	-
Any antibiotic (European Cohorts*)[5]	21	77	73 (56-83)	NA
Penicillins	16	51	69 (45-82)	3549
Macrolides	4	9	56 (-44-86)	3280
Cephalosporins	1	12	92 (36-99)	8002
Other classes	2	11	82 (18-96)	NA

CI, confidence interval; IIV4, inactivated quadrivalent influenza vaccine; N, number of children; NA: not available; RT-PCR, reverse transcription polymerase chain reaction.

*Countries: Belgium, Czechia, Poland, Spain, United Kingdom, Lebanon and Turkey

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Conclusions

Along with the reduction in number of influenza infection via vaccination, we observed decreases in the use of antibiotics across participating European countries and have estimated the benefit at a country level taking Germany as an example. The value of paediatric influenza vaccination becomes apparent when indirect impacts are considered, including reduction in associated antibiotics use. These findings may contribute to decreasing the global threat of antimicrobial resistance.

Clinical Trial Registration (Please input N/A if not registered)

GlaxoSmithKline Biologicals SA funded this study (NCT01439360).

ESPID19-0873
Science and Educational Track

Oral presentation session 08 - Influenza

Pediatric influenza vaccine effectiveness between 2010/11 and 2015/16 in manitoba, canada: a test-negative case-control study

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Background and Aims:

Influenza vaccine effectiveness (VE) studies often use sentinel surveillance networks. We used administrative health databases in the Canadian province of Manitoba for a test-negative case-control study of influenza VE in children.

Methods:

We linked all positive tests (cases) and negative tests (controls) for influenza in Manitoba children aged 6 months to 17 years old(analyzed by one of two government agencies) between November 2010 and May 2016 to the Manitoba Immunization Monitoring System to assess receipt of the seasonal influenza vaccine. We used logistic regression (adjusted for gender, income, physician density, relative local age distribution, and healthcare utilization) to estimate the VE [=100*(1-OR)] of seasonal influenza vaccine against lab-confirmed influenza (LCI).

Results:

We identified 964 cases and 2,678 controls. About 44% of cases and 67% of controls were younger than 5, over one-third of both cases and controls occurred in the lowest income quintile. The number of cases varied by season, from 104 in 2010/11 to 269 in 2015/16. In most years, around a quarter of tests were positive, except for 2015/16 in which 37% tested positive. Vaccine effectiveness varied by season (as did the dominant circulating strain and the antigenic similarity between it and the vaccine) and was mostly higher for children <5 years old than 5-17 year-olds. VE in the season with the most cases (2015/16; 269 cases) was 65 (95% confidence interval, 32-82) for <5 year-olds and 50 (-11-77) for 5-17 year-olds.

Conclusions:

Both the incidence of LCI and the VE against it varied by season, but flu vaccines were generally moderately effective in preventing LCI.

Systematic Review Registration:

N/A

ESPID19-0801
Science and Educational Track

Oral presentation session 08 - Influenza

Analysis of possible influencing factors for influenza-related hospitalization in children

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Background and Aims:

Influenza is a major contributor to the global burden of acute respiratory infection. An annual influenza vaccine is believed to be the best way to prevent influenza-related illnesses. Previous studies have shown that vitamin D supplementation, daily dietary probiotic supplementation seem to decrease the incidence of the common cold and influenza. In this study, we conducted a 4-year, matched case-control study, aiming to find the effectiveness of seasonal influenza vaccine against influenza-related hospitalization in children. We also surveyed the effectiveness of other factors that may affect the hospitalization rate of influenza infection in children.

Methods:

We conducted a matched case-control study along with Taiwan Pediatric Infectious Disease Alliance, which are composed of multiple medical centers in Taiwan. The included cases were influenza-related hospitalized patients aged from 6-month to 5-year-old, during 2012-2013, 2013-2014, 2014-2015, and 2015-2016, 4 consecutive influenza seasons. The controls were comparable to cases in age, sex, and had no influenza-related hospitalization records in the same season. Vaccination histories were taken, and questionnaires were completed. Conditional logistic regression was used to analyze the data.

Results:

A total of 1514 children(421 influenza-infected cases and 1093 controls) attended this study. We found that receiving seasonal influenza vaccination was an independent protective factor against influenza hospitalization($p < 0.01$,OR:0.427,95% CI:0.306-0.594). Children regularly taking dietary probiotic supplement also had less risk for influenza-related hospitalization($p < 0.05$,OR:0.66,95% CI:0.48-0.908). Children with mean sun exposure time greater than 7 hours per week also had a significantly lower risk for influenza-related hospitalization($p < 0.05$,OR:0.667,95% CI:0.491-0.906).

Conclusions:

Seasonal influenza vaccine is an effective way for preventing influenza-related hospitalization in Taiwanese children <5 years old. More than 7 hours sun exposure per week and dietary probiotic supplement may also have protective effects against influenza-related hospitalization of Taiwanese children.

Systematic Review Registration:

N/A

ESPID19-0442
Science and Educational Track

Oral presentation session 08 - Influenza

A systematic review and meta-analysis of the effectiveness of maternal influenza vaccination in preventing maternal and infant influenza

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Background

Pregnant women and their infants are at increased risk of morbidity and mortality due to complications from seasonal and pandemic influenza illness. Although a vaccine exists for pregnant women, no vaccine exists for infants <6 months old. This results in limited infant immunity against influenza infection. However, maternal vaccination may also confer immunity to the infant through trans-placental antibody transfer. There is growing evidence that maternal vaccination reduces infant influenza-illness burden. This systematic review aims to determine the effectiveness of maternal influenza vaccination during pregnancy on mother and infant.

Methods

An electronic search of 6 databases was performed from 1996 to 29th June 2018, including both observational studies and randomised control trials (RCTs). The Cochrane Risk of Bias Tool for RCTs and National Heart, Lung and Blood Institute quality assessment tool for observational studies was used. Meta-analyses of RCTs were undertaken where studies were of low to moderate heterogeneity.

Results

The initial search identified 7220 records; on excluding duplicates, there were 3652 studies. Among 4 RCTs identified, there were 8 published papers deemed high quality. In a random-effects pooled meta-analysis of 2 RCTs maternal influenza vaccination was associated with an overall reduction of Laboratory Confirmed Influenza (LCI) in infants of 34% (95% CI: 0.5-0.85). Random-effects pooled meta-analysis of 2 RCTs showed no protective effect for maternal influenza vaccination on Influenza-like Illness (ILI) in both mother <6 months post-partum and infants <6 months old (RR 0.89 (95% CI: 0.77-1.03), RR 0.99 (95% CI: 0.94-1.05) respectively). Pooled meta-analysis was not possible for other outcomes.

Conclusions

Maternal influenza vaccination was protective against LCI infection in infants. This review supports the targeting of maternal influenza vaccination to partially reduce influenza illness in infants.

Systematic Review Registration (Please input N/A if not registered)

CRD42018102776

ESPID19-0438
Science and Educational Track

Oral presentation session 08 - Influenza

Seasonal influenza vaccine coverage, especially live-attenuated vaccine coverage, increases steadily among children in finland according to a nationwide register-based cohort study

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Background

In the Finnish National Vaccination Programme (NVP), children with chronic underlying conditions have been eligible for free seasonal influenza vaccination (SIV) with trivalent inactivated vaccine (IIV3) since 1980´s, those aged 0.5-2 years since 2007/08. From 2015/16 on, parents of two-year-olds have had choice between IIV3 and quadrivalent live-attenuated vaccine (LAIV4) without recommended preference. Since 2018/19, NVP provides SIV (IIV4/LAIV4) also for 3-6-year-olds. As part of NVP campaigning and impact evaluation, we studied vaccination coverage in these age groups.

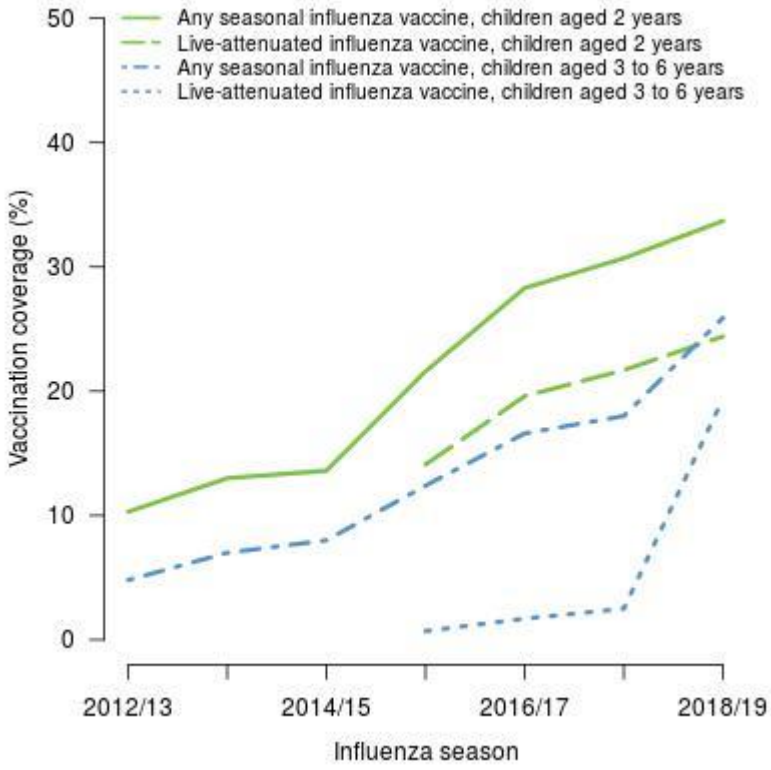
Methods

We conducted a register-based cohort study comprising all children born 2012-2016, currently living in Finland, covered by National Vaccination Register providing children's vaccination records. The vaccination coverage (SIV-COV, proportion vaccinated) was calculated by vaccine type and age group and compared to previous seasons' figures.

Results

As of January, 33.7% of the 53253 2-year-olds and 25.9% of the 233907 3- to 6-year-olds were SIV-vaccinated in 2018/19. SIV-COV among 2-year-olds had increased from 13.6% in 2014/15 to 21.7% in 2015/16 with approximately 2/3 of the vaccinated having received LAIV4. The current, mid-season estimate already exceeds the 2017/18 end-season estimate of 30.7% and the proportion of LAIV4 receivers has increased to almost 3/4. SIV-COV among 3-6-year-olds has grown steadily over past seasons from 8% in 2014/15 to 12.4% (2015/16) and 18.0% (2017/18). The proportion of LAIV4 receivers in this age group has increased from <1/7 to 3/4. Of those eligible for LAIV4 in 2017/18 and 2018/19 (N=55541), 3880 received LAIV4 in 2017/18 but no vaccine in 2018/19, 6825 have taken LAIV4 in both

seasons and 6282 did not receive LAIV4 in 2017/18 but have taken it in



2018/19.

Conclusions

SIV-COV in children in Finland is increasing steadily, and has particularly been boosted by the introduction of LAIV4.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0058
Science and Educational Track

Oral presentation session 08 - Influenza

Associations between body mass index and vaccine responses following influenza vaccination during pregnancy

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Background

Influenza vaccination is recommended for pregnant women, offering the dual benefit of protecting women and their newborn infants. This study aimed to investigate the impact of body mass index (BMI) on vaccine responses following influenza vaccination during pregnancy

Methods

Pregnant women attending antenatal clinics during 2014-2016 were enrolled. Participant's height, weight, age and gestation were recorded prior to administration of licensed seasonal influenza vaccination. Pre- and 1month post- vaccination blood samples were collected to measure antibody responses by haemagglutination inhibition (HI) assay. Responses were compared between women with high (≥30) and normal (<30) BMI for seropositivity (HI titre ≥40), post-vaccination geometric mean titres (GMT), pre/post GMT ratios and seroconversion (≥4-fold rise in titre). Variables associated with seropositivity were assessed by logistic regression.

Results

Most pregnant women (72/90, 80%) demonstrated seropositive antibody titres to all three influenza vaccine strains (H1N1, H3N2 and B) following vaccination. More women were seropositive following vaccination in 2014 (39/43, 91%) compared with 2015 (19/29, 66%) and 2016 (14/18, 78%) (OR 4.1, CI 1.2-13.8; p=0.021). Seropositivity was comparable among high vs normal BMI women (22/24, 92% vs 50/68, 74%; p=0.09). High BMI women had improved odds of seroconversion for H1N1 antibodies compared with normal BMI women (OR 3.1, CI 1.1-9.5; p=0.04). Women vaccinated during their second trimester were more likely to achieve seropositivity to all 3 vaccine antigens (47/53, 88%) compared with women vaccinated during their first trimester (7/12, 58%) (OR 5.6; CI 1.3-23.3; p=0.018).

Conclusions

BMI did not impair influenza vaccine responses in pregnant women and may improve seroconversion. Gestation at vaccination, irrespective of BMI, may be an important consideration for optimising vaccine protection for women and their newborns.

Clinical Trial Registration (Please input N/A if not registered)

ACTRN12614000374662

ESPID19-0676
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Whole genome sequencing of neisseria meningitidis carriage in a randomised controlled trial of 4cmenb vaccination in adolescents

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Background

This study aimed to describe carriage of *Neisseria meningitidis* in vaccinated (4CMenB) and unvaccinated adolescent cohorts in South Australia (SA).

Methods

Posterior oropharyngeal swabs were obtained from senior school students (15-19 years old) at baseline (2017) and 12 months (2018). Carriage of *N. meningitidis* was detected by *porA* real time PCR. All *por*A positive samples were cultured for *N. meningitidis* and isolates underwent whole genome sequencing. Multilocus sequence typing and fine typing were performed (determined using meningotype and PUBMLST database).

Results

Of 900 isolates genotyped in 2017, 277 (31.2%) were genogroup B, 198 (22.3%) genogroup Y, 43 (4.8%) genogroup W, 14 (1.6%) genogroup C, 6 (0.7%) genogroup X and 350 (39.4%) were non-typeable. Sequence type ST-23 (86 isolates; genogroup Y) was the most common sequence type cultured from students in 2017. 110 of the isolates (12%) had a novel sequence type. Clonal complexes 41/44 and 32 accounted for 44% of the genogroup B isolates. The hypervirulent clone, cc41/45 ST-154; P1.7-2,4, the commonest cause of meningococcal disease in SA, was carried by 15 students. At month 12 (2018) there were 325 (27.5%) genogroup B identified, of which 18 were identified as ST-154. The proportion of isolates that were genogroup B did not differ between 2017 and 2018 (31.2% vs 27.5%; p=0.13). Carriage

of the hypervirulent ST-154 genotype was 5.4% vs 5.5% of all genogroup B carriage in 2017 and 2018 respectively (p=0.92). Comparison of hypervirulent genogroup B carriage will be compared between vaccinated and unvaccinated students.

Conclusions

Non-typeable *N. meningitidis* is the predominant meningococcal strain carried by adolescents in SA. Carriage prevalence of genogroup B and the hypervirulent ST-154 were similar in the South Australian adolescent population over the two years of surveillance.

Clinical Trial Registration (Please input N/A if not registered)

NCT03089086

ESPID19-0895
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Invasive meningococcal diseases in italy: an analysis of national surveillance data, 2011-2017

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Background and Aims:

Invasive Meningococcal diseases (IMDs) caused by Neisseria meningitidis (Nm) is one of the most severe vaccine-preventable diseases. In Italy, different anti-meningococcal vaccines are available (Men B, Men C, quadrivalent Men ACYW), but offer and coverage amongst Regions are heterogeneous. In 2017, vaccination coverage rates in 24-month old children were: 83% for Men C, 29% for Men ACYW and 39% for Men B.

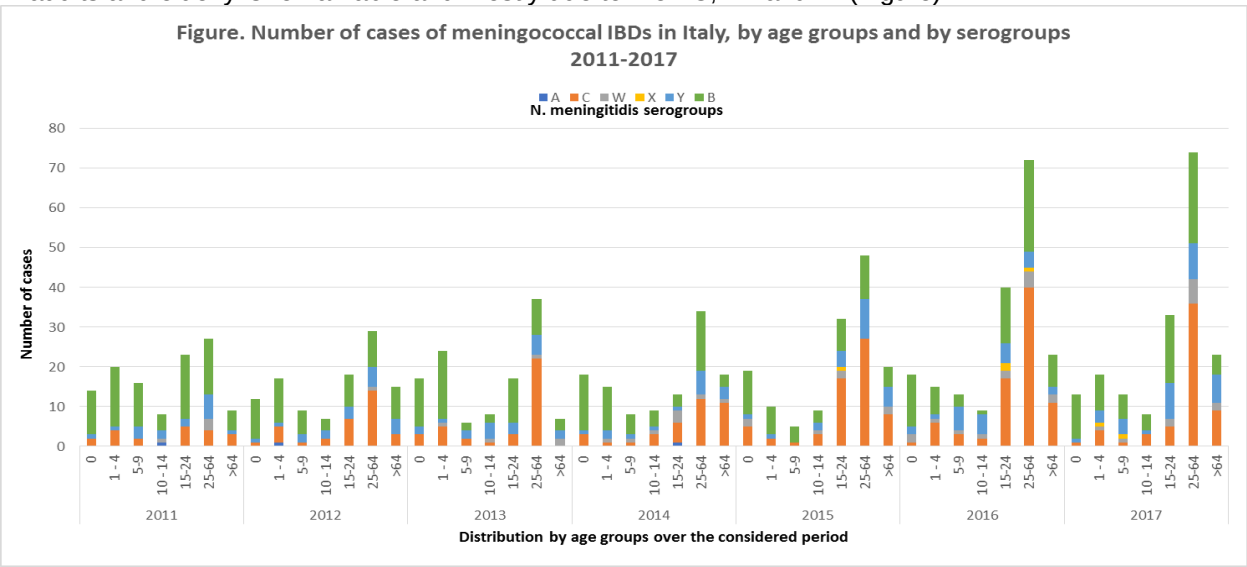
Methods:

We explored IMDs surveillance data from the Italian National Health Institute. Moreover, we analyzed data of notified cases during 2011-2017. Excel 2013 was used for trend analysis, stratifying by serogroups.

Results:

In Italy, during the study period, IMDs overall incidence increased: from 0.25 cases/100,000 inhabitants in 2011 to 0.33 in 2017. Regarding the pediatric population, Nm serogroup B (Men B) was more prevalent until 5 years of age, while non-B serogroups were prevalent in older groups. Serogroups C, W and Y epidemiological trends increased among children over the time. In adolescents, MenB and MenC caused equally most of the cases, Men Y trend increased over the period, and in 2015/2016 a MenC outbreak in Tuscany, and MenX cases were registered. The increase of cases

in adults and elderly is remarkable and mostly due to Men C, W and Y. (Figure)



Conclusions:

Epidemiological trends of IMDs in Italy are dynamic. In fact, the analysis of the national surveillance data showed the emergence of non-B and non-C serogroups among all age groups. Therefore, prevention strategies against all meningococcal serotypes (ACWY and B) should be considered from the primary schedule in infants. Other strategies should be evaluated to include boosters throughout life: pre-school, adolescents and adults. Finally, strengthening overall vaccination coverage against all serotypes is crucial for effective IMDs prevention and control.

Systematic Review Registration:

N/A

ESPID19-0996
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Safety and tolerability of the meningococcal serogroup b vaccine menb-fhbp in children 1 to <10 years of age

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[10]Pfizer Inc, Vaccine Medical and Scientific Affairs, Collegeville PA, USA

Background

MenB-FHbp (bivalent rLP2086) is a serogroup B meningococcal vaccine licensed in multiple countries for adolescents and adults. Two recent phase 2 studies evaluated MenB-FHbp safety in younger children.

Methods

In an ongoing study, 352 toddlers 1–<2 years old were randomized to receive MenB-FHbp (120 µg at months 0,2,6) or hepatitis A virus vaccine (HAV; months 0,6)/saline (month 2). Four hundred children 2–<10 years old were randomized 3:1 to receive 120 µg MenB-FHbp or HAV/saline. Safety outcomes included local reactions, systemic events, and adverse events (AEs); AEs were also evaluated in a pooled analysis (children 1–<10 years old).

Results

Across age groups, local reactions and systemic events, including fever, were more common among MenB-FHbp recipients than controls (local reactions: 82.3%–88.4% vs 39.4%–46.9%; systemic events: 71.1%–85.0% vs 51.9%–62.9%), mostly mild or moderate in severity, transient, and rarely associated with potentiation or study withdrawal (n=1, attributed to injection site pain, decreased appetite, irritability, and somnolence). One serious AE of transient hip synovitis was assessed as vaccine related (MenB-FHbp). Fever rates were higher in toddlers <2 years old vs children 2–<10 years old receiving MenB-FHbp (37.3% vs 24.5%) and declined with subsequent vaccinations; fever >40.0°C was rare (n=3 across age groups). Frequencies of various categories of AEs, newly diagnosed chronic medical conditions, and

medically attended AEs were similar across treatment groups (**Table**).

Table. AEs Among Children 1 to <10 Years of Age Receiving 120 µg MenB-FHbp or HAV/Saline on a 0-, 2-, 6-Month Schedule in the Pooled Analysis

Type of AE Reported	MenB-FHbp (n[a]=514)		HAV/Saline (n[a]=238)	
	n[b] (%)	95% CI[c]	n[b] (%)	95% CI[c]
AEs occurring from dose 1 through 1 month postdose 3	338 (65.8)	(61.5, 69.9)	152 (63.9)	(57.4, 70.0)
Related	37 (7.2)	(5.1, 9.8)	8 (3.4)	(1.5, 6.5)
AEs occurring within 30 days after any dose	258 (50.2)	(45.8, 54.6)	113 (47.5)	(41.0, 54.0)
Related	37 (7.2)	(5.1, 9.8)	8 (3.4)	(1.5, 6.5)
AEs occurring within 30 minutes after any dose	3 (0.6)	(0.1, 1.7)	0 (0.0)	(0.0, 1.5)
SAEs occurring throughout the study[d]	24 (4.7)	(3.0, 6.9)	9 (3.8)	(1.7, 7.1)
Related	1 (0.2)	(0.0, 1.1)	0 (0.0)	(0.0, 1.5)
AEs leading to discontinuation from the study	4 (0.8)	(0.2, 2.0)	1 (0.4)	(0.0, 2.3)
NDCMCs occurring throughout the study[d]	1 (0.2)	(0.0, 1.1)	0 (0.0)	(0.0, 1.5)
MAEs occurring throughout the study[d]	272 (52.9)	(48.5, 57.3)	127 (53.4)	(46.8, 59.8)

AE=adverse event; HAV=hepatitis A virus vaccine; MAE=medically attended adverse event; MenB-FHbp=bivalent rLP2086; NDCMC=newly diagnosed chronic medical condition; SAE=serious adverse event.

[a]Number of subjects in the safety population.

[b]Number of subjects with ≥1 event for the specified analysis interval.

[c]Exact 2-sided CI using the Clopper and Pearson method.

[d]Through approximately 6 months postdose 3.

Conclusions

MenB-FHbp recipients 1–<10 years old more frequently experienced redness, swelling, and fever compared with adolescents in previous studies. Although MenB-FHbp had an acceptable safety and tolerability profile in this age group, this analysis was not powered to detect uncommon AEs; continued safety monitoring of MenB-FHbp in children is warranted.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov, NCT02534935, NCT02531698. Funded by Pfizer.

ESPID19-0992
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Safety and immunogenicity of a quadrivalent meningococcal conjugate vaccine (menacyw-tt) administered in healthy meningococcal vaccine naïve children (2-9 years)

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Background

MenACYW-TT is an investigational quadrivalent meningococcal conjugate vaccine intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT compared to a licensed quadrivalent conjugate meningococcal vaccine (MCV4-CRM; Menveo®) in US children 2-9 years of age.

Methods

In a modified double blind Phase III study, 1000 children were randomized to receive one dose of either MenACYW-TT vaccine or MCV4-CRM vaccine. Serum bactericidal assays with human (hSBA) and baby rabbit (rSBA) complement were used to evaluate antibodies against representative meningococcal serogroup strains at baseline and 30 days after the dose. Safety data were collected up to 6 months post-vaccination.

Results

Non-inferiority of immune responses, based on percentages of participants achieving hSBA vaccine seroresponse, was demonstrated between MenACYW-TT and MCV4-CRM for all four serogroups at Day 30 compared to baseline. The proportions of individuals with hSBA ≥ 1:8 following MenACYW-TT administration were higher than those after MCV4-CRM administration for all four serogroups (A: 86.4% vs 79.3%; C: 97.8% vs 67.1%; W: 94.8% vs 86.3%; Y: 98.5% vs 90.8%). Similar results were observed in the two age substrata (2 to 5 years and 6 to 9 years). Percentages of participants with post vaccination rSBA ≥ 1:128 were comparable between both groups. The safety profiles of MenACYW-TT and MCV4-CRM were comparable. Reactogenicity at the MenACYW-TT injection site was lower than at the MCV4-CRM injection site. There were no immediate adverse events (AEs), no AEs leading to study discontinuation and no related serious adverse events.

Conclusions

MenACYW-TT vaccine was well tolerated and demonstrated a non-inferior immune response compared to the licensed MCV4-CRM vaccine when administered as a single dose to meningococcal vaccine naïve children.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT03077438

ESPID19-0965
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Long-term antibody persistence after primary vaccination with menacwy-tt and immunogenicity of a booster dose in individuals aged 11 to 55 years

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Background

The quadrivalent meningococcal ACWY polysaccharide conjugate vaccine using tetanus toxoid as a carrier protein (MenACWY-TT) is licensed to prevent meningococcal disease caused by meningococcal serogroups A, C, W, and Y in individuals aged ≥6 weeks. In a previous study (NCT00356369), subjects aged 11–55 years received 1 primary dose of MenACWY-TT or a quadrivalent polysaccharide vaccine (MenPS). This study reports long-term antibody persistence in these subjects after the primary MenACWY-TT dose and the safety and immunogenicity of a booster dose.

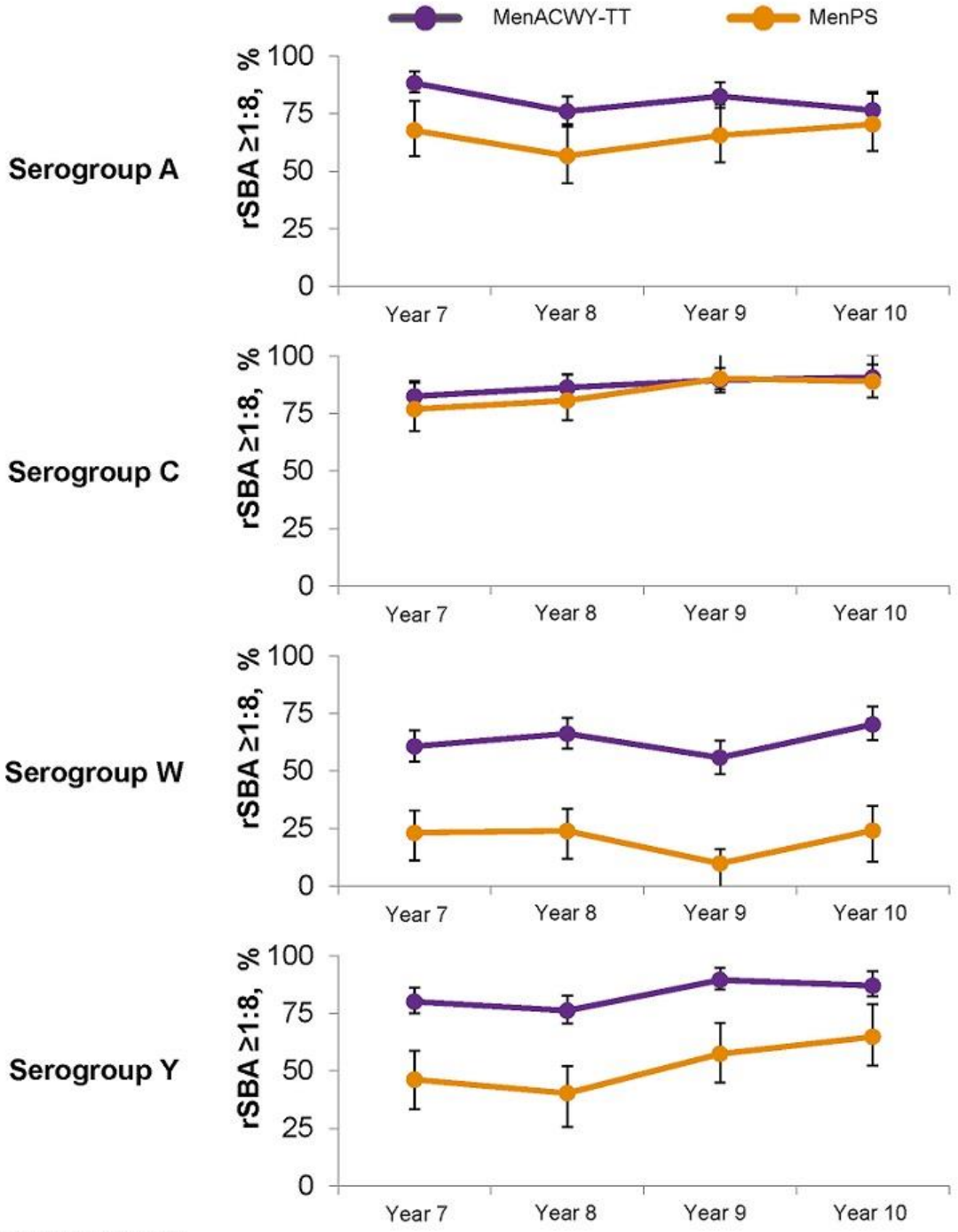
Methods

Antibody persistence 7–10 years post-primary vaccination and immune responses to a MenACWY-TT booster given at year 10 were evaluated by serum bactericidal activity assays using rabbit complement (rSBA); the percentages of subjects with rSBA titers ≥1:8 for each serogroup are reported herein. Safety was evaluated for the booster dose.

Results

Of 400 subjects vaccinated in the primary study, 311 and 220 subjects enrolled in the persistence and booster phases, respectively; 231 and 215 of these subjects completed each phase. From year 7 through year 10, the percentage of subjects with rSBA titers ≥1:8 remained stable for each serogroup. The percentages of subjects achieving titers ≥1:8 were similar for serogroup C in both groups and higher for MenACWY-TT than MenPS recipients for other serogroups at almost all time points (**Figure**). A MenACWY-TT booster dose at year 10 elicited rSBA titers ≥1:8 in ≥98% of all subjects. No new safety signals were observed during the booster phase.

Figure. Percentage of Subjects With an rSBA Titer ≥1:8 up to 10 Years After Primary Vaccination with MenACWY-TT or Men-PS*†



*Adapted ATP cohort.
†Data are from before administration of the MenACWY-TT booster dose.
ATP=according to protocol; MenACWY-TT=meningococcal polysaccharide groups A, C, W and Y conjugate vaccine; MenPS=serogroups A, C, W, and Y polysaccharide meningococcal vaccine; rSBA=serum bactericidal assay using baby rabbit complement.

Conclusions

Functional antibody responses persisted 10 years after primary MenACWY-TT vaccination, indicating long-term protection against meningococcal serogroup A, C, W, and Y disease. A booster dose was safe and immunogenic.

Clinical Trial Registration (Please input N/A if not registered)

NCT01934140. Funded by Pfizer.

ESPID19-0672
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Impact of 4cmenb vaccine on meningococcal carriage density in adolescents

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Background

Previous studies suggest limited or no impact of 4CMenB on carriage of *Neisseria meningitidis* in adolescents. However, it is thought vaccination may reduce the number of bacteria colonising the pharynx, thus reducing transmission and invasive disease. We sought to identify if 4CMenB vaccination is associated with reduced oropharyngeal carriage density.

Methods

In a cluster randomised controlled trial, 237 schools in South Australia in years 10-12 (aged 15-18) were randomized to 4CMenB vaccination at baseline (intervention) or 12 months (control). Carriage density was estimated using a *N. meningitidis* quantitative PCR standard curve, plotting cycle threshold values against colony forming units (CFU/ml). In students who were positive for carriage at 12 months, linear generalized estimating equations (GEE) were used to compare differences between groups. GEE models accounted for clustering by school and adjusted for school size, and social/educational advantage.

Results

During April-June 2017, 24,269 year 10/11 students were enrolled. In students who had carriage at 12 months, vaccination did not reduce the density of disease-causing *N. meningitidis* (vaccinated n=255, mean 238075 CFU/ml [SD 880597]), unvaccinated n=250, mean 184226 CFU/ml [SD 761886], adjusted difference 61813 [95% CI, -84612, 208238]). This was similar for individual genogroups B (vaccinated n=124, mean 274933 CFU/ml (SD 1217845), unvaccinated n=114, mean 238445 CFU/ml (SD 1038070), adj difference 59087 [-235772, 353945]), Y, W, and C. There was also no significant reduction in non-groupable *N. meningitidis* carriage density (vaccinated n=179, mean 156905 CFU/ml (SD 732006), unvaccinated n=229, mean 178747 CFU/ml (SD 617584), adj difference -16734.70 [95% CI, -155934, 122464])

Conclusions

There was no evidence of an impact of 4CMenB on carriage density. Immunisation strategies should focus on direct (individual) protection rather than indirect (herd) protection against invasive group B

meningococcal disease.

Funding:GlaxoSmithKline BiologicalsSA

Clinical Trial Registration (Please input N/A if not registered)

NCT03089086

ESPID19-0631
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Plasma microrna s are potential biomarkers of vaccine reactogenicity in infants: findings from a clinical trial of the reactogenic multicomponent capsular group b meningococcus (4cmenb) vaccine

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Background

Meningitis is a life-threatening, infectious disease. Capsular group B meningococcus (MenB) accounts for most invasive meningococcal disease in developed countries. In 2015, the multicomponent MenB vaccine (4CMenB, Bexsero®) was added to the UK infant vaccination schedule. MicroRNAs (miRNAs) modulate the expression of protein-coding genes. miRNAs are present in plasma and may act as intercellular regulators of gene expression. We investigated the effect of 4CMenB vaccination on plasma miRNA expression.

Methods

4-month-old infants were randomised to receive routine vaccinations with or without 4CMenB. Small RNA sequencing was conducted on plasma RNA pre and 24-hours post vaccination. Whole blood mRNA sequencing data was available from the same participants at the same time-points.

Results

Twenty-one paired samples were sequenced. The proportion of miRNA detected in plasma reduced after vaccination. miR-122 and miR-483-5p were differentially expressed post vaccination in both groups. Enrichment analyses showed that these miRNAs target mitogen activated protein kinases (MAPK) in the toll like receptor cascade (REACTOME pathway). An additional two miRNAs, miR-4497 and miR-576-3p, were differentially expressed in 4CMenB vaccinees. Post vaccination expression of miR-122, miR-483-5p and miR-4497 correlated with fever. We are currently studying the kinetics of differentially expressed miRNAs, and integrating differentially expressed miRNAs into their corresponding regulatory interactions, which may provide biological insights into the reactogenicity of 4CMenB.

Conclusions

We have identified two potential miRNA biomarkers of vaccine reactogenicity. One of these miRNAs, miR-122-5p, is primarily produced by hepatocytes, possibly implicating the liver in vaccine responses.

Funding: European Union’s seventh Framework program under EC-GA no. 279185 (EUCLIDS). NIHR Oxford Biomedical Research Centre. UK MRC.
Acknowledgements: Professor Michael Levin

Clinical Trial Registration (Please input N/A if not registered)

EudraCT number 2014-000126-38

ESPID19-0530
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Gene expression profile of neisseria meningitidis in pharyngeal carriers

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Background

Transcriptomic analysis of the levels of expression of Nm genes in pharyngeal swab samples may help predict which meningococcal protein candidate vaccine antigens might prevent transmission. We aimed for the first time to detect and quantify Nm gene transcripts from in vivo pharyngeal carriage samples and validate the detection of of *fhbP* expression.

Methods

Double headed sterile pharyngeal swab samples were collected from school age children aged 16-19 years in RNA*later* solution and STGG transport medium. 48 samples with medium to high density Nm carriage from 38 subjects were identified by qPCR and RNA was extracted from the RNA*later* swab samples. Probes for 47 Nm genes were used to detect and quantify transcripts on the NanoString nCounter platform. RT-qPCR was done to assess *fhbP* expression for the different variants.

Results

Gene expression was successfully detected and quantified for all 47 genes and varied widely between individual samples. Twenty-two genes were expressed in more than half of the samples, one (*cysT*) was detected in all 38 samples. *Fur, pilE, dsbA_2, opc* and *porA* had the highest mean gene expression (>3800 gene counts/ 1,000 bacteria), whereas *fadD1, csbA, sysW, frpC* and *gna33* had the lowest mean expression (<55 gene counts/1000 bacteria). There was a substantial agreement between RTqPCR and NanoString for *fhbP* detection, Cohen kappa = 72%.

Conclusions

This is the first time that Nm gene expression has been detected and quantified from *in vivo* pharyngeal carriage samples. These studies could help in understanding the effect of current and potential vaccine genes on carriage and transmission.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0180
Science and Educational Track

Oral presentation session 09 - Meningococcal infections

Immunogenicity of the meningococcal serogroup b vaccine menb-fhbp in children 1 to <10 years of age

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Background

MenB-FHbp (bivalent rLP2086) is a serogroup B meningococcal (MenB) vaccine licensed in multiple countries for adolescents and adults. Two recent phase 2 studies evaluated MenB-FHbp immunogenicity in younger children.

Methods

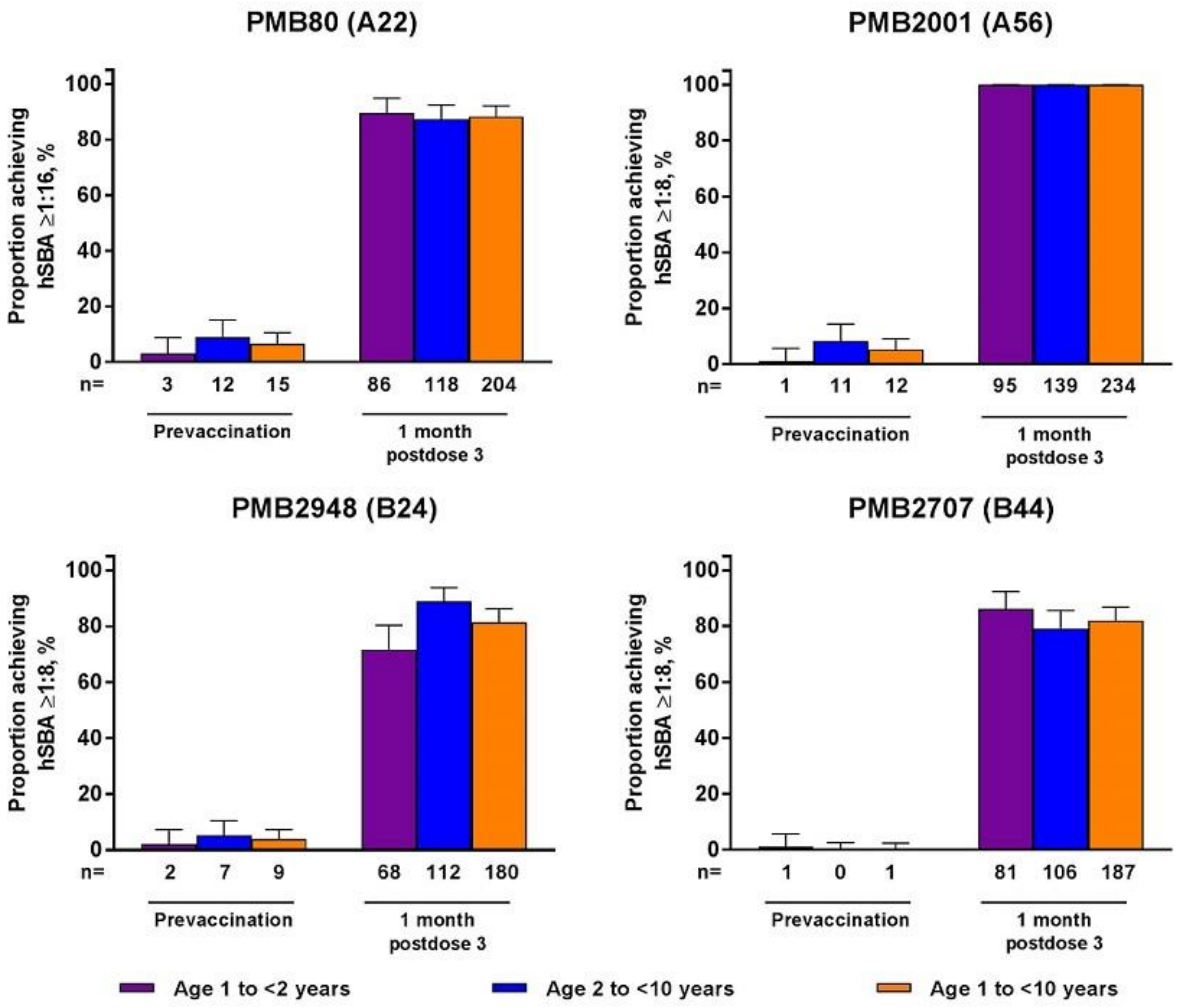
In an ongoing study, 352 toddlers 1–<2 years old were randomized to receive MenB-FHbp (120 µg at months 0, 2, 6) or hepatitis A virus vaccine (HAV; months 0, 6)/saline (month 2). Four hundred children 2–<10 years old were randomized 3:1 to receive 120 µg MenB-FHbp or HAV/saline. Immune responses were evaluated in serum bactericidal assays using human complement (hSBA) against 4 diverse, vaccine-heterologous MenB test strains; the lower limits of quantitation (LLOQs; 1:8 or 1:16) exceeded the accepted correlate of protection (hSBA titers ≥1:4). The current analysis evaluated pooled immune responses in 120-µg MenB-FHbp recipients (1–<10 years old) from the evaluable immunogenicity populations of both studies.

Results

One month postdose 3, 71.6%–100% of toddlers 1–<2 years old receiving 120 µg MenB-FHbp had hSBA titers ≥LLOQ against each of the 4 test strains; percentages were 79.1%–100% in children 2–<10 years old and 81.4%–100% in the pooled analysis (individuals 1–<10 years old; **Figure**). Percentages of subjects in the pooled analysis achieving ≥4-fold rises from baseline in hSBA titers were 74.7%–95.3% at 1 month following dose 3 and were similar across age groups. Geometric mean titers (GMTs) in the

pooled analysis increased from 4.0–8.6 before vaccination to 19.0–178.4 at 1 month postdose 3.

Figure. Proportions of Subjects 1 to <10 Years of Age Receiving 120 μg MenB-FHbp on a 0-, 2-, 6-Month Schedule Achieving hSBA Titers ≥1:16 (PMB80) or ≥1:8 (Other Strains)* Before Vaccination and After Dose 3 in Each Study and in the Pooled Analysis



hSBA=serum bactericidal assay using human complement; LLOQ=lower limit of quantitation; MenB-FHbp=bivalent rLP2086. n=number of subjects with hSBA titer ≥LLOQ.
*Test strains expressing FHbp variants A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively; hSBA LLOQs are 1:16 for strain PMB80, and 1:8 for strains PMB2001, PMB2948, and PMB2707. Due to serum volume constaints, sera from approximately half of subjects in each study were tested against strains PMB80 and PMB2948 while sera from the remaining half of subjects were tested against strains PMB2001 and PMB2707; no subject was tested against all 4 strains.

Conclusions

MenB-FHbp administered on a 0-,2-,6-month schedule induced protective bactericidal antibody responses against diverse MenB strains in subjects 1–<10 years old, supporting its potential for providing children with broad protection against MenB disease.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov, NCT02534935, NCT02531698. Funded by Pfizer.

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Science and Educational Track

Oral presentation session 10 - HIV in children

Comparison of antiretroviral treatment initiation in hiv newly diagnosed adolescents in Spain

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Background and Aims:

Adolescents represent a vulnerable group in acquisition of HIV infection. Differences in management of treatment may occur depending on multiple factors. Our objective is to describe the differences in initiation of antiretroviral treatment (ART) in newly diagnosed HIV adolescents in Spain.

Methods:

Retrospective review of 12-<20 years-old patients included in Spanish HIV cohorts (CoRIS for adults, and pediatric CoRISpe) between 1996 and 2017. A comparative analysis of time to initiation of antiretroviral treatment depending on sociodemographic and clinical data is performed.

Results:

296 HIV newly diagnosed adolescents were included, 77% were male and median age was 18,8 years-old (IQR 17,8-19,5). The way of infection was essentially sexual (89,6%), in men who have sex with men (MSM, 63,2%), mainly born in Spain (57,8%) and Latin America (29,4%). 87,5% of patients were initially followed up in adult units, while 12,5% in pediatric ones. 82,4% have ever received ART; the rest remained without treatment until they abandoned the cohort. Globally, median time from diagnosis to ART initiation was significantly lower in patients followed up initially in pediatric units (30,5 days, IQR 10,3-79,0), compared to adults (181 days, IQR 54,2-931,8) (p<0,001). Regarding the evolution during the study period of Spanish guidelines, median time from treatment indication to ART initiation was significantly lower in pediatric units (16 days, IQR 1,0-45,0) than in adults (33,5 days, IQR 7,0-122,3) (p=0,033). Median time to ART initiation was significantly lower in early adolescents (10-14,9 years-old) than older patients; while no difference was found between origin regions.

Conclusions:

Adolescents followed up initially in Pediatric Units started ART closer from diagnosis and ART Guideline indication compared to Adult Clinics. Further analyses may be useful to elucidate the causes.

Systematic Review Registration:

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Science and Educational Track

Oral presentation session 10 - HIV in children

Differential immunological profiles according to hiv viremia among vertically hiv-infected adolescents on prolonged cart

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Background and Aims:

Vertically HIV-infected adolescents provide a unique opportunity to understand immunological markers according to levels of HIV replication.

Methods:

Thirty antiretroviral treated (ART) vertically HIV-infected adolescents, 12 with detectable viral load (HIV/DVL), 18 with undetectable viral load (HIV/UVL), and 30 HIV negative control adolescents (CONTROL) were evaluated for immune activation and PD-1 expression on different maturation CD4+ T and CD8+ T cell subsets by flow cytometry, and production pattern of 21 cytokines in cell supernatant after *in vitro* stimulation with phytohemagglutinin (PHA) using X-MAP.

Results:

Lower CD4+T cells and higher T cell activation and exhaustion markers were noted on CD4+T and on CD8+T cells and memory subsets from HIV/DVL group, who also produced lower *in vitro* IFN-gamma, IL-10, IL-13, IL-17A, IL-5 and IL-6 than HIV/UVL group. HIV/UVL were comparable with CONTROL group in respect to CD4+T cell counts and T cell activation and exhaustion markers, but with higher *in vitro* production of ITAC (a chemokine with leukocyte recruitment function), IL-4 and IL-23 (Table). An inverse correlation between cytokine production and PD-1 expression on CD4+T and CD8+T subsets

was detected.

Table. Immune activation and exhaustion markers of *ex vivo* CD4+ and CD8+ T cells and cytokine production in pg/mL after *in vitro* stimulation of blood samples from HIV-infected patients with detectable viral load (HIV/DET), undetectable viral load (HIV/UND) and CONTROL groups. Median values are shown, with range in parenthesis. Kruskal-Wallis and Dunn method were used for statistics.

Parameters	HIV/DET	HIV/UND	CONTROL	HIV/DET vs HIV/UND (p)	HIV/DET vs CONTROL (p)	HIV/UND vs CONTROL (p)
CD4+ T cells/mm³	292.2 (203.0 – 880.4)	797.3 (308.7 – 1487.4)	1012.1 (414.6 –1914.6)	**0.033**	**0.001**	0.160
% CD38+HLA-DR+	8.9 (1.7 – 22.9)	3.1 (0.6 – 12.1)	5.1 (0.19 – 20.0)	0.060	0.085	>0.999
%PD1+	30.3 (20.0 – 74.9)	27.7 (13.1 – 34.0)	23.6 (11.9 – 40.2)	0.330	**0.045**	>0.999
CD8+ T cells/mm³	918.7 (402.2 – 1456.7)	788.7 (222.0 – 1760.9)	631.1 (292.1 – 1207.1)	>0.999	0.134	0.262
% CD38+HLA-DR+	17.5 (7.1 – 43.1)	5.8 (1.9 – 13.4)	6.8 (0.6 – 25.3)	**0.002**	**0.002**	>0.999
%PD1+	41.5 (28.2 – 73.3)	26.2 (15.0 – 39.5)	20.4 (8.6 – 35.9)	**0.005**	**<0.001**	0.767
IFN-gamma	7,336.9 (0.4 – 31165.9)	27,511.3 (0.1 – 37767.6)	20,819.6 (757.3 – 33700.8)	**0.048**	0.526	0.431
IL-10	102.8 (0.0 – 324.4)	551.4 (0.8 – 2263.2)	517.5 (66.0 – 4923.8)	**0.003**	**<0.001**	>0.999
IL-13	315.2 (0.0 – 2288.0)	1516.9 (0.0 – 5231.5)	953.7 (174.2 – 3239.8)	**0.045**	0.513	0.423
IL-17A	171.2 (0.0 – 972.5)	931.2 (0.0 – 5097.6)	1004.3 (93.2 – 2223.1)	**0.009**	**0.001**	>0.999
IL-5	145.2 (0.0 – 999.8)	1066.5 (0.0 – 2645.9)	558 (46.9 – 2400.7)	**0.013**	0.074	0.937
IL-6	1275.9 (0.0 – 2429.2)	2733.2 (0.0 – 4677.2)	2813.5 (385.4 – 4659.7)	**0.032**	**0.013**	>0.999
ITAC	189.8 (0.0 – 746.2)	215.0 (0.0 – 312.6)	84.1 (0.0 – 197.7)	>0.999	0.052	**0.006**
IL-4	3.3 (1.0 – 50.3)	3.6 (0.6 – 25.5)	0.6 (0.0 – 16.3)	>0.999	0.080	**0.006**
IL-23	45.9 (4.3 – 148.7)	82.7 (0.0 – 243.5)	35.8 (0.0 – 169.7)	0.551	>0.999	**0.037**

Conclusions:

Despite ART, persistent viremia leads to T cell activation, immune exhaustion and low cytokine production, whereas viral suppression by ART approximates hosts to CONTROL, although HIV still impacts HIV/UVL as indicted by the distinct cytokine profile from CONTROL.

Systematic Review Registration:

FAPESP 2013/21853-1

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Science and Educational Track

Oral presentation session 10 - HIV in children

Pregnancy outcomes in a cohort of perinatally hiv-infected women

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Background and Aims:

An increasing number of perinatally HIV-infected women are reaching adulthood and becoming pregnant. Achieving viral suppression might be challenging in this population frequently exposed to a high number of antiretroviral regimens. The aim of this study was to describe a cohort of vertically HIV-infected mother, prevention strategies and infant outcomes in Spain.

Methods:

Descriptive, retrospective study including perinatally HIV-infected women registered in the Madrid Cohort of HIV-infected children, which gave birth between January 2000 and December 2018.

Results:

48 pregnancies in 43 perinatally HIV-infected women were registered during the study period. Median age was 23.3 years and most were Caucasian. Main characteristics of mother infant pairs are shown in Table 1. Although their immunological situation was generally preserved, half of the study cohort had received six or more ART regimens. Five cases (10%) had detectable viral load (2 >10000 copies/ml) at the moment of delivery. There was one preterm baby and 6 babies were born below 2500 g. There was one case of mother-to-child transmission case in a non-adherent mother in which PMTCT measures could not be implemented.

Ethnicity; N (%)	
Caucasian	38 (88%)
Sub-Saharian	4 (9.5%)
NA	1 (2.3%)
Age at conception (years); mean [SD]	23.3 [6.5]
Previous AIDS diagnosis; N(%)	17 (40.5%)
Previous ART regiments N (%)	
1-2	3 (6.25%)
3-5	5 (10.4%)
>6	23 (47.9%)
Unknown	17 (35.4%)
On ART during pregnancy; n (%)	43 (89.5%)
Maternal CD4 counts at birth; N (%)	
<200 cells/mm3	3 (6.25%)
200-499 cells/mm3	9 (18.75%)
>500 cells/mm3	27 (56.25%)
Unknown	9 (18.75%)
Viral load (copies/mL); n (%)	
<50	43 (89.6)
> 50	5 (10.4%)
Number of deliveries	48
Mode of delivery	
Vaginal	27 (56.25%)
Cesarean	19 (39.5%)
Unknown	2 (4.1%)
Zidovudine intrapartum; N (%)	45 (93.75%)
Newborn gender	
Male	28 (58.3%)
Gestational age (weeks), median (IQR)	38 [37-39]
Birth weight (g); mean (SD)	2950 (563)
Birth weight; n (%)	
<2500 g	6 (12.5%)
<1500 g	1 (2%)
Breastfeeding	0
Postnatal child prophylaxis; n (%)	
Monotherapy	36 (75%)
Dual or triple therapy	10 (20.8%)
none	0
Unknown	2 (2%)
Mother-to-child-transmission rate; N (%)	1(2%)

Conclusions:

The unique population of vertically HIV-infected youths poses particular challenges for health care providers. Specific strategies to minimize perinatal transmission risks and adherence in this unique population are needed.

Systematic Review Registration:

NA

ESPID19-0376
Science and Educational Track

Oral presentation session 10 - HIV in children

HIV-exposure and delayed bcg vaccination do not affect bcg scarring in infants

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Background

Bacillus Calmette-Guerín (BCG) vaccination is routinely recommended at birth in most developing countries. There is no validated immunological correlate of protection for BCG. BCG scar is frequently used a marker of vaccination uptake. Delayed vaccination may be a strategy to overcome immature immune responses to BCG given at birth, especially in the context of infant HIV exposure and safety concerns of live BCG vaccine in HIV-infected infants.

Methods

We analyzed BGC scar status, size and ulceration in South African HIV-exposed and unexposed infants in a randomized controlled trial investigating immunological and clinical effects of delayed BCG vaccination. Infants were randomized to receive Danish strain BCG (Statens Serum Institute, Copenhagen) intradermally at birth or delayed vaccination at 14 weeks of age. BCG scar formation, size of scar and ulceration were assessed at 28 weeks and at 18 months.

Results

180 infants (113 HIV-exposed, 67 unexposed) were randomized. Assessment was completed in 135 infants (75%) at 28 weeks; 76 (56.3%) birth and 59 (43.7%) delayed vaccination group. Baseline characteristics were similar. All infants formed a BCG scar. At week 28, infants with delayed vaccination had a greater scar size (7.31 mm versus 5.97 mm, p=0.003). Ulceration was less frequent in the birth vs. delayed group [OR=0.02, 95% CI (0.00-0.15), p<0.001]. There was no difference in frequency of BCG scarring by HIV exposure status. HIV-exposed infants vaccinated at birth had greater scar size compared to HIV-unexposed infants at week 28. Scarring persisted at 18 months in 110/114 (96.5%) with no effect of timing of vaccination or HIV exposure.

Conclusions

BCG scarring occurred in infants regardless of timing of vaccination and HIV exposure status. Immunological effects of HIV exposure and timing vaccination should be further investigated.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0256
Science and Educational Track

Oral presentation session 10 - HIV in children

Measles immunity at 4.5 years of age following vaccination at 9 and 15-18 months of age among hiv-infected, hiv-exposed-uninfected and hiv-unexposed children

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Background

HIV-infected and HIV-exposed-uninfected (HEU) children may be at increased risk of measles infection due to waning of immunity following vaccination. We evaluated persistence of antibodies to measles vaccination at 4.5 years of age in HIV-unexposed, HEU, and HIV-infected children with CD4+≥25% previously randomised to immediate antiretroviral therapy interrupted at 12 months (HIV/Immed-ART-12), 24 months (HIV/Immed-ART-24), or when clinically/immunologically indicated(HIV/Def-ART). The HIV/Def-ART group had ART initiated by median 5.8 (interquartile range 4.4-10.3) months of age.

Methods

This cohort study followed participants from 6-12 weeks through 4.5 years of age. HIV-unexposed (n=95), HEU (n=84), HIV/Immed-ART-12 (n=70), HIV/Immed-ART-24 (n=70), and HIV/Def-ART (n=62) children were scheduled to receive measles vaccination at 9 and 15-18 months of age. Anti-measles serum IgG titres were quantified using enzyme-linked immunosorbent assay at 4.5 years.

Results

Compared with HIV-unexposed children (2860 mIU/ml; 95% confidence interval [CI] 2373-3446), measles antibody geometric mean titres (GMTs) were significantly lower in both HIV/Immed-ART-12 (571; 95%CI 409-796; p<0.001) and HIV/Immed-ART-24 (1136; 95%CI 791-1633; p<0.001), but similar in the HIV/Def-ART (2777; 95%CI 2008-3841); p=0.675) and HEU (3242; 95%CI 2617-4014; p=0.525) groups. Furthermore, compared with HIV-unexposed, antibody titres ≥330 mIU/mL (i.e. presumed sero-correlate for protection; 99%) were also significantly lower in HIV/Immed-ART-12 (70%; p<0.001) and HIV/Immed-ART-24 (83%; p<0.001); but similar in the HIV/Def-ART (90%) and HEU (98%) groups.

Conclusions

HIV-infected children in whom ART was interrupted at either 12 or 24 months of age had lower GMTs and lower proportions with seroprotective titres than HIV-unexposed children; indicating a potential downside of ART treatment interruption.

Clinical Trial Registration (Please input N/A if not registered)

The ClinicalTrials.gov registry numbers for the parent studies are NCT00099658 and NCT00102960

ESPID19-0249
Science and Educational Track

Oral presentation session 10 - HIV in children

Immunogenicity and safety of an early 2-dose measles vaccination schedule at 6 and 12 months of age in hiv-exposed uninfected and hiv-unexposed south african children

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[4]*Division of Epidemiology and Biostatistics- School of Public Health- Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*
[5]*Clinical Epidemiology- University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands*

Background

Measles morbidity and mortality are greatest in children <12 months old, with increased susceptibility in HIV-exposed children. Furthermore, a recent measles epidemic in South Africa observed increased susceptibility to measles in infants <9 months of age. We evaluated the immunogenicity and safety of an early 2-dose measles vaccine regimen administered at 6 and 12 months of age in South Africa.

Methods

HIV-unexposed (n=212) and HIV-exposed uninfected (HEU) (n=71) children received measles vaccination (CAM-70) at 6 and 12 months of age. Blood samples were collected before and one month after each vaccine dose. Anti-measles immunoglobulin G titers were measured by enzyme-linked immunosorbent assay. Safety data were collected by active surveillance during 7 days following vaccination and passive surveillance for serious adverse events (SAEs) throughout the study period.

Results

The majority of children (88.2% HIV-unexposed, 95.8% HEU; p=0.044) had seronegative antibody titers (<150 mIU/mL) to measles at 4.2 months of age. Post-primary measles vaccination, 42.3% of HIV-unexposed and 46.4% of HEU had seroprotective titers ≥330 mIU/mL. Post-second dose, measles geometric mean titers and proportions with antibody titers ≥330 mIU/mL were similar between groups, with 99.0% of HIV-unexposed and 95.3% in HEU children being seroprotected. Solicited reactions following vaccination and SAEs occurred with similarly frequency and severity in HIV-unexposed and HEU children.

Conclusions

Early 2-dose measles vaccination at 6 and 12 months of age with the CAM-70 strain was well tolerated and induced antibody responses in HIV-unexposed and HEU children, which could partly offset the early loss of maternally derived antibodies in infants born to predominantly measles-vaccinated mothers.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0235
Science and Educational Track

Oral presentation session 10 - HIV in children

Increasing contribution of sexually-transmited hiv diagnoses in adolescents in spain

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[2]Hospital Universitario Gregorio Marañón, Departmnet of Pediatrics, Madrid, Spain
[3]Centro Sanitario Sandoval, Infectious Diseases, Madrid, Spain
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[5]Hospital General de La Rioja, Infectious Diseases, Logroño, Spain
[6]Hospital Sant Joan de Deu, Departmnet of Pediatrics, Barcelona, Spain
[7]Hospital Universitario Carlos III-La Paz, Departmnet of Pediatrics, Madrid, Spain
[8]Hospital Vall d'Hebron, Departmnet of Pediatrics, Barcelona, Spain
[9]Hospital Clínico San Carlos, Departmnet of Pediatrics, Madrid, Spain

Background and Aims:

A specific approach of HIV in adolescents is of global concern. Data about new HIV diagnoses in adolescents is scarce. Describing this population will contribute to better approach this problematic situation.

Methods:

Description of HIV new diagnoses in patients 12-20 years-old included in CoRIS (adult) and CoRISpe (pediatric) Spanish cohorts until end 2017. Demographic, clinical, biological data and way of transmission were analysed.

Results:

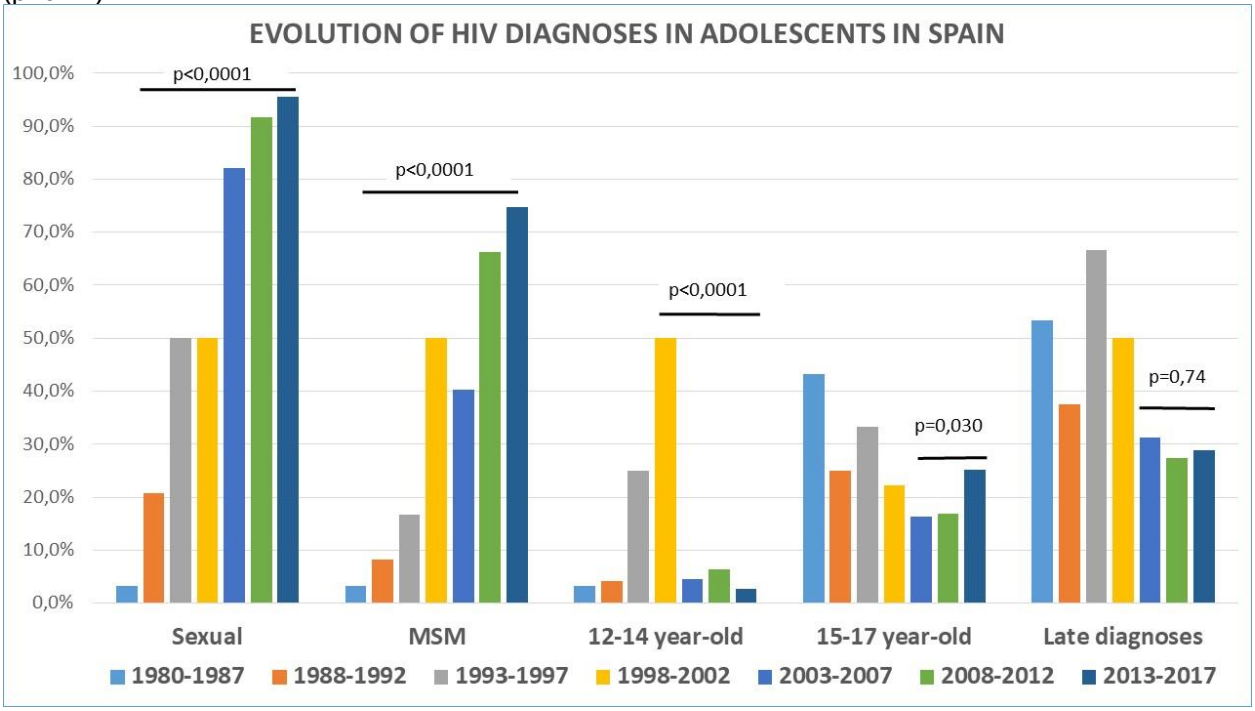
For 357 adolescents, new HIV diagnosis was made; 75.4% were male. Median age at diagnosis was 18.7 years. Middle adolescents (15-17 year-old) significantly increased, from 2003-2007 (16.4%) to 2013-2017 (25.2%, p=0.030).

In 275 of cases (77%) way of infection was sexual (53.5% men who have sex with men, MSM; 23.5% heterosexual contact), 54 (15.1%) people who injected drugs, 10 (2.8%) vertical transmission and 6 (1.7%) hemoderivates receivers. Sexual transmission and MSM increased significantly over time to 95.5% and 74.8% respectively in 2013-2017.

Regarding the origin, 131 (36.7%) adolescents were born outside Spain; 71% of them in Latin-America. For Latin-American, in 93.5%, transmission was sexual vs 72.0% for other origins (p=0.0002).

Late diagnosis (CD4<350/mm^3 or AIDS at diagnosis) was made for 123 adolescents (34.5%). This was more frequent for transmission by heterosexual contact (41.7%) than MSM (23.0%, p=0.0023). Late diagnoses among adolescents decreased over time but not in last 15 years: 21/67 (31.3%) in 2003-2017 vs 32/111 (28.8%) in 2013-2017

(p=0.74).



Conclusions:

There is an increasing contribution of sexual transmission and MSM in new HIV diagnoses in adolescents. HIV-newly infected adolescents are younger, with a growing rate of 15-17 year-old. More than 1/3 present late diagnosis and did not decrease in last 15 years. This emphasizes the vulnerability of this population and the need to develop more effective preventive actions.

Systematic Review Registration:

N/A

ESPID19-0044
Science and Educational Track

Oral presentation session 10 - HIV in children

Response to direct acting antivirals in vertically hiv/hcv co-infected youths

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[8]La Paz University Hospital, Infectious Diseases, Madrid, Spain
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[11]Gregorio Marañon University Hospital, Infectious Diseases, Madrid, Spain
[12]CoRISpe Study Group, Pediatrics, Spain, Spain

Background and Aims:

New direct acting-antivirals (DAA) have altered HCV treatment in recent years. The absence of authorized drugs in children along with the natural evolution of the infection in childhood, generally asymptomatic until adolescence, results in little treatment experience in the population of vertically HIC/HCV co-infected subjects. The objective of this study is to describe response to DAA treatment in this unique population.

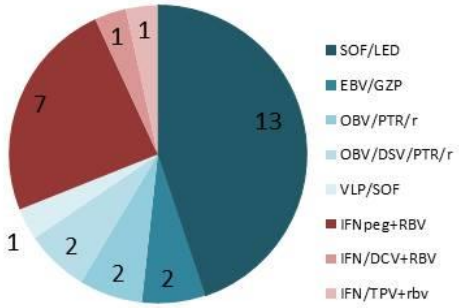
Methods:

Longitudinal observational study within The Spanish National Cohort of HIV-infected children and adolescents (CoRISpe) including vertically HIV/HCV co-infected children that had received treatment against HCV when visiting adult units. Demographic, analytical, clinical and virological parameters were collected before, and 12 weeks after finishing HCV treatment.

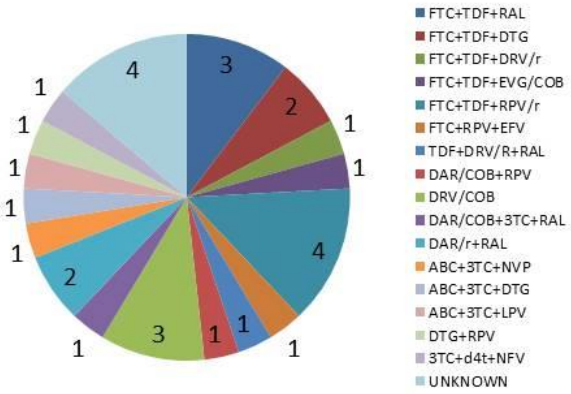
Results:

Fourty-six patients were analyzed (3 lost and 5 deceased). 52.2% were women, median age: 26.5 years (IQR 24-30). Thirty patients received treatment, median age: 22 years (IQR 19.7-25). At HCV treatment initiation, all patients were on ART (antiretroviral treatment), 92% virollogically suppressed, median CD4-T cells: 646 cel/ul (IQR 551-1039), 13.3% below CD4<500cel/ul. 24.1% presented advanced fibrosis (F3-F4), 17.2% F2 and 55% F0-F1. Overall, 70% were treated with direct action antivirals (DAA); plus RBV in 23% [100% sustained virological response (SVR)]. Nine patients received interferon therapies (88%

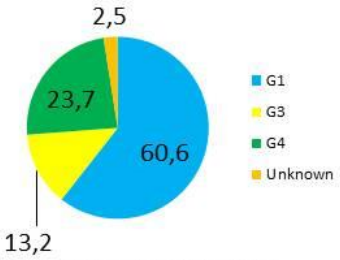
SVR).



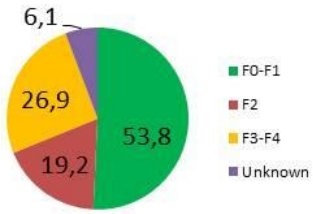
HCV treatment



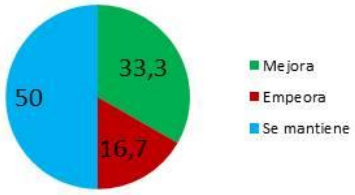
HIV treatment (ART)



Genotipical distribution



Fibrosis status before treatment



Fibrosis status post treatment

Conclusions:

In our study, new DAA treatment guidelines achieved excellent cure rates (100%) in vertically HIV/HCV co-infected patients. However, 24.1% of these patients showed advanced fibrosis (F3-F4) at treatment initiation with no improvement despite treatment in 60%. To speed up access to new DAA treatments for pediatric populations is an urgent need.

Systematic Review Registration:

No systematic review registration

ESPID19-0019
Science and Educational Track

Oral presentation session 10 - HIV in children

Incidence of tuberculosis in hiv infected children in india – is there a role of isoniazid preventive therapy?

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Background and Aims:

To determine the role of Isoniazid Preventive Therapy (IPT) in children with HIV.

Methods:

Eighty-one HIV infected children were classified according to the CDC classification at the time of presentation. The development of TB at the time of presentation or on follow up was noted and was analyzed with various risk factors.

Results:

Mean age of presentation was 6.36±3.67 years. According to CDC classification, 4.9% patients were in class N, 11.1% were in class A, 56.8% were in class B, 27.2% were in class C at presentation. TB at presentation was seen in children in CDC class B and C (p=0.026). Ten patients had TB at the time of presentation and 48(59.3%) patients developed TB after a mean duration of 12.2±23.4 months from presentation. No statistical significance was present between incidence of TB and gender, CD4 count, TB contact and prior tubercular infection and ART status. Children upto 3 years of age developed TB after 6.23±14.07 months, those between 3-6 years developed TB after 14.6±23.27 months, those between 6-9 years developed TB after 6.54±21.23 months, those between 9-12 years developed TB 40.2±35.98 months after presentation (p=0.042). Eight(16.7%) had multidrug-resistant (MDR) TB and 1 patient (2.08%) had extensively drug-resistant (XDR) TB.

Conclusions:

Children at younger age develop TB within a year of presentation whereas those in the adolescent age group develop TB after 3 years of diagnosis of HIV. Thus, role of IPT in adolescents at the time of diagnosis may not be useful whereas IPT may be useful in the younger age group. With high incidence of MDR-TB, role of IPT in HIV infected children in India needs to be re-assessed.

Systematic Review Registration:

N/A

ESPID19-0894
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Group a streptococcal carriage rates in portuguese children of nursery age

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Background

Streptococcus pyogenes, or Group A streptococcus (GAS), is a Gram-positive bacterium of clinical importance, causing a variety of diseases from mild and self-limiting conditions such as pharyngitis and impetigo, to more severe conditions such as necrotising fasciitis, rheumatic heart disease and invasive disease. A small proportion of individuals carry GAS asymptomatically in the upper respiratory tract; while their role in transmission in the community is unclear, it is possible that those harbouring high densities of GAS could transmit to others.

Methods

We carried out a cross-sectional observational study series in children in nurseries from Coimbra, Portugal, to look for patterns in GAS carriage rates and carriage density over several years. Nasal swab samples (n=2,884) were collected from children aged 5-84 months between 2011 and 2016; a subset of children also gave matched saliva samples (n=209). The presence and density of important bacterial species was determined using qPCR, including for GAS (*ntpC*).

Results

Overall, the carriage rate of GAS in the nasopharynx was 9.3%, and the range in densities of GAS carriage was similar to that of pneumococcus (in positive samples). Of those who gave saliva samples, the carriage rate of GAS was found to be higher than in the nose (12.4% compared to 3.8% in matched samples). We observed a trend towards higher nasal carriage rates in those with more symptoms of rhinitis, and fluctuations in overall carriage rates between months and years of sampling, indicating a potential relationship between other respiratory infections and GAS carriage in the nose.

Conclusions

In conclusion, we describe the carriage rates of GAS in children of nursery age, and report on factors which may relate to increasing transmission of GAS in this age group.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0686
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Burden of rotaviral diarrhoea and its risk/associated factors among under-five children: a case-control study in bangladesh

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Background and Aims:

Diarrhoea due to rotaviral infection is a universal health problem including Bangladesh. Data on epidemiology and risk/associated factors of rotavoral-diarrhoea are limited. An analysis was carried out on data collected between 1996-2014 in a hospital-based Diarrhoeal-Disease-Surveillance-System (DDSS) in the 'Dhaka Hospital' of International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). The DDSS enrolls a 2% systematic sample, regardless of age, sex, and diarrhoea severity.

Methods:

The data included information on socio-demographic factors, environmental history, clinical characteristics, nutritional status, and diarrhoea pathogens. After cleaning of data, relevant information of 21,626 children (40.3% female children) aged <5-years (mean±SD age of 14.9±11.7 months) were available who reported with diarrhoea. Of them 1,901 (8.7%) were *Escherichia coli*, 994 (4.5%) were *Shigella*, 2,264 (10.3%) were *Vibrio cholera* positive; and 9,137 (41.7%) children admitted with rotaviral-diarrhoea. Thus, children with rotavirus positive from stool sample comprised the cases, and the rest 12,489 children were considered as controls.

Results:

Variables found significantly associated with rotaviral-diarrhoea in bi-variate analysis were used in logistic regression analysis, which revealed that diarrhoea with <7 days duration, absence of mucous and/or blood in stool, no abdominal pain, presentation without some/severe dehydration, use of drug before hospital reporting, infancy (<12 months of age), not suffering from stunting and/or wasting, reporting during cooler months (October to March), were the associated/risk factors ($p<0.05$ for all adjusted-odds-ratio) of rotaviral-diarrhoea.

Conclusions:

The most common cause (42%) of diarrhoeal illness in inder-5 is rotavirus. The above mentioned associated or risk factors in under-5 children would help to differentiate rotaviral-diarrhoea (who do not need antibiotic) from other common causes of bacterial diarrhoea, that may help in reducing the rampant use of antibiotic and appropriate management of diarrhoeal illness.

Systematic Review Registration:

Not applicable

ESPID19-1075
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Pre-school osteoarticular infections (poi) – study a multicenter multinational retrospective study of osteomyelitis and septic arthritis in young children in australia and new zealand

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[2]University of Otago, Department of Population Health, Christchurch, New Zealand
[3]Christchurch Hospital - Christchurch- Kidz First Children's Hospital - Auckland- Starship Children's Health - Auckland- Royal Darwin Hospital - Darwin- Lady Cilento Children's Hospital - Brisbane- John Hunter Children's Hospital - Newcastle- Sydney Children's Hospital - Sydney- The Children's Hospital at Westmead - Sydney- The Royal Children's Hospital - Melbourne- Monash Children's Hospital - Melbourne- Princess Margaret Hospital for Children - Perth, Paediatrics, Australia and New Zealand, Australia

Background and Aims:

Australia and New Zealand have a particularly high incidence of osteoarticular infections in preschool aged children, possibly due to an increased burden of disease in Indigenous ethnic groups. This study aimed to review the clinical presentations, microbiology and management of osteomyelitis and septic arthritis in preschool aged children.

Methods:

ICD-10 codes were used to identify children between 3-60 months of age who presented with osteomyelitis, septic arthritis or spondylodiscitis between January 2012 and December 2016. Eleven different hospitals across Australia and New Zealand contributed data on the demography, clinical presentation, microbiology and antibiotic treatment of pre-school children admitted with osteoarticular infections. The study has been endorsed by the ANZPID Research Network.

Results:

1252 cases were entered into the database of which 920 met our inclusion criteria. 517 patients had septic arthritis, 473 osteomyelitis and in 34 patients the spine was involved. Nearly 20% of children tested had a positive blood culture. PCR was seldom used for diagnosis on surgical specimens but led to a higher rate of pathogen detection, particularly for *Kingella kingae* (Figure 1). Intravenous Flucloxacillin and oral cephalexin were the choice of antibiotic in the majority of cases with a total duration of antibiotic use of 35.3 days on average.

Figure 1: Microbiological samples taken and their results

	Blood		Bone or joint aspirate		Tissue sample	
	Culture	PCR	Culture	PCR	Culture	PCR
Total number of samples	788	1	439	49	292	16
Positive results (%)	154 (19.5%)	0	165 (37.6%)	22 (44.8%)	129 (44.2%)	9 (56.3%)
MSSA	75	0	55	1	50	0
MRSA	20	0	16	0	26	0
Streptococcus pyogenes	23	0	17	0	16	0
Streptococcus pneumoniae	4	0	17	2	7	0
Kingella kingae	16	0	31	13	17	9
Other causative microorganism	16	0	29	6	13	0

Conclusions:

This is one of the largest studies performed on the epidemiology of paediatric osteoarticular infections. The preliminary results indicate that in the majority of cases no micro-organism is identified but increased use of molecular diagnostic methods may lead to increased detection of pathogens. Further analysis will be presented on the microbiology and spectrum of clinical management. Our data can support the development of guidelines for diagnosis and management of pre-school osteoarticular infections.

Systematic Review Registration:

N/A

ESPID19-1012
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

An evidence-based cognitive behavioral intervention designed for ethnic minority adolescent women with abuse history and sti

J. Champion[1]
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Background

Ethnic minority adolescent women with sexual or physical abuse histories and sexually transmitted infections (STI) are at-risk for HIV. Community-based interventions for behavior modification and subsequent risk reduction have not been effective among these women.

Objective: Evaluate longitudinal effects of theory-based (AIDS Risk Reduction Model) cognitive behavioral intervention model versus enhanced counseling for abused ethnic minority adolescent women on STI incidence.

Methods

Design: Randomized controlled trial

Setting: Community-based clinics

Participants: Mexican-and-African American adolescent women aged 14-18 years with abuse history or STI seeking sexual health care

Extensive preliminary study for intervention development included individual interviews, focus groups, secondary data analysis, pre-testing and feasibility testing for modification of an evidence-based intervention prior to testing. Informed consent preceded detailed interviews concerning demographics, abuse history, sexual behavior and physical exams at study entry and randomization into control or intervention groups. Intervention participants received workshop, support group and individual counseling sessions. Control participants received abuse and enhanced clinical counseling. Follow-up detailed interviews and physical exams at 6 and 12 months assessed for STI. Intention to treat analysis assessed intervention effects using chi-square and multiple regression models.

Results

409 Mexican-(n=342) and African-(n=67) American adolescent women; 90% intervention attendance; follow-up at 6 (93%) and 12 (94%) months. Intervention (n=199) versus control (n=210) experienced fewer infections at 0-6 (0% vs. 6.6%, p=0.001), 6-12 (3.6% vs. 7.8%, p=0.005, CI 95% lower-upper .001-.386) and 0-12 (4.8% vs. 13.2%, p=0.002, CI 95% lower-upper, .002-.531) month intervals.

Conclusions

A cognitive behavioral intervention, Project IMAGE, designed for ethnic minority adolescent women with abuse history and STI was designated as effective by the Centers for Disease Control, providing

evidence for STI/HIV evidence-based interventions. Implications include translation to community-clinic-based settings for sexual health promotion among adolescent women.

Clinical Trial Registration (Please input N/A if not registered)

NCT01387646

ESPID19-0484
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Rainfall and agents of gastroenteritis in costa rican children: a nine-year study

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Background and Aims:

Diarrheal disease is one of the main public health problems worldwide, with more than 1700 million episodes per year in the pediatric population and more than half a million deaths.

We studied the frequency and distribution of pathogens associated with gastroenteritis at the National Children's Hospital of Costa Rica (NCH-CCSS) and their relationship with rainfall rates.

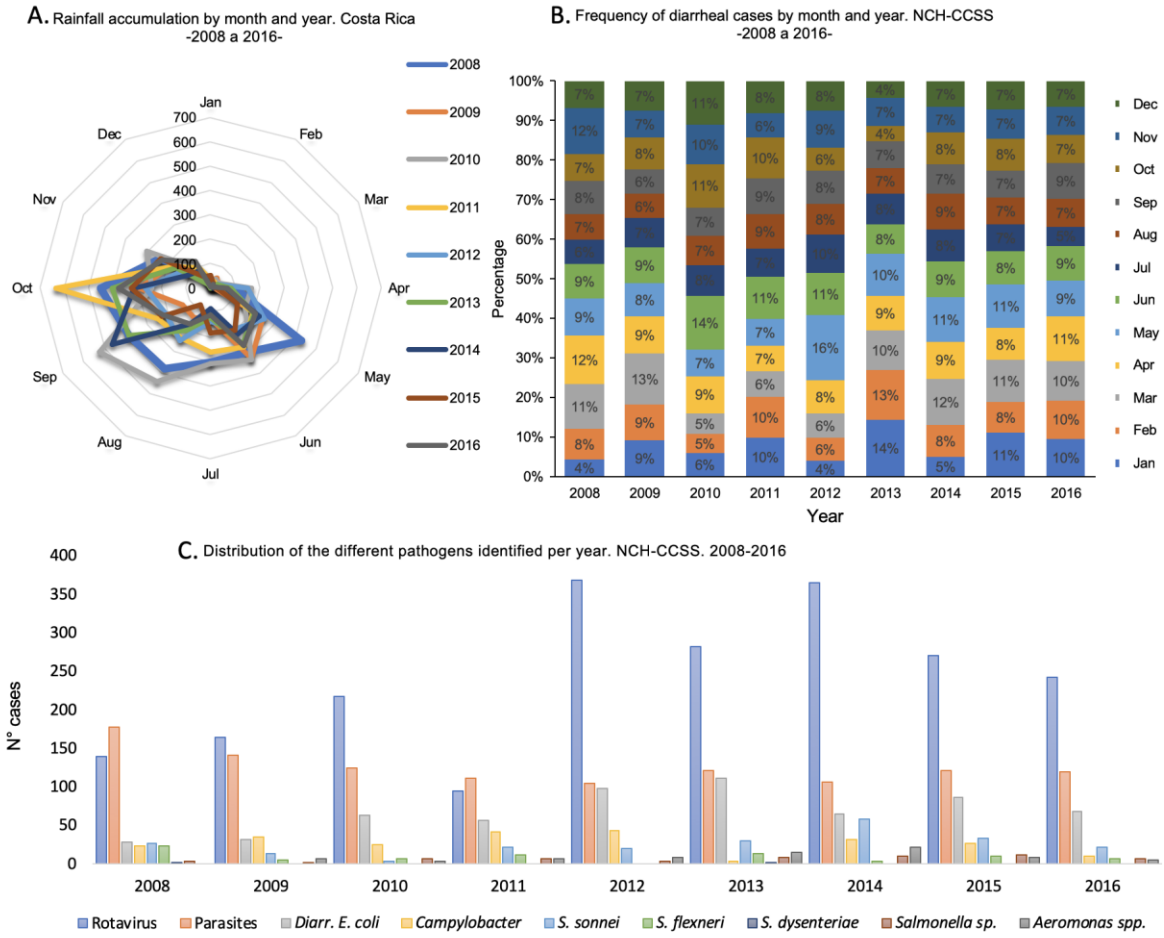
Methods:

A retrospective observational study from January 2008 to December 2016 was conducted. Data were retrieved from NCH-CCSS's clinical and laboratory databases, as well as national rainfall records. Nine major pathogen groups were included: Rotavirus, intestinal parasites, diarrheagenic *Escherichia coli* (DEC), *Shigella* spp., *Salmonella* sp., *Aeromonas* spp., and *Campylobacter* spp. Generalized additive models (GAM) with Poisson distribution were fitted to evaluate the relationship of rainfall with the number of cases per pathogen.

Results:

46 906 fecal samples were studied. Only 12 247 (26 %) corresponded to cases of diarrhea. The most frequent agents were Rotavirus, intestinal parasites and DEC.

According to the GAM, Rotavirus was the only pathogen to show a significant interaction with rainfall ($X^2 = 10.86$; $p < 0.05$). For every increment of 1 mm/m^2 in monthly rainfall, the incidence of Rotavirus fell by 0.1%.


A. Rainfall accumulation by month and year. Costa Rica
-2008 a 2016-
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
700
600
500
400
300
200
100
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
B. Frequency of diarrheal cases by month and year. NCH-CCSS
-2008 a 2016-
Percentage
Year
Dec
Nov
Oct
Sep
Aug
Jul
Jun
May
Apr
Mar
Feb
Jan
C. Distribution of the different pathogens identified per year. NCH-CCSS. 2008-2016
N° cases
Rotavirus
Parasites
Diarr. E. coli
Campylobacter
S. sonnei
S. flexneri
S. dysenteriae
Salmonella sp.
Aeromonas spp.

ESPID19-0313
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Nationwide cohort study on prevention for mother to child transmission of htlv-1 in japan

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Background and Aims:

To prevent mother-to-child transmission (MTCT) of human T-lymphotropic virus type 1 (HTLV-1), the most reliable way is to refrain from breast milk containing infected cells and to provide exclusive formula-feeding. In Japan, short-term breastfeeding (<3 months) or freeze-thawing breast milk can also be selected. However, no sufficient evidence has been established to support these approaches.

Methods:

Children born from HTLV-1 career mothers, who were registered at 92 facilities from 2012 to 2015, were followed up until 3 years of age. The MTCT rate was evaluated according to the nutritional method selected by the mothers.

Results:

Of the 757 children, 267 tested for HTLV-1 antibody at 3 years of age were analyzed. The seropositive rate was 20% (2/10) with long-term breastfeeding, 6.1% (6/98) with exclusive formula-feeding, 2.1% (3/142) with short-term breastfeeding, and 5.9% (1/17) with freeze-thawing breast milk. There was no significant difference between exclusive formula-feeding and short-term breastfeeding. Of mothers who selected short-term breastfeeding, 6.7% had continued breastfeeding to their infants 12 months of age.

Accumulating data, including the Health Labour Sciences Research Grant studies (2009), showed that the seropositive rate was 17.8% (95/535) with long-term breastfeeding, 3.5% (57/1651) with exclusive formula-feeding, 2.0% (6/304) with short-term breastfeeding, and 3.7% (3/81) with freeze-thawing breast milk. Compared with exclusive formula-feeding, the relative risk for MTCT was 6.04 (95% confidence interval [CI]: 4.3-8.5) with long-term breastfeeding and 0.56 (95% CI: 0.24-1.32) with short-term breastfeeding

	n	number of seropositive children	MTCT rate	95% CI			relative risk	95% CI		
long-term breastfeeding (≧3 months)	535	95	17.8%	14.5%	–	21.0%	6.04	4.28	–	8.53
excluseve formula-feeding	1651	57	3.5%	2.6%	–	4.3%	reference		–	
short-term breastfeeding (<3months)	304	6	2.0%	0.4%	–	3.5%	0.56	0.24	–	1.32
freeze-thawing breast milk	81	3	3.7%	-0.4%	–	7.8%	1.08	0.33	–	3.51

(table).

Conclusions:

There was no significant difference in MTCT rate between exclusive formula-feeding and short-term breastfeeding. HTLV-1-carrier mothers who select short-term breastfeeding may fail to stop breastfeeding, resulting in provision of long-term breastfeeding. Therefore, providing support for mothers is necessary before the age of 3 months.

Systematic Review Registration:

N/A

ESPID19-0177
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Breastfeeding and the risk of hospitalisations for infectious diseases in early childhood: a cohort study

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Background

There is strong evidence that breastfeeding protects infants from infectious diseases in both low/middle- and high-income countries. The World Health Organization recommends that all infants should be breastfed exclusively until six months of age. However, there is a lack of studies examining breastfeeding practices in high-income settings. This study aimed to measure the associations between breastfeeding practices i.e. duration and intensity, and hospitalisations for infectious diseases in children under two year of age, in Uppsala County (Sweden).

Methods

We conducted a register-based cohort study including children born in Uppsala County between 1998 and 2012. The Uppsala Child Health database was combined with the Swedish Medical Birth Register, the National Inpatient Register, the Cause of Death Register, the Total Population Register and the Longitudinal integration database for health insurance and labour market studies. Breastfeeding was classified by duration (<1 week (not breastfeed), <4 months, 4-<6 months, 6-<9 months and ≥9 months) and intensity (exclusive or partial). The outcome was total number of hospital admissions for infectious diseases. Crude and adjusted associations between breastfeeding practices and hospitalisations for infectious diseases, were calculated using Poisson regression models.

Results

We followed 58,540 children until two years of age or censoring. The study included 5086 hospital admissions for infectious diseases. The risk of hospitalisations for infectious diseases decreased with the duration of breastfeeding. For children who were breastfed until 6-<9 months, we found no difference between “exclusive breastfeeding” and “partial breastfeeding with exclusive breastfeeding until 4-<6 months” (table).

Table: Breastfeeding and the risk of hospitalisations for infectious diseases

	Crude IRR (95% CI)		Adjusted* IRR (95% CI)	
Not BF	2.61	(2.06 - 3.32)	2.08	(1.62 - 2.66)
Partial BF<4 MO	1.55	(1.31 - 1.83)	1.42	(1.18 - 1.70)
Exclusive BF<4 MO	1.53	(1.29 - 1.82)	1.39	(1.17 - 1.66)
Partial BF 4-<6 MO	1.48	(1.17 - 1.88)	1.36	(1.05 - 1.76)
Partial BF 4-<6 MO with exclusive BF <4 MO	1.27	(1.01 - 1.61)	1.23	(0.96 - 1.56)
Exclusive BF 4-<6 MO	1.26	(1.02 - 1.57)	1.19	(0.95 - 1.49)
Partial BF 6-<9 MO	1.37	(1.11 - 1.70)	1.25	(0.99 - 1.58)
Partial BF 6-<9 MO with exclusive BF <4 MO	1.33	(1.08 - 1.64)	1.31	(1.06 - 1.63)
Partial BF 6-<9 MO with exclusive BF 4-<6 MO	0.95	(0.82 - 1.10)	0.97	(0.83 - 1.13)
Exclusive BF 6-<9 MO	1	ref	1	ref
BF ≥ 9 mo	0.99	(0.86 - 1.13)	0.96	(0.83 - 1.10)

*Adjusted analyses were adjusted for maternal age, maternal education level, maternal country of birth, maternal smoking, number of previous births, gestational age, small for gestational age, large for gestational age and time trends (year of birth).
BF, breastfeeding. MO, months. IRR, Incidence Rate Ratios. CI, Confidence Interval.

Conclusions

Our results suggest that breastfeeding until at least six months of age with exclusive breastfeeding until at least four months, is associated with a decreased risk of infectious diseases in early childhood.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0066
Science and Educational Track

Oral presentation session 11 - Public health and epidemiology

Disease burden of neonatal invasive group b streptococcus infection in the netherlands

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Background

Group B Streptococcus (GBS) is the leading cause of neonatal sepsis and meningitis worldwide. We aimed to estimate the current burden of neonatal invasive GBS disease in the Netherlands, as a first step in providing an evidence base for policy makers on the potential benefits of a future maternal GBS vaccine.

Methods

We constructed an incidence-based disease progression model informed by literature and expert consultation. Incidence in children age 0-90 days was based on nationwide surveillance data from the Netherlands Reference Laboratory for Bacterial Meningitis. Medical microbiology departments routinely send GBS isolates cultured in blood or cerebrospinal fluid to the reference laboratory. Culture underestimates neonatal GBS disease. We used previous studies to estimate the incidence of proven and probable GBS disease for sensitivity analyses.

Results

The incidence of culture positive neonatal invasive GBS infection in the Netherlands in 2017 was 57 (95% CI 55-59) cases per 100.000 live births. This incidence comprised 15 cases of meningitis and 42 cases of sepsis per 100.00 births, with a mortality of 3.8 per 100.000 live births. Further, an estimated disease burden of 460 DALY (95% CI 380-540) per 100.000 live births was attributable to neonatal invasive GBS infection. In the sensitivity analysis combining proven and probable neonatal GBS disease the estimate for all neonatal invasive GBS increased to 110 (95% CI 100-110) cases and 550 DALY (95% CI 460-650) per 100.000 live births.

Conclusions

Neonatal invasive GBS infection currently causes a substantial disease burden in the Netherlands. However, important evidence gaps are yet to be filled, especially the burden of long-term sequelae after neonatal GBS sepsis. Furthermore, cases of probable GBS sepsis may contribute substantially to this burden potentially preventable by a GBS vaccine.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0934
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Protective antibody levels and timeliness of primary immunizations in preterm infants.

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Background

The Dutch National Immunization program (NIP) schedule currently includes a primary vaccination series at 2-3-4 and a booster at 11 months of age. To examine the influence of a delayed start of immunizations in preterm infants, we compared the timeliness of immunizations with the vaccine induced antibody levels after the primary series.

Methods

In this prospective observational study, preterm infants were recruited and stratified according to gestational age (GA) (< 28, 28-32 and 32-36 weeks). Blood samples were collected at 6 weeks and one month after the primary series. Immunization dates were collected from vaccination certificates and medical data from monthly parental questionnaires and patient records. Serum antibody levels were measured against all vaccine components with multiplex immunoassay using Luminex technology.

Results

In total, 296 preterm infants were enrolled (GA<28: n=87; GA 28-32: n=119; GA 32-36: n=90). Of all infants, 60.1% received their first immunization on time (6-9 weeks after birth). This proportion varied by GA group between 36.7%, 72.8% and 65.1%, respectively.
The proportion with protective antibody levels was high for pertussis, diphtheria and tetanus in all GA groups and did not differ by immunization timeliness (Table).
Insufficient protection (< 80%) was observed for Hib and several pneumococcal serotypes (4, 6B, 18C and 23F) with the lowest levels for GA<28 weeks. Higher antibody levels, for most pneumococcal serotypes, were observed with delayed start of first immunization in infants <28 weeks, but not in older GA

groups.

Table .
Geometric mean concentrations and percentages of protected antibody levels per antigen, per GA group and timeliness of vaccination.

		All GA		< 28 weeks		28-32 weeks		32-36 weeks	
		GMC	% protected	GMC	% protected	GMC	% protected	GMC	% protected
PT	*On time*	63.4	92.2	62.5	95.8	55.5	89.7	78.1	94.2
	Delayed	69.6	94.2	61.8	95.8	66.0	89.7	90.9	96.3
FHA	*On time*	67.0	95.4	65.7	91.3	62.6	93.6	74.8	100
	Delayed	66.1	89.4	65.8	89.6	56.4	86.2	79.1	92.6
Prn	*On time*	89.6	93.5	98.9	95.8	91.2	96.2	83.5	88.5
	Delayed	101.8	96.2	101.1	100	99.1	89.7	106.0	96.3
Diphtheria	*On time*	0.32	89.0	0.37	87.5	0.34	94.9	0.27	80.8
	Delayed	0.43	94.2	0.48	95.8	0.45	96.6	0.35	88.9
Tetanus	*On time*	1.16	96.8	1.31	91.7	1.11	98.7	1.19	96.2
	Delayed	1.28	100.0	1.48	100	1.28	100	0.98	100
Hib	*On time*	0.11	40.3	0.06	25.0	0.10	39.7	0.16	48.1
	Delayed	0.11	38.5	0.09	39.6	0.13	37.9	0.14	37.0
Ps1	*On time*	0.98	82.4	1.38	58.3	0.96	80.8	1.38	96.1
	Delayed	1.02	80.8	0.99	83.3	0.74	79.3	0.99	77.8
Ps4	*On time*	0.77	76.0	0.36	52.0	0.76	74.4	0.46	90.2
	Delayed	0.67	71.2	0.78	79.2	0.58	65.5	0.59	63.0
Ps5	*On time*	1.61	89.5	0.87	79.2	1.65	88.5	2.06	96.1
	Delayed	1.44	91.0	1.95	93.8	1.23	86.2	0.99	77.8
Ps6B	*On time*	0.26	47.7	0.09	25.0	0.30	52.6	0.33	51.0
	Delayed	0.18	41.3	0.24	45.8	0.16	41.4	0.14	33.3
P7F	*On time*	2.15	95.4	1.74	95.8	2.07	93.6	2.52	98.0
	Delayed	2.05	95.0	2.70	97.9	1.57	89.7	1.67	81.5
Ps9V	*On time*	0.97	87.5	0.75	78.3	0.91	83.3	1.18	98.0
	Delayed	1.00	81.7	1.44	85.4	0.74	79.3	0.74	77.8
Ps14	*On time*	2.24	87.5	1.53	78.3	2.08	84.6	2.96	96.1
	Delayed	2.04	82.7	2.30	79.2	2.26	93.1	1.49	77.8
Ps18C	*On time*	0.67	68.4	0.48	65.2	0.58	64.4	0.98	74.5
	Delayed	0.57	61.5	0.78	66.7	0.49	55.2	0.39	59.3
Ps19F	*On time*	2.17	90.1	1.66	91.3	2.18	89.7	2.45	90.2
	Delayed	2.05	83.7	2.64	89.6	2.19	86.2	1.22	70.4
Ps23F	*On time*	0.38	56.6	0.25	43.5	0.38	53.8	0.48	66.7
	Delayed	0.32	53.8	0.41	56.3	0.29	85.6	0.23	44.4

Legend: Yellow boxes indicates protective antibody levels < 80%

Conclusions

These findings indicate that premature infants are insufficiently protected for multiple, in particular conjugated, vaccine components. Overall, limited differences in protective antibody levels were observed between the three GA groups. The role of timing of immunizations in antibody responses needs further exploration.

Clinical Trial Registration (Please input N/A if not registered)

NTR 7340

ESPID19-0869
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Safety and immunogenicity of an investigational quadrivalent meningococcal conjugate vaccine (menacyw-tt) when co-administered with other vaccines in healthy adolescents

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Background

MenACYW-TT is an investigational quadrivalent meningococcal conjugate vaccine intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT compared to a licensed quadrivalent conjugate meningococcal vaccine (Menveo®; MCV4-CRM) and when co-administered with tetanus, diphtheria, acellular pertussis (Tdap) and human papilloma virus (HPV4) vaccines in healthy meningococcal vaccine naïve adolescents (10-17 years of age) in USA.

Methods

In a pivotal Phase II study, 1715 subjects randomly received MenACYW-TT; MCV4-CRM; MenACYW-TT co-administered with Tdap and HPV4; or Tdap and HPV4 vaccines. Serum bactericidal assays with human (hSBA) and baby rabbit (rSBA) complement were used to measure antibodies against representative serogroup strains. Safety data were collected up to six months post-vaccination.

Results

Non-inferiority of immune response, based on percentages of participants achieving hSBA vaccine seroresponse at Day 30 from D0 baseline, was demonstrated for MenACYW-TT vs MCV4-CRM; and MenACYW-TT co-administered with Tdap and HPV4 vaccines vs when administered alone,. The proportions of individuals with hSBA ≥ 1:8 after MenACYW-TT administration were higher than those after MCV4-CRM administration for all serogroups (A: 93.5% vs 82.8%; C: 98.5% vs 76.0%; W: 99.1% vs 90.7%; Y: 97.2% vs 83.2%). Co-administration of MenACYW-TT, Tdap and HPV4 vaccines did not generate evidence suggestive of clinically significant interference. The safety profiles of MenACYW-TT and MCV4-CRM; and Tdap and HPV4 vaccines (administered with or without MenACYW-TT) were comparable. There were no vaccine related serious adverse events.

Conclusions

MenACYW-TT vaccine was well tolerated and generated an immune response that was non-inferior to the licensed MCV4-CRM vaccine. The immunogenicity and safety profiles were comparable when vaccine was administered with or without Tdap and HPV vaccines in meningococcal vaccine naïve adolescents.

Clinical Trial Registration (Please input N/A if not registered)

NCT# 02199691

ESPID19-0849
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Safety of typhoid conjugate vaccine in nepal:preliminary results from a randomized control trial

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Background

Enteric fever caused by *Salmonella enterica* serovar Typhi is a major public health problem in developing countries, which could be controlled through widespread deployment of typhoid conjugate vaccine (TCV). Vaccine safety and tolerability is an important consideration in vaccine rollout. The recently WHO-prequalified TCV has been reported to be safe in infants, young children and adults in trials in India, though data remain limited.

Methods

A randomised controlled trial is underway in Nepal to assess safety and efficacy of TCV in children from 9 months to 15 years of age, in which participants were randomised 1:1 to TCV or a capsular group A meningococcal vaccine. Telephone follow-up seven days after vaccination was conducted to solicit local and systemic reactions in all participants. All serious adverse events (SAE) were assessed in person, when feasible, or via phone call, recorded in CRFs and reported by the local study paediatrician.

Results

20,019 children were randomised and vaccinated. In the seven days post-vaccination, fevers occurred in 7.8% of under-5s and 4.2% of children 5-15 years. 6% of children felt pain at vaccination, 0.8% experienced swelling and 0.2% redness. Few children experienced system reactions, the most common being nausea (1.4%) and diarrhoea (1.8%).

Within one month of vaccination 17 participants experienced 18 SAEs; the most common being pyrexia, pneumonia, and febrile convulsions. One SAE was identified as vaccine-related; a participant developed high-grade fever within 24 hours of vaccination and required hospital admission.

Conclusions

The unblinded data show that TCV and the control vaccine were well tolerated, and an interim unblinded analysis is in preparation. This safety data supports the usage of TCV in populations where *Salmonella* Typhi remains problematic.

Clinical Trial Registration (Please input N/A if not registered)

ISRCTN43385161

ESPID19-0808
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Reactogenicity and safety of 2 or 3 doses of takeda's bivalent virus-like particle (vlp) norovirus vaccine (nov) in infants

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Background

Acute gastroenteritis due to norovirus infection can have severe consequences in very young children. Takeda's bivalent vaccine candidate (NoV) has been shown to be safe and well tolerated in recipients from 6 months to 100 years of age; we assessed tolerability of two or three doses in infants aged 6 week to 6 month-old.

Methods

In this phase 2 dose-finding study in Colombia and Panama , 359 children were randomized to eight groups to receive two (n = 180) or three (n = 179) intramuscular doses of NoV containing 15/15, 15/50, 50/50, or 50/150 µg GI.1/GII.4c genotype VLPs and 0.5 mg $Al(OH)_3$. Doses 1 and 2 were given on Days 1 and 56, dose 3 or saline placebo on Day 112. Parents recorded solicited adverse events (AEs) for 7 days and any unsolicited AEs for 28 days following each dose, and serious adverse event (SAE) throughout the study.

Results

There were no deaths or vaccine-related SAEs or withdrawals. Generally mild-to-moderate AEs were reported after 51% and 41% of first- and second-dose recipients, rates after the third dose being similar in vaccinees (30%) and placebo-recipients (32%). Overall, the most frequent local reaction was pain in ≤24% of vaccinees, while irritability (≤29%) and drowsiness (≤23%) were the most frequent systemic AEs. Rates did not increase with subsequent doses nor with the increasing dosages of VLP used. Unsolicited AEs mainly consisted of typical mild-to-moderate AEs and only two severe AEs, neither of which lead to withdrawal.

Conclusions

All NoV candidates were well tolerated with clinically acceptable reactogenicity profiles in infants aged 6 weeks to 6 months, irrespective of VLP dosage supporting the further clinical exploration of this vaccine candidate.

Clinical Trial Registration (Please input N/A if not registered)

Clinical Trial Registration (clinicaltrials.gov: NCT02153112; EudraCT: 2014-000778-20)

ESPID19-0794
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Immunogenicity of takeda's bivalent virus-like particle (vlp) norovirus vaccine (nov) in young infants

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Background

Norovirus infection can cause frequent diarrhoeal episodes with dehydration, hospitalisations and fatalities in very young children. We assessed the immunogenicity of 2 or 3 doses of investigational Takeda bivalent NoV candidate formulations in Colombian and Panamanian children aged 6 weeks to 6 months.

Methods

This was a double-blind, randomised, phase 2 dose-finding study of NoV formulations with 15/15, 15/50, 50/50 or 50/150 µg dosages of GI.1/GII.4c genotype VLPs and 0.5 mg $Al(OH)_3$. Two groups aged 3.1 ± 1.3 months (Mean ± SD, n = 180) or 3.0 ± 1.4 months (n = 179) received either two or three intramuscular doses, respectively, of the different formulations on Days 1, 56 and 112; the two-dose groups received saline placebo as dose three. Antibody responses to each VLP were measured on days 56, 84 and 140 as functional histo-blood group binding antigen blocking antibodies (HBGA), expressed as seroresponse rate (≥ 4-fold increase over baseline, SRR), and geometric mean titres (GMT).

Results

On Day 1 88% and 58% of children were seronegative for HBGA against GI.1 and GII.4c, respectively. There were HBGA responses against GI.1 across all formulation groups 56 days after one dose (SRR: 35–52%), which increased significantly at 84 days after a second dose (SRR: 88–96%). SRR for GII.4c were 12–18% and 40–61% after doses 1 and 2, respectively. At Day 140 HBGA GMTs in 2-dose groups declined against GI.1 and had plateaued against GII.4c, but were further increased against both antigens in all 3-dose groups.

Conclusions

In young infants aged 6 weeks to 6 months, high HBGA antibody responses were observed after two vaccinations 8 weeks apart, and further increased by a third vaccination 8 weeks later.

Clinical Trial Registration (Please input N/A if not registered)

Clinical Trial Registration (clinicaltrials.gov: NCT02153112; EudraCT: 2014-000778-20)

ESPID19-0403
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

A recombinant lipoprotein of zika virus induced anti-zika immune responses

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Background

Zika virus is a RNA virus belongs to Flaviviridae family closely related to dengue, yellow fever and West Nile viruses. Recently, the rapid spread of Zika virus in tropical and subtropical areas has become great concerns for public health.

Methods

Currently, specific treatments to cure Zika virus infection or approved vaccines to prevent Zika virus infection are unavailable. Therefore, development of therapeutic agents or vaccines against Zika virus is very important. The objective of this report is to develop Zika subunit vaccine using recombinant lipoprotein technology. We lipidated Zika virus envelope protein domain three (rlipo-ZIKE3) by *E.coli* expression system.

Results

The lipidated protein can activate dendritic cells through Toll-like receptor (TLR) 2 but not non-lipidated protein. The co-stimulatory molecule CD80, CD40 could be up-regulated after treatment with lipidated protein. Accordingly, the TNF-αand IL-6 secretion were increased in the lipidated protein-treated dendritic cells. After immunization with mouse, the sera of lipidated protein rlipo-ZIKE3 immunization can neutralize the Zika virus infection but not non-lipidated protein rZIKE3. Furthermore, we found that lipidated protein immunization can prolong mice survival after Zika virus challenge.

Conclusions

These results suggested that the lipidated protein rlipo-ZIKE3 is a potential vaccine candidate.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0195
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Immunization with skp delivered on outer membrane vesicles protects mice against enterotoxigenic escherichia coli challenge

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Background

Outer membrane vesicles (OMVs) are promising vaccine components because they combine antigen and adjuvant in a single formulation. Detoxified Salmonella enterica strains that express penta-acylated lipid A retain OMV immunogenicity but with reduced reactogenicity. We have previously shown that a recombinant form of the enterotoxigenic *Escherichia coli* (ETEC) seventeen kilodalton protein (Skp) protects mice in a pulmonary challenge model, when fused to the glutathione-S-transferase (GST) epitope and combined with cholera toxin.

Methods

Here we compared directly the efficacy of expressing Skp in detoxified Salmonella OMVs to GST-Skp for their ability to protect mice against ETEC challenge.

Results

We observed that the display of Skp on OMVs, in the absence of exogenous adjuvant, protects the mice as well as the recombinant GST-Skp with adjuvant, showing that we can achieve protection when antigen and adjuvant are administered as a single formulation.

Conclusions

Collectively, these data demonstrate the utility of using OMVs for the expression and display of antigens for use in vaccine development and validate previously published work demonstrating that immunization with Skp is efficacious in protecting mice against ETEC challenge.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0153
Science and Educational Track

Oral presentation session 12 - Vaccine development and immunogenicity

Recombinant lipidated dengue envelope protein domain iii induces robust immune responses and reduces antibody-dependent enhancement risks

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Background

Dengue virus is a mosquito-transmitted virus that can cause self-limiting dengue fever, severe life-threatening dengue hemorrhagic fever and dengue shock syndrome. The existence of four serotypes of dengue virus has complicated the development of an effective and safe dengue vaccine. Currently, there is no effective vaccine to provide full protection against four serotypes of dengue virus for children. New approaches to dengue vaccine development are urgently needed. Our approach represents a promising method of dengue vaccine development.

Methods

Two important components of a vaccine, the immunogen and immunopotentiator, were combined into a single construct to generate a new generation of vaccines. In this study, dengue-2 envelope protein domain III (D2ED III) was used as the vaccine candidate. Recombinant D2ED III and recombinant lipidated D2ED III (LD2ED III) were prepared from an *Escherichia coli*-based system. The immune responses and protective efficacy induced by LD2ED III were evaluated in mice.

Results

The formulation containing lipidated D2ED III (LD2ED III) in the absence of exogenous adjuvant elicited higher D2ED III-specific antibody responses than those obtained from its nonlipidated counterpart, D2ED III, and dengue-2 virus. In addition, the avidity and neutralizing capacity of the antibodies induced by LD2ED III were higher than those elicited by D2ED III and dengue-2 virus. Importantly, we showed that after lipidation, the subunit candidate LD2ED III exhibited increased immunogenicity while reducing the potential risk of antibody-dependent enhancement of infection in mice.

Conclusions

Our study suggests that the lipidated subunit vaccine approach could be applied to other serotypes of dengue virus and other pathogens.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0959
Science Track

ESCMID/ESPID Joint symposium 05 - Novelties in diagnostic microbiology in paediatrics

Performance of quantiferon-tb plus in the diagnosis of tuberculosis infection in children

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Background

QuantiFERON-TB Gold Plus (QTF-Plus) is a new generation assay that measures IFN-γ produced by CD4+ and CD8+ T-cells in response to *M. tuberculosis* antigens. This test has never been evaluated in a pediatric population to date.

Methods

We prospectively enrolled children assessed for TB by QTF-Plus from February 2017 to July 2018. Children with latent tuberculosis (LTBI) were divided in two groups: recent close contacts of an active TB case (C-LTBI) and adopted/immigrated children (S-LTBI). C-LTBI were considered to have a recent TB infection, while S-LTBI group a long-lasting infection. Descriptive statistics, Mann-Whitney U test and Cohen's kappa coefficient were used for analysis.

Results

Overall, 713 children were evaluated. Children were diagnosed as uninfected (n=585), LTBI (n=105) and active TB (n=23). There was an agreement between TB1 and TB2 in active TB, while two positive results only in TB2 were found in LTBI. Sensitivity and specificity of QTF-Plus for active TB were 91,3% and 100%, respectively. Statistically significant difference (p<0,001) was found between IFN-γ median values of active TB [TB1: 2,86 IU/ml (IQR 1,19-9,45); TB2: 2,96 IU/ml (IQR 1,34-10,06)] *vs* LTBI [TB1: 0,03 IU/ml (IQR 0-1,52); TB2: 0,02 IU/ml (IQR 0-1,36)] groups. Furthermore, there was a significant difference (p<0,001) between median concentrations measured in C-LTBI *vs* S-LTBI.

Conclusions

Sensitivity and specificity of QTF-Plus in diagnosing active TB in children were similar to those previously reported for QTF-GIT and for QTF-Plus in adults, showing a good performance of the test in children. The finding of two children with LTBI only TB2 responders, suggests that QTF-Plus could be more sensitive in diagnosing LTBI in children. Our results suggest a possible use of QTF-Plus in differentiating between LTBI and active TB and in discriminating recent infections.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0853
Science Track

ESCMID/ESPID Joint symposium 05 - Novelties in diagnostic microbiology in paediatrics

Molecular antimicrobial resistance surveillance for gram negative bacteria in a pediatric intensive care unit (picu)

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Background and Aims:

Antimicrobial drug resistance is recognized as one of the most important global public health concerns. Infections caused by highly resistant bacteria (HRB) in pediatric patients significantly increase morbidity, mortality rates and costs allocated to healthcare systems. The aim of this project was to develop high clinical value molecular diagnostics directly to clinical samples as a tool for active surveillance of antimicrobial resistance in a PICU endemic for HRB.

Methods:

This study was conducted in an 8-bed pediatric intensive care unit (PICU), located in a tertiary level general hospital. Patients hospitalized for at least 7 days were included. Stool samples were collected between July and December 2018 and stored at -80oC until processed. The burden of resistance to antibiotics was assessed using PCR following DNA isolation directly from stool samples. The presence of four carbapenemases: *blaKPC*, *blaOXA-48*, *blaVIM*, and *blaNDM* as well as of *blaTEM* and *blaSHV* were evaluated.

Results:

A total of 39 patients were admitted. Stool samples were processed from 25 patients (64%). In sixteen of the 25 patients (64%), at least one carbapenemase was detected: 7 patients carried blaKPC gene, 3 *blaVIM* and 6 both *blaKPC* and *blaVIM*. *blaOXA-48* and *blaNDM* were not detected. The *blaTEM* was detected in 15 patients and half of them co-carried *blaVIM* and *blaKPC*. The *blaSHV* was detected in 7 patients, four of them co-carried *blaKPC* and *blaVIM*.

Conclusions:

Implementation of a targeted and customized rapid molecular detection assay directly to clinical samples was efficient to detect the burden of bacterial resistance in this clinical setting endemic to highly resistant bacteria. These results are part of a multidisciplinary research to integrate methodologies and develop efficient strategies to combat antimicrobial resistance.

Systematic Review Registration:

N/A

ESPID19-0802
Science Track

ESCMID/ESPID Joint symposium 05 - Novelties in diagnostic microbiology in paediatrics

Do host genetics determine disease phenotype and outcome from ebola virus disease?

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Background

The West African Ebola epidemic of 2013-2016 was the largest Ebola epidemic in history. The epidemic highlighted the varying clinical phenotypes of Ebola virus disease (EVD); from those who were exposed, infected and died a catastrophic death, to those who were highly exposed yet remained asymptomatic. We sought to understand whether host genetic differences contributed to outcome from EVD.

Methods

A cross sectional study conducted in 32 community regions of Sierra Leone, 2529 participants were recruited from affected communities. This constituted 1021 household contacts, 1004 community controls and 504 Ebola survivors. Participants provided a saliva sample for DNA analysis and an oral fluid sample for serology. A detailed questionnaire was completed, including a risk exposure stratification. Furthermore 242 samples from deceased patients and 77 samples from surviving patients were obtained through the Ministry of Health and Sanitation-Public Health England Ebola biobank. DNA was extracted from all samples, and 2153 samples were genotyped using the Illumina H3 Africa array, 250 of these samples also underwent whole exome sequencing. Anti-EBOV IgG antibodies were identified using the Kalon Diagnostics Ltd EBOV IgG Enzyme Immuno-sorbent Assay.

Results

Analysis of the genomic data is currently being conducted, formal results will be available from March 2019. Case studies of communities in Sierra Leone, alongside serological results, reveal several distinct disease phenotypes described in the table below. Children demonstrated some of the most discrete phenotypes.

	Category	Exposed	PCR status	Anti-EBOV IgG	Symptomatic (case definition)	Outcome
1	Exposed uninfected	Yes	Not tested	Negative	No	Alive
2	Exposed infected	Yes	Not tested	Positive	No	Alive
3	Ebola survivor	Yes	Positive	Positive	Yes	Alive
4	Ebola deceased	Yes	Positive	Not tested	Yes	Deceased
5	Control	No	Not tested	Negative	No	Alive

Conclusions

Early data indicate that a host genetic predisposition to outcome from infection with Ebola virus is likely. Two mechanisms are proposed; a rarer trait providing protection from infection, and a more common immune mediated mechanism that reduces the chance of an infected patient suffering a severe disease process with a negative outcome.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESPID19-0324
Science Track

ESCMID/ESPID Joint symposium 05 - Novelties in diagnostic microbiology in paediatrics

Targeted metagenomic sequencing of respiratory syncytial virus: a comprehensive method for studying viral genomics and beyond

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Background

We conducted a pilot study to validate the performance of target enrichment in sequencing respiratory syncytial virus (RSV) directly from paediatric nasopharyngeal swabs collected in the European Commission Innovative Medicines Initiative REspiratory Syncytial virus Consortium in EUrope (RESCEU) clinical studies, which are investigating the virological and immunological features of RSV infection using various samples.

Methods

RSV-positive swabs from participants <1-year-old were used to construct sequencing libraries following the published veSEQ-HIV protocol. Target enrichment was performed using an in-house probe panel, targeting >100 bacterial and viral pathogens, including RSV. Sequencing was performed on the Illumina MiSeq platform, generating 265-bp paired-end reads. Following taxonomic classification with Kraken 2, complete RSV genomes were reconstructed with *shiver*. RAxML was used for phylogenetic inference.

Results

17 samples were sequenced. The complete RSV genome was recovered in 13 samples, 50% of the genome in 2, and <10% of the genome in the other 2. The samples for which whole-genome reconstruction was not successful had a viral load $<2\times10^3$ copies/mL. Viral loads were positively correlated with RSV read counts ($R^2=0.64$, $p<0.001$). 4 strains were classified as RSV subgroup A (genotype ON1) and 13 were RSV subgroup B (genotype BA9). In addition to RSV, we identified a significant number (>20,000) of reads classified as *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* in 8, 4, and 1 samples, respectively.

Conclusions

These preliminary data suggest that targeted metagenomic sequencing is feasible for use in diagnostics (e.g., quantification, genotyping, co-detection of other pathogens), epidemiological (e.g., phylogeny, transmission dynamics), and virological studies (e.g., strain variation, evolution dynamics). We will apply this method in the ongoing RESCEU studies to evaluate the molecular epidemiology of RSV and genomic factors associated with severe RSV infection.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT03627572, NCT03756766

ESPID19-0654
Science Track

ESID/ESPID Joint symposium 12 - Infections which define immune responses - or the other way around?

Disseminated bacillus-calmette-guerin infection and primary immunodeficiency disorders: a 15-year retrospective review

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Background

Disseminated Bacillus Calmette-Guérin (BCG) disease (BCGosis) can occur in patients with primary immune deficiency disorders (PIDs). They often present with non-specific symptoms, and with hard-to-treat multi-focal sites of dissemination. We present a 15-year retrospective review of patients admitted to KK Hospital in Singapore, from 2003 to 2018.

Case Presentation Summary

18 patients were identified, mostly male (13, 72.2%). The median age of first presentation was 5.5 (range 0.5–74) months. The underlying diagnoses of PIDs included Mendelian Susceptibility to Mycobacterial Diseases (MSMD) (due to IL-12R or IFNgR1 defects, or STAT1 loss-of-function mutation) (8, 44.4%), Severe Combined Immunodeficiency (SCID) (7, 38.9%), Chronic Granulomatous Disease (CGD) (1, 5.6%), Anhydrotic Ectodermal Dysplasia with Primary Immunodeficiency (EDA-ID) (1, 5.6%), and undefined innate immunity defect (1, 5.6%). Sites of microbiologically-confirmed BCGosis were cutaneous (9, 50.0%), musculoskeletal (7, 38.8%), lymph nodes (6, 33.3%), blood (5, 27.8%), spleen (5, 27.8%), liver (3, 16.7%), bone marrow (3, 16.7%), central nervous system (2, 11.1%), intra-abdominal (2, 11.1%), and pulmonary (1, 5.6%). All received a three- or four-drugs first-line therapy (combination of Rifampicin, Ethambutol, together with Aminoglycosides, Quinolones or Isoniazid) for a median of 14 (range 4*–25) months. 3 patients required second-line therapy, which included a combination of Ethionamide, Cycloserine, Para-aminosalicylic acid (PAS), Moxifloxacin, or Linezolid. 18 patients (44.4%; 5 SCID, 1 CGD, 1 EDA-ID, 1 undefined innate immunity defect) underwent stem cell transplant, of which 6 (75%) are doing well. 5 died (27.8%), of which 2 were due to BCGosis, and both (1: MSMD with STAT1 loss-of-function, 1: SCID) did not receive stem cell transplant.

Learning Points/Discussion

Disseminated BCG disease (BCGosis) should prompt further immunology evaluation to determine the diagnosis and severity of the immune defect. Stem cell transplant should be considered for severe immunodeficiency.

ESPID19-0321
Science Track

ESID/ESPID Joint symposium 12 - Infections which define immune responses - or the other way around?

Diagnosis of tuberculosis disease in immunocompromised children – a multi-centre paediatric tuberculosis network european trials group (ptbnet) study

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Background

The number of immunocompromised children in Europe is expanding, due to greater survival of children with chronic conditions and increasing use of immunosuppressive agents. The diagnosis of tuberculosis (TB) in this patient group is often challenging, potentially resulting in delayed treatment and poorer outcomes. This study aimed to describe the clinical features at presentation and to assess the performance of immune-based and microbiological tests in immunocompromised children with TB.

Methods

We collected cases of active TB in children with immunocompromise at 27 European centres retrospectively from 2000 to 2017. Each case was age- and sex-matched to 2 previously healthy children with active TB, considered controls. Data were collected in the ptbnet database using a secure web-based instrument (REDCap). Descriptive statistics, chi-square and Mann-Whitney-U tests were used for analysis.

Results

Sixty-two immunocompromised children (20 HIV-infected, 19 drug-induced, 4 primary immunodeficiency, 19 other conditions) and 124 controls were included. Immunocompromised children presented more frequently extrapulmonary TB (36.2% vs. 22.8%; p=0.04). The comparison of immunocompromised children versus controls (Table 1) showed significant differences in i) clinical presentation [fever, p=0.004; respiratory distress, p=0.02; low BMI, p=0.002; weight loss, p=0.003; headache, p=0.003; hepatosplenomegaly, p=0.0001], ii) tuberculin skin test (TST) diameter (p=0.02), and iii) QuantiFERON-TB negative results (12.7% controls vs. 37.5% immunocompromised cases; p=0.02). Compared to controls, children receiving immunosuppressive drugs had a significantly higher proportion of false-negative TST results (5mm cutoff) (4.9% vs. 41.7%, p=0.001), and a non-significantly higher rate of microbiological confirmation (45.9% vs. 61.1%, p=0.23).

Table 1. Baseline characteristics, presenting features and diagnostic test performance in immunocompromised children with TB

	Controls Previously healthy children (n=124)	Cases Immunocompromised children (n=62)	p
Sex (female)	66 (53.2)	33 (53.2)	1.00
Age (median (IQR)	8.1[4.0-13.8]	9.9 [6.8-12.7]	.16
Reason for consultation			
Contact tracing	52 (42.6)	11 (18.3)	.001
Migrant screening	3 (2.5)	3 (5.1)	.36
Clinical signs/symptoms consistent with TB	64 (52.5)	46 (74.2)	.004
TB screening before biological agents	0 (0)	1 (3.7)	.29
Screening for suspected immunocompromise	0 (0)	8 (29.6)	.0001
Other	14 (11.5)	5 (8.5)	.37
Extrapulmonary TB	26 (22.8)	21 (36.2)	.04
Clinical features at presentation	17.0 [15.2-20.6]	15.5 [14.1-17.3]	.002
BMI (median (IQR)	45 (37.2)	37 (59.7)	.004
Fever	55 (45.1)	26 (42.6)	.44
Cough	11 (9.0)	13 (21.3)	.02
Respiratory distress	24 (19.8)	24 (40.7)	.003
Weight loss	34 (28.6)	24 (40.0)	.12
Malaise	2 (4.7)	4 (16.7)	.09
Vomiting	3 (2.5)	8 (14.0)	.003
Headache	4 (3.3)	9 (15.5)	.006
Lethargy	0	1 (3.6)	.30
Other CNS symptoms	7 (10.6)	9 (30.0)	.02
Other gastrointestinal symptoms	3 (2.5)	13 (21.0)	.0001
Hepatomegaly	5 (4.1)	12 (19.4)	.001
Splenomegaly			
TST (median (IQR)	15.0 [12.0-20]	14.0 [2.5-19.0]	.02
<5 mm	5/103 (4.9)	10/37 (27.0)	
5-10 mm	13/103 (12.6)	4/37 (10.8)	
>10mm	85/103 (82.5)	23/37 (62.2)	.01
QTF*			
Negative	9/71 (12.7)	10/28 (37.5)	
Indeterminate	2/71 (2.8)	0/28 (0)	
Positive	60/71 (84.5)	18/28 (64.3)	.02
TB confirmation (by culture or PCR)	51/111 (45.9)	31/58 (53.4)	.22
***M. tuberculosis* culture positive**	42/111 (37.8)	27/58 (46.6)	.17
***M. tuberculosis* PCR positive**	22/111 (19.8)	17/58 (29.3)	.12

All data are represented in n (%) unless stated otherwise
Abbreviations: BMI = body mass Index, CNS = central nervous system, IQR = interquartile range, PCR = Polymerase Chain Reaction, QFT = QuantiFERON-TB Gold assay, TB = tuberculosis, TST = tuberculin skin test.

Conclusions

Existing immune-based TB tests have suboptimal sensitivity in immunocompromised children, but microbiological tests have similar confirmation rate compared to immunocompetent children. Tests with better performance characteristics are needed to enable early diagnosis and treatment in this high-risk population.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0283
Science Track

ESID/ESPID Joint symposium 12 - Infections which define immune responses - or the other way around?

Waning immunity against streptococcus pneumoniae, pertussis, and tetanus in children treated for acute lymphoblastic leukemia: a canadian immunization research network study

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Background

Children with acute lymphoblastic leukemia (ALL) require prolonged immunosuppressive chemotherapy, which may affect immunity to previously received vaccinations. Immunization recommendations post-chemotherapy vary across jurisdictions worldwide. We compared immunity to *S. pneumoniae*, tetanus and pertussis among previously vaccinated children who had completed chemotherapy for ALL and immunocompetent children.

Methods

We conducted a multi-center trial of children with ALL 6-12 months post-chemotherapy completion. We excluded children with infant ALL, relapsed ALL, and stem cell transplant recipients. Controls with no history of immunocompromising conditions were matched 1:1 to ALL participants by age +/- 6 months at blood collection. We measured IgG levels to pneumococcal conjugate vaccine (PCV) serotypes, pertussis toxin (PT), and tetanus toxoid. We compared geometric mean concentrations (GMCs) between ALL participants and controls using linear random effects models.

Results

Seventy participants with ALL and 70 matched controls were included in the analysis. Before enrollment, 51% and 32% of ALL participants had received 4 and ≥5 doses of DTaP-containing vaccines, respectively versus 24% and 53% of controls (p<0.001); 60% of ALL participants and 53% of controls had received ≥3 doses of PCV7 or PCV13 (p=0.02). Serology results are shown below.

	Subjects with ALL		Controls	
	GMC	**95% Confidence Interval**	**GMC**	**95% CI**
Pneumococcal Serotype (mg/ml)				
6B	0.4	0.3-0.5	1.3	1.0-1.7
7F	0.3	0.2-0.3	0.7	0.6-0.9

	Subjects with ALL		Controls	
9V	0.5	0.4-0.6	0.9	0.8-1.2
14	0.5	0.3-0.6	1.7	1.2-2.5
18C	0.2	0.2-0.3	0.5	0.4-0.7
19F	1.0	0.8-1.2	3.3	2.8-3.9
23F	0.3	0.2-0.4	1.2	0.9-1.6
Pertussis toxin (IU/ml)	4.1	3.7-4.6	10.3	8.1-13.2
Tetanus toxoid (IU/ml)	0.2	0.1-0.2	1.7	1.3-2.4

Conclusions

Children who completed chemotherapy for ALL had lower vaccine immunity against *S. pneumoniae*, pertussis and tetanus than immunocompetent children. Children with ALL would benefit from systematic booster immunizations after chemotherapy.

Clinical Trial Registration (Please input N/A if not registered)

NCT02447718

ESPID19-0200
Science Track

ESID/ESPID Joint symposium 12 - Infections which define immune responses - or the other way around?

Studies into the mechanism of measles-associated immune suppression during a measles outbreak in the netherlands

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Background

Measles causes a transient immune suppression, leading to increased susceptibility to opportunistic infections. Measles virus (MV) infection of immune cells is facilitated by the cellular receptor CD150. In experimentally infected non-human primates, MV infects and depletes $CD150^+$ memory lymphocytes. Based on this finding, we postulated the 'immune amnesia' model to explain the mechanism of measles immune suppression. A measles outbreak in the Dutch Orthodox Protestant community in 2013 provided a unique opportunity to test this hypothesis in unvaccinated children.

Methods

We performed an observational cohort study and enrolled more than 100 unvaccinated children before or early after MV infection. To determine levels of virus shedding and phenotypes of MV-infected cells (Cohort A), nose and throat swabs and blood samples were collected from patients with clinical signs of prodromal measles. To determine whether lymphocyte populations were depleted after measles (Cohort B), we collected paired blood samples from healthy children before and after measles.

Results

In Cohort A, we found that virus was shed more efficiently in the nose than in the throat. In the PBMC, we detected MV-infected memory $CD4^+$ T, $CD8^+$ T and B cells. In Cohort B, we found reduced frequencies of circulating memory B cells and increased frequencies of regulatory T and transitional B cells after measles.

Conclusions

We show that measles viraemia in prodromal measles patients is largely mediated by MV-infected memory lymphocytes. Measles had a lasting impact on circulating lymphocyte subsets after recovery from the disease. These data support our immune amnesia hypothesis and offer an explanation for the previously observed long-term effects of measles on host resistance.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0400
Science Track

ESPID Plenary symposium 04 - New research approaches in the study of infectious diseases in children

Application of microsampling to facilitate clinical pharmacokinetic studies of antibiotics in critically ill paediatric patients

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Background

Performing clinical studies can be challenging in critically ill neonates, infants and children due to the burden of blood sampling. Innovation in the quantitative analysis of clinical samples, led by improved sensitivity of methods such as LC-MS/MS, has enabled the reduction of blood sample volumes to less than 0.05 mL or 'microsamples'. These samples can potentially be acquired from a finger or heel prick.

Methods

We assessed the suitability of implementing microsampling for clinical pharmacokinetic studies by performing a two-stage investigation: an *ex-vivo* validation and a clinical bridging study, in accordance with international regulatory agency guidelines. Plasma from critically-ill adult patients receiving vancomycin or piperacillin-tazobactam was collected as both a traditional liquid sample from an arteriovenous catheter and as a capillary liquid plasma sample from a finger-prick. Samples of plasma were extracted and analysed for vancomycin or piperacillin-tazobactam concentrations using a Shimadzu LC-MSMS 8030+[1,2].

[1] Parker (2017) Bioanalysis 9(12): 911-924
[2] Naicker (2018) J Pharm Biomed Anal 148: 324–333

Results

Bioanalytical validation testing met acceptance criteria for linearity, accuracy and precision. Stability, selectivity and matrix effects testing were within acceptance criteria. Figure 1 shows a Bland-Altman plot for the comparison between peripheral and arterial plasma for (a) vancomycin and (b) piperacillin-tazobactam concentrations for critically ill patients. The results of peripheral and arterial plasma met acceptance criteria as an incurred sample reanalysis test.

Conclusions

The bioanalytical validation found our methods were suitable for measuring vancomycin or piperacillin-tazobactam concentrations in microsamples of liquid plasma. The clinical bridging study found samples collected using peripheral capillary sampling were a valid alternative to samples collected from an arterial line. Based on the results of this research, a clinical pharmacokinetic study using microsampling is underway at the Queensland Children's Hospital.

Clinical Trial Registration (Please input N/A if not registered)

ACTRN12618001469202

ESPID19-0238
Science Track

ESPID Plenary symposium 04 - New research approaches in the study of infectious diseases in children

Caesarean section is associated with increased risk of infection-related hospitalisation in childhood: a data linkage study of 7.3 million births from four countries

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Background and Aims:

The striking individual differences in the severity of childhood infections are poorly understood. The postnatal microbiome, which varies with mode of delivery, is important for the development of early immune responses. Limited data suggest caesarean section (CS) is associated with increased infection-related hospitalisation (IRH). We investigated the relationship between mode of delivery and subsequent childhood IRH.

Methods:

We conducted a multi-country population-based cohort study of all singleton live births from 1996-2015 using record-linked birth registry and hospitalisation data from Australia (NSW and WA), England, Scotland and Denmark. Mode of delivery was categorised as vaginal or CS (emergency/elective) and by premature rupture of membranes (PROM). We defined IRH (overall, by clinical type) as a recorded relevant primary / secondary ICD-10 diagnosis code for a child aged <5 years. Analysis was conducted using Cox regression models for recurrent events, adjusting for maternal factors, birth parameters and socio-economic status, and results pooled using meta-analysis.

Results:

Overall, 7.29 million children were included, of whom 1.55 million (21.3%) had at least one IRH. On average one-quarter (18-29%) of deliveries were by CS, of which half (39-57%) were elective. Caesarean section was associated with increased risk for IRH compared to vaginal delivery (hazard ratio, HR 1.10, 95%CI 1.09-1.10), and the risk of IRH was higher following elective CS (Figure). The HR for overall IRH

was 1.18 (1.10-1.28) following elective CS delivery with PROM. For specific infection groups, the HR was 1.26 (1.16-1.37) for lower respiratory infection and 1.38 (1.06-1.79) for gastrointestinal infection.

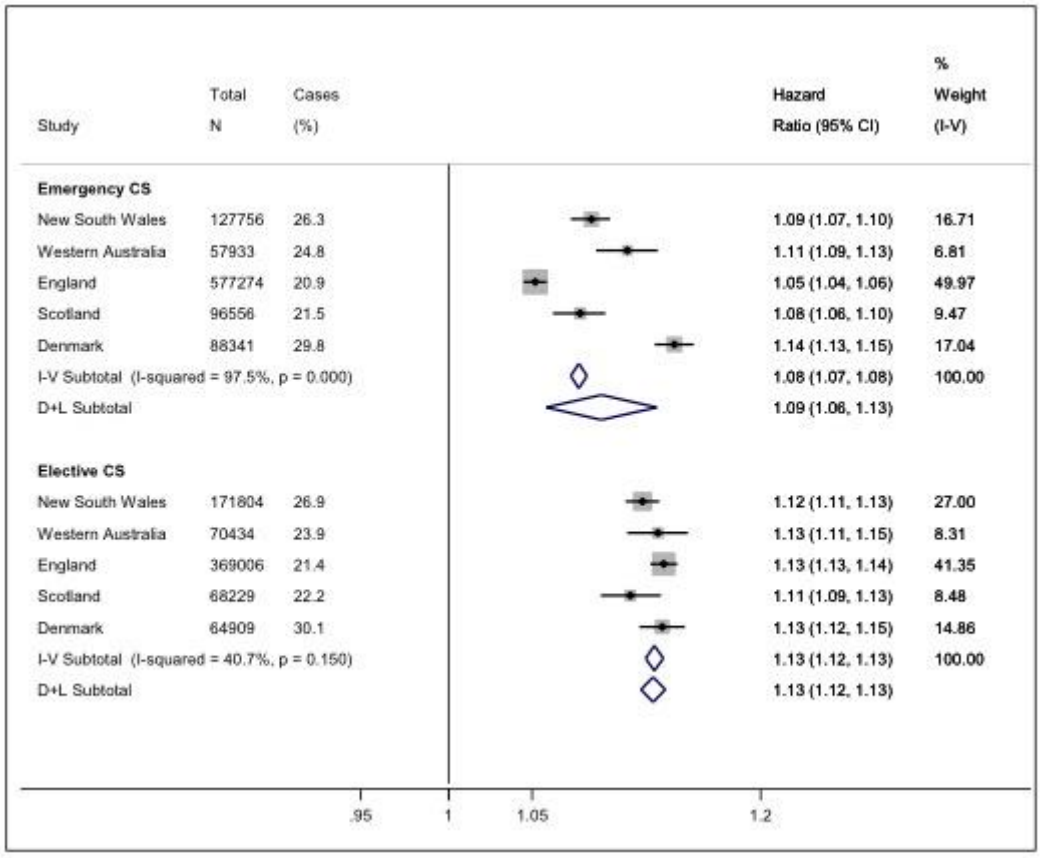
Conclusions:

Caesarean section is associated with increased risk of IRH in young children. Differences in early microbial exposure by mode of delivery are likely determinants. Mechanistic studies are warranted and intervention trials should be considered.

Systematic Review Registration:

N/A

Figure: Hazard ratios for infection-related hospitalisation following delivery by emergency or elective caesarean section, compared to vaginal delivery



All models adjusted for: sex, gestational age, birth weight, smoking during pregnancy (not available for England data), maternal age at birth, parity, area level deprivation, birth year, indication for type of delivery and season of birth

ESPID19-1133
Science Track

ESPID Symposium 01 - Paediatric sepsis

Diagnostic accuracy of presepsin in infants younger than 3 months with fever without a source: preliminary data

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Background

Infants with fever without source (FWS), have an increased risk of severe (SBI) and invasive (IBI) bacterial infection. Differentiate between infants with IBI, SBI or a viral infection remains a challenge. Procalcitonin (PCT) and C-reactive protein (CRP) were proven accurate biomarkers for bacterial infections. The sCD14-subtypes (Presepsin, P-SEP) seems to be a promising biomarker for sepsis in neonates and adults. Objective of the study was to determine the accuracy of P-SEP in identifying IBI and SBI in infants younger than 3 months with FWS.

Methods

This multi-center, prospective, clinical trial of infants younger than 3 months with FWS presenting to 6 pediatric emergency departments. P-SEP, CRP and PCT levels were measured, urinary dipstick and a blood culture were performed.

Results

Of the 284 enrolled patients, 16 had IBI and 60 SBI. P-SEP achieved the best accuracy for IBI at the cutoff of 449 pg/mL (sensitivity 81.2%, specificity 76.1%). The ROC curve of P-SEP values had the area under the curve (AUC) of 0.85 (95% CI 0.70–0.90), compared an AUC of 0.82 for PCT (95% CI 0.69–0.95). At the same cutoff PSEP showed inadequate accuracy for SBI (sensitivity 36.7%, specificity 75.4%).

Conclusions

P-SEP is a promising new biomarker. P-SEP accuracy for IBI is comparable to PCT. Eventhough, P-SEP is probably not enough accurate to be use as a stand-alone marker to rule in an IBI. Future researches

should demonstrate if P-SEP could be used in combination with other biomarkers or clinical findings in clinical prediction models to increase the accuracy to discriminate high risk patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0863
Science Track

ESPID Symposium 01 - Paediatric sepsis

Microorganism profile & antimicrobial resistance pattern in neonatal sepsis over 6 years: experience from tertiary care hospital in india

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Background and Aims:

Sepsis, a leading cause of neonatal mortality worldwide, contributes to almost one third neonatal deaths in India. Microorganism profile, resistance pattern and epidemiology of sepsis are poorly understood prompting us to study the microorganism profile and antimicrobial resistance(AMR) pattern of neonatal sepsis over six years.

Methods:

Over Six years(Jan'13 to Dec'18) demographic profile of neonates labelled as sepsis(based on clinical signs and/or lab criteria) was noted along with a meticulous record of microorganisms isolated and AMR profile. Multidrug resistance(MDR) among gram negative(GN) isolates was defined as resistance to ≥ 3 antibiotic classes. Unit protocol for empirical antibiotic therapy was: First line: Piperacillin tazobactum and Amikacin, Second line: Meropenam and Amikacin, Third line: Colistin and Amikaicn and Vancomicin(in MRSA).

Results:

Over the study period, 79655 neonates were delivered, 16015(20%) required admission with 60%(n=9700) being preterm. Overall incidence of sepsis was 23% and that of culture positive sepsis 5%. Of total sepsis, Early onset(≤ 72 hours of life) developed in 53% and 14% had meningitis. Three-fifths of all deaths were attributable to sepsis. Out of 795 isolates, 60% were GN. Klebsiella was the most common organism(30%) followed by Staphylococcus aureas(23%), CONS(14%), E.coli(10%) and Acinetobacter(10%). A high level of MDR was observed in GN(54%) isolates: Acinetobacter(63%), Klebsiella(55%) and E.coli(50%). Among gram positive, high Methicillin resistance was seen; Staphylococcus aureas(62%) and CONS(56%). Rising trend of MDR and methicillin resistance over the years was disturbing(Fig 1).

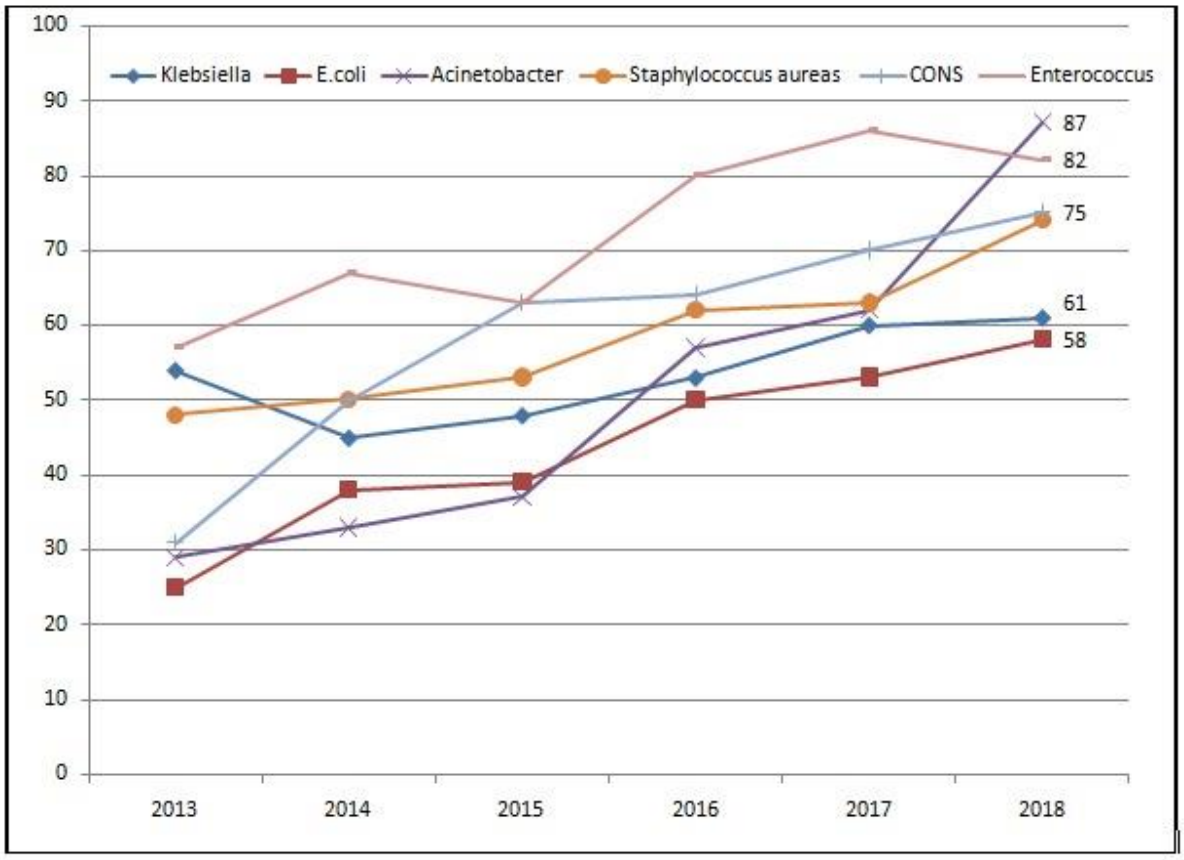

Fig 1: Multidrug resistance over 6 years among commonly isolated gram negative organisms
X axis depicts time period from 2013 to 2018 and Y axis depicts percentage of MDR

Conclusions:

The study provides insight into the common pathogens responsible for neonatal sepsis along with their antibiotic susceptibility pattern. Alarming degree of AMR underscores the need to understand the pathogenesis of Neonatal sepsis in LMICs as well as conduct trials to determine the best possible antibiotic regimens.

Systematic Review Registration:

None

ESPID19-0193
Science Track

ESPID Symposium 01 - Paediatric sepsis

Development and validation of a novel adapted qsofa score to predict intensive care unit admission in febrile children presenting to the emergency department

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Background and Aims:

Age-adjusted quick Sequential Organ Failure Assessment score(qSOFA), P-MODS and PELOD-2 have been validated in the PICU setting in children with sepsis, but qSOFA, in the Emergency Department (ED) showed only moderate prognostic accuracy for PICU transfer and/or mortality.

Methods:

A novel bedside score was developed using qSOFA components; altered mentation, systolic blood pressure and respiratory rate, and adapted with age-adjusted heart rate (HR), respiratory rate (RR), capillary refill (CR) and conscious level on the Alert, Responds to Voice, Responds to Pain and Unresponsive (AVPU) scale. HR and RR> 99thcentile using the Bonafide age-adjusted thresholds, CR≥ 3 seconds and VPU of the AVPU score, were each assigned a score of 1. Primary outcome was ICU admissions within 48 hours of ED presentation.

Results:

The score was developed using a derivation cohort of 1121 febrile children presenting to the ED with suspected bacterial infection, and predicted ICU admission with an area under the curve (AUC) of 0.78. The score was validated retrospectively on a cohort of 12266febrile children presenting to the ED. There were 12 ICU admissions and 58 (0.5%) children had a score of ≥2. The score predicted ICU admission with an AUC= 0.66. For a score of ≥2, the odds ratio was 95 (95% CI:17-516)for admission to ICU.

Conclusions:

This study of over 15,000 children is the largest study evaluating an age-adjusted qSOFA score for the diagnosis of sepsis. In febrile children presenting to the ED, a novel bedside, age-adjusted qSOFA score shows moderate predictive ability for ICU admission in the subsequent 48 hours. Paediatric-specific criteria could potentially improve the rapid identification and treatment of children with sepsis presenting to the ED.

Systematic Review Registration:

N/A

ESPID19-0118
Science Track

ESPID Symposium 01 - Paediatric sepsis

Predictive value of ‘signs and symptoms’ in diagnosis of culture proven early onset neonatal sepsis (eons) in preterm neonates

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Background

Clinical diagnosis of Early onset neonatal Sepsis (EONS) is difficult because of non specific 'signs and symptoms' and inability of laboratory test to identify infected neonates. Clinician is often faced with a dilemma regarding starting antibiotics in preterm neonates suspected of being septic. This study was planned to evaluate predictive accuracy, if any, of signs and symptoms in culture proven EONS in preterm neonates

Methods

This prospective observational study enrolled 1120 preterm infants between 26 and 34 weeks of gestation over 22 months. Demographic and clinical data along with 23 possible signs and symptoms for EONS were recorded and analyzed through univariate followed by multivariate logistic regression to predict presence of culture proven EONS.

Results

Out of 23934 infants delivered during this period, 4250 (18%) were preterm with 1120 between 26 and 34 weeks of gestation. Mean gestation and birth weight were 29 weeks and 1190 grams. On univariate analysis (Table 1), 19 signs and symptoms namely RD persisting beyond 4 hours of life, grunt, hypoxia, apnea, shock, temperature abnormality, abnormal HR, feed intolerance, altered muscle tone, encephalopathy, seizure, sclerema, oliguria, unexplained bleeding, requirement of mechanical ventilation, requirement of CPR, metabolic acidosis and Intravenous fluid usage were found to be significant for predicting EONS. However, on multivariate analysis only 5 were significance namely: apnea, abnormal HR, unexplained bleeding, altered muscle tone and temperature abnormality.

Table 1: Univariate anlysis of signs and symptoms of sepsis in study groups

Signs of sepsis	Culture		P value	Odd's ratio (OR)	95% confidence interval
	Positive(n= 166)	Negative (n= 954)			
Respiratory distress persists >4hrs	136(81.93%)	479(50.21%)	0.001	4.495	2.967-6.809
MV support required	44(26.51%)	107(11.22%)	0.001	2.854	1.915-4.254
Altered muscle tone	29(17.47%)	23(2.41%)	0.001	8.568	4.817-15.240
Feed intolerance	72(43.37%)	92(9.64%)	0.001	7.176	4.933-10.430
Abnormal heart rate	89(53.61%)	101(10.59%)	0.001	9.761	6.754-14.107
Apnea	112(67.47%)	182(19.08%)	0.001	8.797	6.121-12.643
Signs of encephalopathy	14(8.43%)	26(2.73%)	0.01	3.287	1.678-6.437
Temperature abnormality	34(20.48%)	73(7.65%)	0.001	3.108	1.987-4.856
Unexplained bleeding	53(31.93%)	34(3.56%)	0.001	12.691	7.909-20.365
Seizure	28(16.87%)	36(3.77%)	0.001	5.173	3.059-8.748
Altered glucose homeostasis	24(14.46%)	115(12.05%)	0.385	1.233	0.767-1.981
Local signs of sepsis	1(0.6%)	17(1.78%)	0.265	0.334	0.044-2.527
Sclerema	34(20.48%)	55(5.77%)	0.001	4.210	2.644-6.702
Shock	52(31.33%)	123(12.89%)	0.001	3.081	2.110-4.500
Grunt	121(72.89%)	332(34.8%)	0.001	5.037	3.489-7.272
Feeding difficulties	5(3.01%)	25(2.67%)	0.773	1.154	0.435-3.058
Requirement of CPR	40(224.1%)	93(9.75%)	0.001	2.939	1.940-4.451
Oliguria	19(11.45%)	47(4.93%)	0.001	2.494	1.423-4.369
Metabolic acidosis	39(23.49%)	100(10.48%)	0.001	2.622	1.732-3.968
Hypoxia	118(71.08%)	397(41.61%)	0.001	3.449	2.400-4.940
Jaundice with in 24hrs	5(3.01%)	14(1.47%)	0.155	2.08	0.740-5.860
PPHN	2(1.2%)	3(0.31%)	0.112	3.865	0.641-23.313
IV fluid usage	123(74.1%)	317(33.23%)	0.001	5.748	3.960-8.410

Conclusions

Although symptomatology is often considered non-specific for clinical decision making regarding antibiotic therapy in the management of EONS, symptoms consisting of one or more of unexplained bleeding, altered muscle tone, temperature abnormality, abnormal heart rate or apnea, may help the clinician for initiating antibiotics in preterm infants between 26 and 34 weeks of gestation.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0953
Science Track

ESPID Symposium 02 - Vaccine challenges

Evaluation of vaccine safety during the first public sector introduction of typhoid conjugate vaccine, navi mumbai, india, 2018

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Background

In 2018, the World Health Organization prequalified the first typhoid conjugate vaccine (TCV) (Typbar-TCV). During July – August 2018, The Navi Mumbai Municipal Corporation (NMMC) launched the first public sector TCV introduction in the world. Following the Global Advisory Committee on Vaccine Safety recommendations, we systematically evaluated adverse events to characterize the safety profile of TCV

Methods

We collected data using the following methods: 1) telephone interviews among a randomly selected subset (5%) of vaccine recipients at 48 hours and 7 days following TCV using a standard questionnaire, 2) chart abstraction for adverse events of special interest (AESI) using the Brighton Collaboration criteria for diagnostic certainty followed by ascertainment of vaccination status in five hospitals in Navi Mumbai.

Results

According to administrative reports, 113,420 children aged 9 months to <15 years old received TCV during the campaign. Among 5,605 interviews completed at 48 hours, 33% reported one or more adverse event; pain at the injection site (26%, n=1452), local injection site swelling (8%, n=419), and fever (7%, n=416) were most commonly reported. At 7 days, among 4,728 interviews completed, the most commonly reported events included fever (4%, n=200), pain (1%, n=52) and headache (1%, n=42). The most common AESI identified in hospitals were thrombocytopenia (n=43) and seizures (n=18), though these were more than 6 times more commonly identified among unvaccinated patients. A total of 225 (0.2%) events were reported through the NMMC AEFI surveillance system using national guidelines; none of the severe or serious events were attributed to vaccination.

Conclusions

Navi Mumbai TCV introduction provides further evidence of an excellent safety profile of TCV when administered to children 9 months to < 15 years of age.

Clinical Trial Registration (Please input N/A if not registered)

NCT03554213

ESPID19-0491
Science Track

ESPID Symposium 02 - Vaccine challenges

Memory b cell responses in infants after reduced schedule (2+1) of 4cmenb vaccine

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Background

Following the introduction of 4CMenB vaccine in the UK vaccine effectiveness of 82.9% was estimated, but memory B (memB) cells responses has yet to be reported. Here, we describe 4CMenB-specific memB cell frequencies and their correlation with hSBA titres.

Methods

8-12 week old, healthy infants (N=187) were randomised to receive either 4CMenB vaccine plus routine immunisations (test group) at 2, 4 and 12 months of age or to receive delayed 4CMenB (control group) at 6, 8 and 13 months. We analysed memB cell responses to specific proteins (fHbp, NadA, NHBA and PorA) in the test and control groups using a cultured ELISpot assay. In the test group, the memB cell ELISpot was performed 4 weeks post-primary immunisation, at pre-boost (12 months of age) and 4 weeks post-boost.

Results

There was no difference in frequency of memB cells 4 weeks post-primary immunisation in the test group (N=43) when compared with pre-immunisation frequencies in controls (N=17), demonstrating a lack of detectable memory after primary immunisations. A decline in hSBA protective titers (reference strain 44/76-SL) from post-primary (97.3%) to pre-boost (29.1%) was also observed.
From the post-primary immunisation time point to post-boost, a significant increase in memB cell frequency was observed for all antigens. A weak but significant correlation (spearman rho:0.44, p=0.0035) was identified between the post-boost hSBA and the fHbp specific memB cells performed one month after primary immunisation in test group.

Conclusions

No detectable memB cells were identified after primary immunisations in the test group when compared with controls.
Booster immunisation with 4CMen B is fundamental for the induction of detectable memB cell populations in a reduced schedule.

Funding: European Union’s seventh Framework program under EC-GA no. 279185 (EUCLIDS). NIHR Oxford Biomedical Research Centre

Clinical Trial Registration (Please input N/A if not registered)

EudraCT number 2014-000126-38

ESPID19-0436
Science Track

ESPID Symposium 02 - Vaccine challenges

Longitudinal study of capsular group b protein-based vaccine antigens in carried meningococci in oxfordshire, uk, 1999 and 2014/15

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Background

Meningococci exclusively colonise the human oropharynx. The biodiversity and complex interactions within the oropharyngeal microbiota contribute to preventing hyperinvasive organisms causing disease. The impact of protein-based vaccines is being examined in large-multicentre trials in Australia and the UK. The aim of this study was to analyse the distribution and diversity of vaccine antigenic variants in whole genome sequences (WGS) of meningococcal carriage isolates from 1999 and 2014/15 in Oxfordshire.

Methods

Meningococcal carriage WGS from 1999 (n=498) and 2014/15 (n=149) were analysed using novel genomic typing methods, Bexsero® Antigen Sequence Type (BAST) and Outer Membrane Vesicle peptide Types (OMVT) on the web-accessible database PubMLST.org/neisseria. Seventy-four disease-causing meningococci from South East England (2014/15) were included for comparison.

Results

Oxfordshire carriage rates fell from 21.9% (1999) to 7.0% (2014/15). Secular changes in clonal complexes led to changes in genogroup distribution. There were 32.5-36.2% carried meningococci that possessed exact and putatively cross-reactive Bexsero® antigenic variants, compared to 63.5% in disease. Isolates with exact or putatively cross-reactive fHbp peptide variants from Bexsero® (24.2% 2014/15 Carriage) and Trumenba® (67.1% 2014/15 Carriage) showed different distributions, with Trumenba® variants predominantly found in genogroups B, C, W, X, Y, or Z, and Bexsero® variants in genogroups E, L, or capsule null. Compared to the antigenic profile of MeNZB™ (OMVT-1), most isolates had 0-4/24 matching loci, not changing over time.

Conclusions

To date, there is limited data on effects of vaccine-induced antibodies on carried meningococci. Mouse models suggest clearance of carriage maybe associated with high numbers of antigenic targets, but only 3.6% (1999) and 1.3% (2014/15) isolates contained >1 vaccine antigen in our study. In Western Australia, Bexsero® did not eliminate carriage of disease-causing meningococci, but impact on non-disease causing meningococci remains unclear.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0162
Science Track

ESPID Symposium 02 - Vaccine challenges

A phase 2, double-blind, randomized, multicenter trial to evaluate the safety and immunogenicity of 15-valent pneumococcal conjugate vaccine (pcv15) compared to pcv13 in healthy infants

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Background

A phase 2 study to compare safety and immunogenicity of PCV15 (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19F, 19A, 22F*, 23F, 33F*) to PCV13 in infants.

Methods

In this randomized, blinded, comparator-controlled study to evaluate lot consistency, vaccines were administered concomitantly with other routine pediatric vaccines recommended by Advisory Committee on Immunization Practices at 2, 4, 6, and 12-15 months of age. Subjects received either Lot 1 PCV15 [n=350], Lot 2 PCV15 [n=347], or PCV13 [n=347]. Safety profiles were compared after each dose. The primary outcome measure was serotype-specific IgG≥0.35 µg/mL for the 13 serotypes shared with PCV13 and IgG geometric mean concentrations (GMCs) for all 15 serotypes were measured by the pneumococcal electrochemiluminescence (Pn ECL) assay at 1-month post-dose 3 (PD3).

Results

At PD3, PCV15 met non-inferiority criteria for 13 of 13 shared serotypes with PCV13. In particular, higher percentage point differences of response rates for serotype 3 in PCV15 versus PCV13 were observed (PCV15 Lot 1 – PCV13: 24.2% [18.6%, 30.0%]; PCV-15 Lot 2 – PCV13: 22.3% [16.5%, 28.3%]). Both lots of PCV15 induced higher GMCs than PCV13 to serotypes 22F* and 33F*.

Most subjects in each group reported clinical AEs, and a comparable proportion of subjects reported serious AEs across groups (Lot 1 PCV15: 4.0%; Lot 2 PCV15: 3.7%; PCV13: 2.9%).

Conclusions

Both lots of PCV15 were non-inferior to PCV13 based on the proportion of subjects meeting the threshold value of ≥0.35 µg/mL for serotype-specific IgG at 1-month PD3. Tolerability was comparable in all vaccine groups, and no safety signals were observed.

*Serotypes unique to PCV15

Clinical Trial Registration (Please input N/A if not registered)

NCT02987972

Table 1:Serotype-specific IgG and Geometric Mean Concentrations for PCV15 Lot1, PCV15 Lot2, and PCV13

Pneumococcal Serotype	Endpoint	PCV15 Lot 1 (N = 350)			PCV15 Lot 2 (N = 347)			PCV13 (N = 347)		
		n	Observed Response	95% CI	n	Observed Response	95% CI	n	Observed Response	95% CI
PCV13 Types										
1	% ≥ 0.35µg/mL	277	96.8% (268/277)	(93.92, 98.50)	273	97.8% (267/273)	(95.28, 99.19)	291	96.9% (282/291)	(94.21, 98.58)
	GMC (µg/mL)	277	1.19	(1.10, 1.27)	273	1.37	(1.26, 1.49)	291	1.65	(1.50, 1.82)
3	% ≥ 0.35µg/mL	276	96.0% (265/276)	(92.98, 97.99)	273	94.1% (257/273)	(90.66, 96.61)	291	71.8% (209/291)	(66.28, 76.92)
	GMC (µg/mL)	276	1.04	(0.97, 1.12)	273	1.02	(0.93, 1.11)	291	0.53	(0.48, 0.58)
4	% ≥ 0.35µg/mL	272	98.2% (267/272)	(95.76, 99.40)	272	97.1% (264/272)	(94.29, 98.72)	288	95.1% (274/288)	(91.98, 97.32)
	GMC (µg/mL)	272	1.30	(1.20, 1.40)	272	1.27	(1.17, 1.37)	288	1.26	(1.14, 1.38)
5	% ≥ 0.35µg/mL	277	96.0% (266/277)	(93.01, 98.00)	272	96.0% (261/272)	(92.88, 97.96)	290	96.6% (280/290)	(93.75, 98.33)
	GMC (µg/mL)	277	1.37	(1.25, 1.49)	272	1.45	(1.32, 1.59)	290	1.75	(1.58, 1.94)
6A	% ≥ 0.35µg/mL	277	90.6% (251/277)	(86.55, 93.78)	273	95.6% (261/273)	(92.45, 97.71)	290	96.2% (279/290)	(93.31, 98.09)
	GMC (µg/mL)	277	1.42	(1.26, 1.59)	273	1.48	(1.34, 1.63)	290	2.62	(2.35, 2.92)
6B	% ≥ 0.35µg/mL	275	90.5% (249/275)	(86.45, 93.73)	273	92.3% (252/273)	(88.48, 95.18)	290	91.4% (265/290)	(87.54, 94.34)
	GMC (µg/mL)	275	1.95	(1.67, 2.27)	273	1.71	(1.49, 1.96)	290	1.89	(1.64, 2.18)
7F	% ≥ 0.35µg/mL	277	99.6% (276/277)	(98.01, 99.99)	273	99.3% (271/273)	(97.38, 99.91)	290	99.0% (287/290)	(97.01, 99.79)
	GMC (µg/mL)	277	2.43	(2.25, 2.62)	273	2.42	(2.23, 2.62)	290	2.98	(2.72, 3.26)
9V	% ≥ 0.35µg/mL	277	97.1% (269/277)	(94.39, 98.75)	273	97.8% (267/273)	(95.28, 99.19)	289	95.8% (277/289)	(92.86, 97.84)
	GMC (µg/mL)	277	1.39	(1.28, 1.52)	273	1.70	(1.56, 1.86)	289	1.59	(1.44, 1.76)
14	% ≥ 0.35µg/mL	276	99.3% (274/276)	(97.41, 99.91)	273	97.4% (266/273)	(94.79, 98.96)	289	97.2% (281/289)	(94.62, 98.80)
	GMC (µg/mL)	276	5.08	(4.63, 5.58)	273	4.78	(4.27, 5.34)	289	5.79	(5.11, 6.55)
18C	% ≥ 0.35µg/mL	277	96.8% (268/277)	(93.92, 98.50)	273	98.2% (268/273)	(95.78, 99.40)	291	95.5% (278/291)	(92.48, 97.60)
	GMC (µg/mL)	277	1.24	(1.14, 1.35)	273	1.65	(1.52, 1.79)	291	1.67	(1.52, 1.82)
19A	% ≥ 0.35µg/mL	277	98.9% (274/277)	(96.87, 99.78)	273	98.5% (269/273)	(96.29, 99.60)	290	98.6% (286/290)	(96.51, 99.62)
	GMC (µg/mL)	277	1.63	(1.51, 1.75)	273	1.64	(1.51, 1.78)	290	1.99	(1.83, 2.18)
19F	% ≥ 0.35µg/mL	277	100.0% (277/277)	(98.68, 100.00)	273	98.9% (270/273)	(96.82, 99.77)	290	99.7% (289/290)	(98.09, 99.99)
	GMC (µg/mL)	277	2.25	(2.09, 2.43)	273	2.33	(2.15, 2.53)	290	2.57	(2.38, 2.78)
23F	% ≥ 0.35µg/mL	277	92.4% (256/277)	(88.64, 95.25)	273	94.9% (259/273)	(91.55, 97.17)	290	90.7% (263/290)	(86.74, 93.77)
	GMC (µg/mL)	277	1.21	(1.10, 1.35)	273	1.47	(1.32, 1.63)	290	1.25	(1.11, 1.40)
Non- PCV13 Types										
22F	% ≥ 0.35µg/mL	277	98.9% (274/277)	(96.87, 99.78)	273	98.5% (269/273)	(96.29, 99.60)	291	1.7% (5/291)	(0.56, 3.96)
	GMC (µg/mL)	277	4.80	(4.39, 5.24)	273	4.18	(3.76, 4.63)	291	0.05	(0.05, 0.06)
33F	% ≥ 0.35µg/mL	277	87.7% (243/277)	(83.27, 91.35)	273	90.1% (246/273)	(85.94, 93.38)	289	2.1% (6/289)	(0.77, 4.46)
	GMC (µg/mL)	277	1.58	(1.34, 1.86)	273	1.51	(1.30, 1.75)	289	0.05	(0.04, 0.05)

GMC = Geometric mean concentration.
N = Number of subjects randomized and vaccinated. n = Number of subjects contributing to the analysis. CI = Confidence interval.

ESPID19-0286
Science Track

ESPID Symposium 03 - Perinatal infections - The mother - Infant pair

Antibody responses to primary and booster immunizations in infants born to women immunized with pertussis-containing vaccines in pregnancy versus unimmunized women: systematic review and meta-analysis

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Background

Several countries have recommended pertussis immunization in pregnancy. We aimed to determine if pertussis immunization in pregnancy modifies the active immune response to primary/booster infant immunizations.

Methods

A systematic review and meta-analysis of studies reporting antibody levels to primary/booster immunization in infants born to women immunized against pertussis in pregnancy vs. unimmunized women was performed. The geometric mean ratios (GMRs) of anti-tetanus toxoid (TT), anti-diphtheria toxoid (DT), anti-*Streptococcus pneumoniae*(SPN) and anti-pertussis antibodies in infants born to women immunized in pregnancy vs. unimmunized women were calculated (random-effects model).

Results

8 studies (3 RCTs) were included. After primary immunization, infants born to women immunized in pregnancy had significantly (P<0.05) lower anti-pertussis toxin (PT) [GMR, 0.72; 95% CI, 0.59-0.86], anti-pertactin (PRN) [0.65;0.54-0.77], anti-fimbriae 2+3 (FIM2+3) [0.46;0.37-0.56],anti-DT [0.67;0.53-0.83], anti-SPN1 [0.65;0.46-0.91], anti-SPN3 [0.44;0.24-0.79], anti-SPN4 [0.69;0.59-0.79], anti-SPN5 [0.58;0.49-0.68], anti-SPN6A [0.57;0.46-0.70], anti-SPN7F [0.76;0.64-0.88], anti-SPN19A [0.75;0.61-0.90] antibody levels, but not significantly lower anti-TT [1.09;0.82-1.44], anti-SPN6B [1.08;0.88-1.32], anti-SPN9V [0.62;0.37-1.03], anti-SPN14 [0.68;0.35-1.30], anti-SPN18C [0.89;0.74-1.06], anti-SPN19F [0.85;0.71-1.01], anti-SPN23F [0.89;0.72-1.10] antibody levels compared with infants born to unimmunized women (Figure). After booster immunization, infants born to women immunized in pregnancy had significantly (P<0.05) lower anti-PT [0.79;0.68-0.92], anti-FHA [0.75;0.64-0.86], anti-FIM2+3 [0.43;0.32-0.58], anti-DT [0.86;0.75-0.98] antibody levels, but not significantly lower anti-PRN [1.02;0.81-1.28] nor anti-TT [1.58;0.72-3.43] antibody levels, compared with infants born to unimmunized women (Figure). Results remained significant in sensitivity analysis restricted to RCTs except for anti-PT and anti-DT antibodies post-primary and post-booster immunization, respectively.

Conclusions

This is the first meta-analysis supporting interference of pertussis immunization in pregnancy with infants' active immune responses. These findings support the need for enhanced surveillance of pertussis, diphtheria and pneumococcal diseases after primary and booster vaccinations in infancy to determine the clinical significance of this effect.AAfter

Systematic Review Registration (Please input N/A if not registered)

Systematic Review Registration: PROSPERO CRD42017079171.

ESPID19-1072
Science Track

ESPID Symposium 03 - Perinatal infections - The mother - Infant pair

Epidemiology of invasive group B streptococcal disease and maternal colonisation in a UK cohort of pregnant women and their infants

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Background

Group B streptococcus (GBS) remains the leading cause of invasive infectious disease in newborns and young infants. In the UK, where intrapartum antibiotic prophylaxis is risk-based, the incidence of invasive GBS disease in infants has increased recently (0.95/1000 births).

Methods

Pregnant women from 5 different hospitals in England were recruited for a 6-month period. In 2 hospitals rectovaginal swabs from women 35 weeks gestation onwards were processed, tested for antimicrobial resistance to penicillin and erythromycin and serotyped with a rapid latex agglutination test followed by PCR if non-typable by latex. A follow-up telephone call was made at 90 days as well as a broader national surveillance.

Results

A total of 1805 women were recruited for surveillance and 614 were screened for GBS finding a colonisation rate of 22%. The serotype distribution was 25% Ia, 14% Ib, 16% II, 30% III, 1% IV and 14% V. All strains were sensitive to penicillin but 20% were found to be resistance to erythromycin. From the surveillance cohort, 4 newborns developed early onset disease during the study period (2.2/1000 births). A total of 15 bacterial isolates from infant cases were analysed showing the following serotype distribution: 42% Ia, 8% Ib, 17% II, 25% III and 8% V.

Conclusions

The colonisation rate and GBS resistance to erythromycin in our cohort is concordant with the estimates for the UK. However, we found a higher incidence of invasive GBS disease. The serotype distribution in colonised women was similar to the distribution described globally but we found more cases due to serotype Ia followed by III. To conclude, intrapartum antibiotic prophylaxis policies should be reconsidered in the UK while vaccine development is pursued.

Clinical Trial Registration (Please input N/A if not registered)

ESPID19-0796
Science Track

ESPID Symposium 03 - Perinatal infections - The mother - Infant pair

Oral amoxicillin/clavulanic acid in newborns: do we reach target levels?

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Background

Oral antibiotic use is scarce in neonates due to pharmacokinetic uncertainties in the first weeks of life. Amoxicillin/clavulanic acid covers most causative pathogens of early-onset neonatal sepsis, eg. group B streptococci (GBS) and *E. coli*. Efficacy of amoxicillin depends on time above MIC; for clavulanic acid the area under the curve (AUC) and peak concentration are used. It has a good bio-availability in children and adults, but evidence in neonates is lacking. We evaluated the pharmacokinetics of oral amoxicillin/clavulanic acid in term newborns (0-28 days of age).

Methods

This study is part of a multicenter RCT evaluating the non-inferiority of neonatal intravenous-to-oral switch therapy in probable bacterial infection. Pharmacokinetic analysis was performed in patients allocated to the switch group. After 48 hours of intravenous penicillin/gentamicin, they switched to amoxicillin/clavulanic acid suspension (25/6.25 mg/kg tid). Two bloodsamples from different dosing intervals were obtained and directly stored at -80°C. Analysis was performed batchwise using Liquid Chromatography and Mass Spectrometry. For amoxicillin, an MIC of 8 mg/L for ≥50% of time was considered appropriate. Unfortunately, for clavulanic acid, a target is currently lacking.

Results

Samples of the first 15 patients have been analysed. Patients switched to oral therapy on average after 2.5 days. Amoxicillin levels were all above MIC of *GBS* (0.25 mg/L) and *E. coli* (8 mg/L); range: 9.10-30.6 mg/L. Clavulanic acid was absorbed in all patients but a great variance in serum level was observed (range: 0.26-4.82 mg/L), as showed in figure

1.

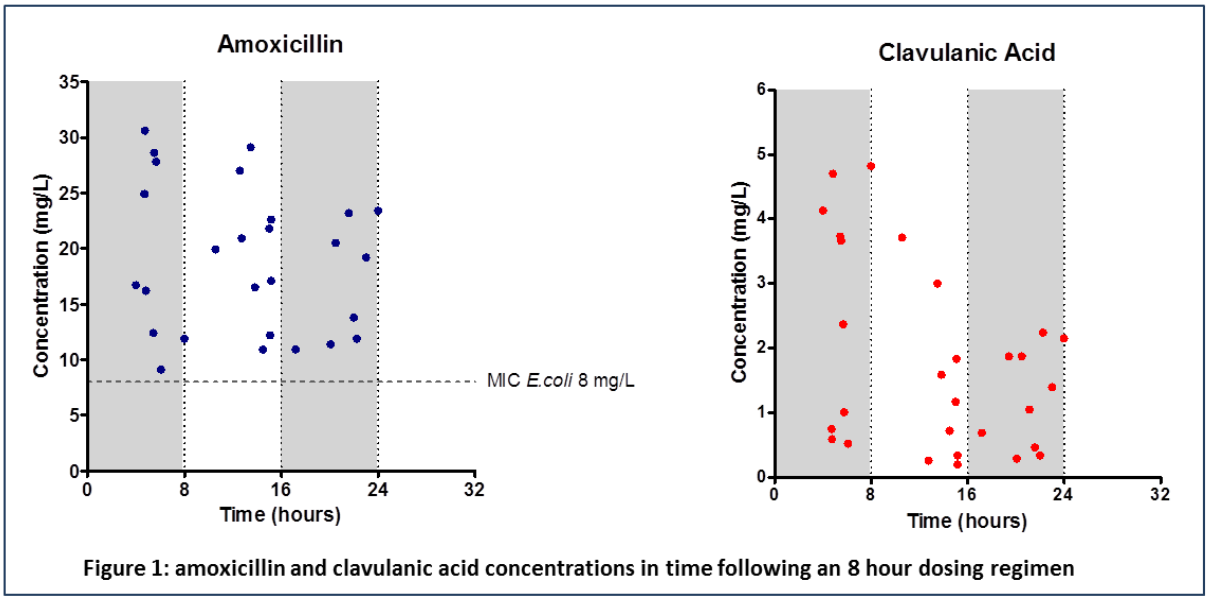

Figure 1: amoxicillin and clavulanic acid concentrations in time following an 8 hour dosing regimen

Conclusions

Oral amoxicillin is well absorbed in newborns leading to adequate serum levels. Clavulanic acid is absorbed as well, but great variance is seen in through levels. Data on peak levels and AUC will follow soon.

Clinical Trial Registration (Please input N/A if not registered)

Clinicaltrials.gov Trial number NCT03247920

ESPID19-1174
Science Track

ESPID Symposium 08 - Congenital CMV infection

Baseline brain magnetic resonance imaging (mri) for children with congenital cytomegalovirus (ccmv) – a retrospective analysis

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Background and Aims:

All infants referred to our team had baseline brain MR imaging. Many had white matter changes as well as classic CMV findings (cysts, ventricular stranding, polymicrogyria, calcification, etc). We devised an image scoring system which was applied retrospectively to infants presenting < 4months of age (Table 1). The scoring system differentiated those with white matter changes only.

Methods:

Retrospective clinical data analysis and imaging review by 3 paediatric-neuro-radiologists, of infants presenting January 2010-December 2018. Anonymized data was analyzed in Excel, infants were categorized according to presentation with symptoms at birth(“symptomatic”) or not(“asymptomatic”)(1).

Results:

Of 59 infants referred, 25 were symptomatic at birth. Thirteen of 34 asymptomatic referrals failed the newborn hearing test, and 11 were for obstetric and 10 for other reasons.

In total, 56% had abnormal imaging, 72% symptomatic and 44% asymptomatic (Table1). Twenty six had sensory-neural-

Table 1 MRI scoring system showing distribution of MRI Findings in patients with different presentations of congenital CMV

	Score*†	Abnormal MRI (%)	Normal MRI (%)	Abnormal MRI VL c/ml median (range)	Normal MRI VL c/ml median (range)
All infants		33 (56)	26 (44)	3755 (0-690,000)	166 (0-45610)
Symptomatic CCMV (all)	-	18 (72%)	7 (28%)	2500 (0-45,610)	2500 (358-690,000)
Presented > 4mths of age, so no MRI score	-	1			
	1	1	-		
	2	3	-		
	3	13	-		
Symptomatic CCMV (+SNHL- 1 or 2 ears)	-	10 (91%)	1 (9%)	47052 (2500-690,000)	N/A
Presented > 4mths of age, so no MRI score	-	1			
	1	1	-		
	2	2	-		
	3	6	-		
Asymptomatic CCMV (all)	-	15 (44%)	19 (56%)	728 (0-24.930)	166 (0-26.926)
Presented > 4mths of age, so no MRI score	-	2			
	1	2	-		
	2	4	-		
	3	7	-		
Asymptomatic CCMV (+SNHL- 1 or 2 ears)	-	7 (47%)	8 (53%)	0 (0-2449)	182 (0-364)
Presented > 4mths of age, so no MRI score	-	1			
	1	1	-		
	2	2	-		
	3	3	-		
*†MRI Scoring System 1 Lesions other than white matter (calcification, cysts, polymicrogyria etc) 2 White matter changes only 3 White matter + other changes as in 1					

Reference: (1) SE Luck PIDJ 2017 Dec; 36(12):1205-1213

hearing loss (SNHL) in one ear or two (11 symptomatic, 15 asymptomatic), and of those 65% had abnormal imaging. Isolated white matter changes occurred in 3/17 symptomatic and 4/12 asymptomatic infants.

Children with abnormal MRI had significantly higher plasma viral loads than those with normal MRI(*p=0.049)(Table 1).

All infants symptomatic at birth with abnormal imaging were treated with ganciclovir / valganciclovir, 2 started after 28 days. Eighteen (53%) asymptomatic infants were treated, 5 of 6 with SNHL and abnormal imaging started late. Five asymptomatic infants, with normal imaging, were treated.**Conclusions:**

Without screening for CCMV, the full spectrum of brain impact cannot be defined. In our cohort, 44% of “asymptomatic” infants had abnormal imaging, notably affecting white matter. We believe all infants with CCMV should have a baseline MRI, and an international scoring system is required, to prospectively link infant imaging with long term clinical outcomes.

Systematic Review Registration:

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ESPID19-1043
Science Track

ESPID Symposium 08 - Congenital CMV infection

Using a disease-based registry to review neurodevelopmental progress in congenital cmv-infected children at age 6 months: the european congenital cytomegalovirus initiative (ecci) registry v2.0

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Background

Congenital CMV (cCMV) infection is an important cause of neurodevelopmental problems, particularly sensorineural hearing loss (SNHL), but data on long term neurodevelopment in untreated cases is limited. One aim of the ECCI Registry V2.0 is to fill this research gap.

Case Presentation Summary

Baseline (demographics, signs and symptoms, investigations, treatment) and subsequent (neurodevelopmental progress at specified age ranges) assessments of cCMV-infected children are entered onto a study-specific electronic database.

104 cases from Greece, Italy and the UK were entered. Of 65 cases with 6 months follow-up, 46 were suitable for analysis. 24 (52%) were symptomatic in the neonatal period and 20 (40%) received antiviral treatment.

14 (58%) of the cases symptomatic in the neonatal period had no neurodevelopmental impairment at age 6 months, of which 5 (36%) were untreated. Most (96%) asymptomatic cases in the neonatal period remained asymptomatic at age 6 months. 2 (8%) of the 26 untreated cases had neurodevelopmental impairment at age 6 months, of which one was asymptomatic in the neonatal period.

37 (80%) cases had repeat auditory brainstem responses entered; 34 (92%) had stable or no SNHL, 1 (3%) had improved SNHL and 2 (5%, both treated) had worsening SNHL.

Learning Points/Discussion

At age 6 months, most cCMV-infected children had stable SNHL and there was a trend towards good neurodevelopmental outcome in treated symptomatic cases. However, many untreated symptomatic cases also had good outcomes at 6 months, supporting the need for controlled trials of new treatments.

Longer-term follow-up from a range of European paediatric ID centres gives us the unique opportunity to compare outcomes in children with similar clinical phenotypes who are both treated and untreated.

ESPID19-1015
Science Track

ESPID Symposium 08 - Congenital CMV infection

Maternal cytomegalovirus infection and negative amniotic fluid cmv-pcr: infant outcomes at 1 year of age.

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Background and Aims:

Cytomegalovirus (CMV) PCR in amniotic fluid (AF) is a helpful tool to rule. out fetal CMV infection, but false negative results can be present.

Methods:

A retrospective study of infants born from mothers with CMV infection during pregnancy and AF CMV-PCR performed in a tertiary hospital from 2009 to 2017 was carried out. Hearing loss and neurologic abnormalities were evaluated at birth and at 12 months of age.

Results:

AF CMV-PCR was performed in 45 women (one twin pregnancy, 46 fetuses). AF CMV-PCR was positive in 27 cases: in 3 of those cases intrauterine demise was present, in 10 cases termination of pregnancy was performed, 13 infants were born infected and one was lost of follow up. AF CMV-PCR was negative in 18 fetuses: 16 of them were born uninfected. In two of those pregnancies AF CMV-PCR was negative (performed at 20 and 30 weeks of gestation, respectively), but children were born infected with normal physical and blood exams. One of those infants showed germinolysis in cranial ultrasonography at birth and mild white matter abnormalities in MRI and received oral valganciclovir. None of them showed any sequelae at 12 months of age. One fetus of a twin pregnancy died in utero and the other fetus had a negative AF CMV-PCR and was born uninfected. Sensitivity of CMV-PCR in AF was 86.7%(CI95%:59.6%-98.3%) and specificity 100%(CI95%:79.4%-100%) with a negative predictive value of 88.9%(68.8-96.7%).

Conclusions:

In case of CMV infection during pregnancy and negative amniocentesis, congenital CMV should be ruled out at birth. Infected children with negative amniocentesis did not present any sequelae at 12 months of age.

Systematic Review Registration:

ESPID19-0926
Science Track

ESPID Symposium 08 - Congenital CMV infection

Neurodevelopmental outcome in children with congenital cmv infection asymptomatic at birth

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Background and Aims:

Almost 90% of children with congenital CMV (cCMV) born asymptomatic; among them 5-15% develop sequelae, mainly auditory impairment. For this reason international guidelines suggest to follow up babies with cCMV until 6 years old. Nevertheless almost 30% of children that reach the 3 years follow up without symptoms are lost to further follow up. The aim of this retrospective study is to evaluate the neurocognitive development in a cohort of asymptomatic cCMV

Methods:

We evaluated 21 patients with cCMV asymptomatic at birth followed up at the Immunological and Infectious Disease Unit at Chidren's Hospital Bambino Gesù in Rome. All parents consented to partecipate to the study. We performed neurodevelopment assessment using the Bayley III scale for children 6 months- 3 years of age and the Wippsi III scale for children above 3 years.

Results:

We analyzed 10 patients in the age range 6months-3 years with a mean age of 2 years. At the Bailey III scale we observed score in the normal range for motor and linguistic ability (mean linguistic QI 95, mean motor QI 96); interestingly, although not significant, both were -0,5 standard deviation. 11 patients in the age range 3,5-7 years were enrolled, with a mean age 4,7 years. In these children we performed the wippsi III scale and we observed in 25% difficulties in the "stimuli processing speed", in 35% low score in "general language" and in 10% low score in "fluid intelligence capacity".

Conclusions:

Our data suggest that children with cCMV asymptomatic at birth have normal neurodevelopment assessment in the first 3 years of life but later can show difficulties in processing speed and general language. These findings reinforce the necessity of 6 years follow up for cCMV

Systematic Review Registration:

na

ESPID19-0386
Science Track

ESPID Symposium 11 - Prevention of meningococcal disease - The way forward

Meningococcus protein-antigen vaccines' effects on carriage and transmission – are we asking the right questions?

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Background

Meningococcus(Nm) conjugate vaccines can have powerful indirect effects. Whether protein-antigen vaccines similarly reduce transmission population-wide when used in teenagers has not been tested. Attempts to answer this question are studying throat carriage rates in individuals immunised 6-12 months earlier. So far, results seem disappointing. We have conducted longitudinal studies which challenge this approach.

Methods

917 16-17 year old school students had throat swabs(TS) taken at one month intervals through wintertime. 416 students had 4CMenB vaccine 2 doses one month apart with TS at immunisation and 3 months later. This group also gave weekly saliva samples throughout the study. Samples were analysed for Nm and capsular genogroups (B,C,Y,W,X) by qPCR of DNA extracts of samples and of products of culture on selective media. In study 1 a panel of respiratory viruses were also detected by PCR.

Results

Nm throat carriage episodes were significantly shorter than previously reported (median 29 days, 95%CI 26-32) with spikes in carriage density crossing 2-4 decile logs and often associated with respiratory viral infection ($p<0.03$). Observed weekly in saliva, colonisation persisted for >20 weeks in 5 individuals. Among carriers (6.3-8.7%), high density carriage in the throat (>300 gene copies/ml) was seen before but not 3 months after Bexsero administration (n=4 vs 0, NS).

Conclusions

Nm carriage is usually brief and dynamic. Mucosal immune responses to protein-antigen vaccines may impact on carriage and transmission but, unlike conjugate vaccines', may not reliably prevent acquisition. In the absence of population-wide experiments (as conducted with MenA and MenC vaccines), studies to evaluate protein antigen vaccines should focus on carriage duration, density and rates of onward transmission to contacts rather than on impact on late carriage rates in vaccine recipients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-1048
Science Track

ESPID Symposium 11 - Prevention of meningococcal disease - The way forward

Antibody persistence up to 10 years after menacwy-tt vaccine administration and immunogenicity of a booster dose in adolescents and young adults

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Background

The meningococcal ACWY polysaccharide conjugate vaccine using tetanus toxoid as a carrier protein (MenACWY-TT) is licensed to prevent disease caused by meningococcal serogroups A, C, W, and Y. This study reports long-term antibody persistence after 1 dose of MenACWY-TT; safety and immunogenicity of a booster dose were also assessed.

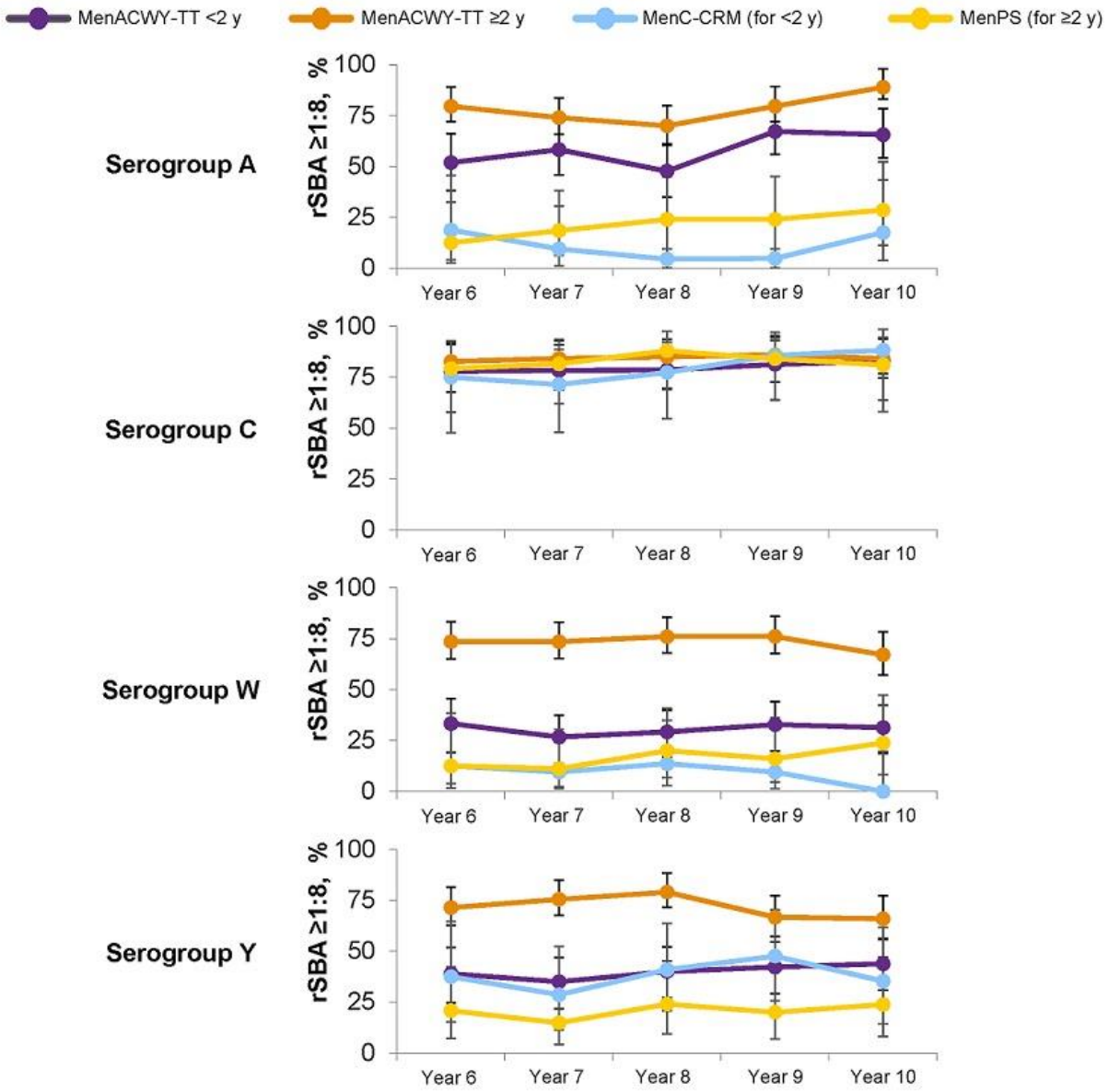
Methods

Previously, participants aged 1–10 years received primary vaccination with MenACWY-TT or a control vaccine: monovalent serogroup C polysaccharide conjugate vaccine (MenC-CRM; subjects aged <2 years), or quadrivalent polysaccharide vaccine (MenPS; subjects aged ≥2 years (NCT00427908). Immunogenicity was measured by serum bactericidal activity assays using rabbit complement (rSBA) to determine percentages of subjects with titers ≥1:8 for each serogroup at 6–10 years postprimary vaccination and 1 month after a booster dose given at year 10. MenACWY-TT analyses were stratified by age at primary vaccination (<2y and ≥2y). Safety was evaluated for the persistence and booster phases.

Results

Of 243 subjects enrolled in the long-term persistence phase, 191 and 181 completed the persistence and booster phases, respectively. Percentages of MenACWY-TT recipients with rSBA titers ≥1:8 for each serogroup remained stable through year 10. The group initially given MenACWY-TT at age ≥2 years had the highest percentage of subjects with rSBA titers ≥1:8 for all serogroups at nearly all time points (**Figure**). After a booster dose at year 10, ≥94% of all subjects achieved rSBA titers ≥1:8 for all serogroups. No new safety signals were observed during the persistence or booster phases.

Figure. Percentage of Subjects With rSBA Titers ≥1:8 up to 10 Years After Primary Vaccination With MenACWY-TT, MenPS, or MenC-CRM*



*Adapted ATP (according to protocol) cohort.
ATP=according to protocol; MenACWY-TT=meningococcal polysaccharide groups A, C, W, and Y conjugate vaccine; MenPS=serogroups A, C, W, and Y polysaccharide meningococcal vaccine; MenC-CRM=meningococcal serogroup C oligosaccharide conjugate vaccine; rSBA=serum bactericidal assay using baby rabbit complement.

Conclusions

Functional antibody responses persisted 10 years after 1 dose of MenACWY-TT, indicating long-term protection against meningococcal A, C, W, and Y disease. A booster dose was well tolerated and elicited robust immune responses.

Clinical Trial Registration (Please input N/A if not registered)

NCT01962207. Funded by Pfizer.

ESPID19-0255
Science Track

ESPID Symposium 11 - Prevention of meningococcal disease - The way forward

4cmenb, a multicomponent meningococcal vaccine developed for serogroup b meningococci elicits cross-reactive immunity also against serogroups c, w and y

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Background

Invasive meningococcal disease, mainly caused by 6 meningococcal serogroups (MenA, MenB, MenC, MenW, MenX and MenY), remains a major public health concern worldwide. The 4-component MenB vaccine (4CMenB) contains 4 main antigens (factor H binding protein [fHbp], *Neisseria* adhesin A [NadA], Neisserial heparin binding antigen [NHBA] and porin A [PorA]) that are also conserved in some non-MenB strains. This study evaluated the ability of sera from infants and adolescents vaccinated with 4CMenB to induce complement-mediated killing of MenC, MenW, and MenY strains collected in 3 European countries and Brazil.

Methods

227 non-MenB clinical isolates collected in 01/07/2007-30/06/2008 by reference laboratories in the UK, Germany and France (Euro-3 panel), and 41 non-MenB isolates collected in 2012 in Brazil were classified by serogroup, multilocus sequence typing (MLST) and antigen genotypes. 147 strains representative of STs and antigen genotypes were randomly selected and tested in a serum bactericidal antibody (SBA) assay using pooled immune sera from infants and adolescents immunized with 4CMenB.

Results

In the Euro-3 panel, MenC represented 57%, MenY 22% and MenW 16% of the isolates that mainly belonged to the ST-11, ST-23/ST-167 and ST-22 clonal complexes, respectively. In the Brazilian panel, MenY represented 49%, MenW 39% and MenC 12% of the isolates that belonged to the ST-22, ST-11 and ST-103 clonal complexes, respectively.
The SBA assays with MenC, MenW, and MenY strains showed that 74.1% and 61.9% of the non-MenB strains tested were killed by infant and adolescent sera, respectively, with SBA titers ranging from ≥4 to ≥128.

Conclusions

4CMenB can provide cross-protection against non-MenB strains in both infants and adolescents, which represents an added benefit of this vaccine.

Clinical Trial Registration (Please input N/A if not registered)

NCT00518180, NCT00661713, NCT00944034, NCT00847145, NCT00657709

ESPID19-0182
Science Track

ESPID Symposium 11 - Prevention of meningococcal disease - The way forward

Antibody persistence up to 26 months after booster dosing in adolescents 4 years following a 2- and 3-dose primary vaccination series of menb-fhbp

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Background

Antibody persistence after booster vaccination with MenB-FHbp (bivalent rLP2086) has not been previously described. This adolescent study evaluated antibody persistence following a MenB-FHbp booster dose administered 4 years after primary vaccination.

Methods

This phase 3 open-label extension of a phase 2 randomized study included adolescents 11–18 years of age who received MenB-FHbp on 2- and 3-dose schedules (including licensed 0-,6-month and 0-,2-,6-month schedules). Booster vaccination was administered 48 months after the primary series. Immune responses were evaluated in serum bactericidal assays with human complement (hSBAs) using 4 vaccine-heterologous meningococcal serogroup B (MenB) test strains. Immunogenicity endpoints included percentages of subjects with hSBA titers ≥ the lower limit of quantitation (LLOQ; 1:8 or 1:16; titers ≥1:4 correlate with protection) at 1 and 48 months postprimary and 1, 12, and 26 months postbooster. Post-booster safety was evaluated.

Results

The booster stage included 58 and 62 subjects on 0-,2-,6-month and 0-,6-month primary schedules, respectively. Persistence data following primary vaccination and through 26 months postbooster indicated that percentages of subjects with protective hSBA titers were similar across primary series. Percentages at 1, 12, and 26 months after boosting (93.4%–100%, 59.0%–89.1%, and 57.5%–82.8%, respectively) were similar or higher compared with 1, 12, and 24 months after primary vaccination (77.9%–99.1%, 16.5%–76.1%, and 15.7%–68.6%, respectively; **Figure**). No safety concerns were identified with up to 26 months of postbooster follow-

up.

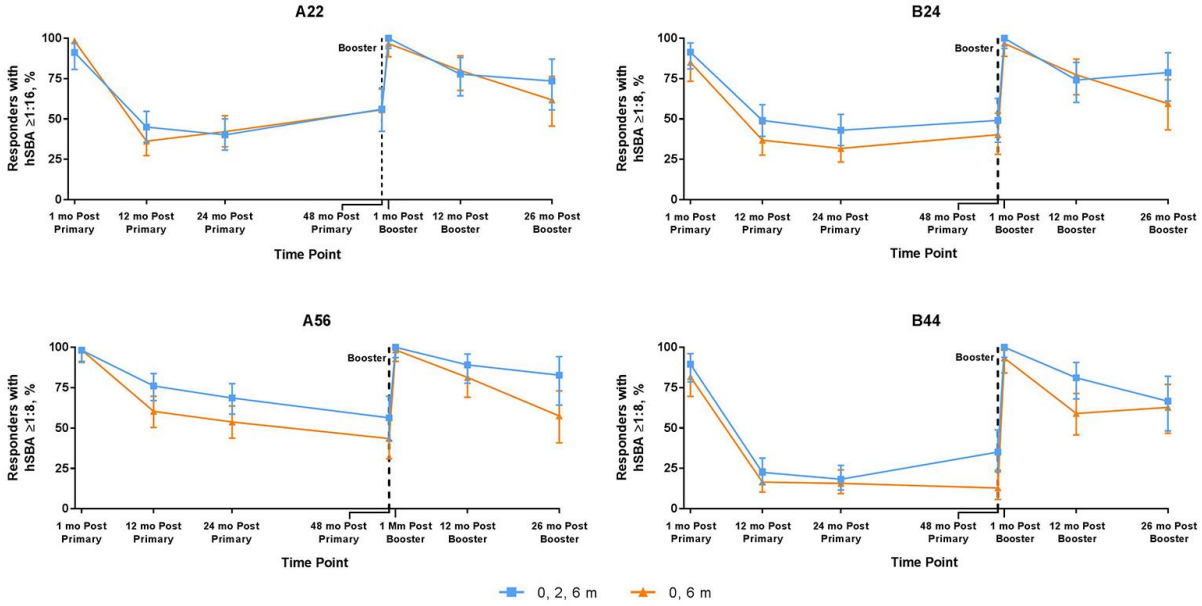

Figure 1. Percentages of subjects acheiving hSBA titers ≥LLOQ against each of the 4 primary strains by time point. Error bars represent 95% CIs. Strains are indicated by the FHbp variants they express. Data for 1 and 48 mo post primary and all postbooster time points used the evaluable immunogenicity population; n=29-58 (0, 2, 6 months); n=40-62 (0, 6 months); data at 26 mo were only available for subsets of subjects in the 0-, 2-, 6- and 0-, 6-month groups. Data for 12 and 24 mo post primary used the modified intent-to-treat population; n=102-111 (0, 2, 6 months); n=103-115 (0, 6 months). Samples for 1 and 48 mo post primary were rerun concomitantly with all post booster samples to allow for comparison. Samples for 12 and 24 mo were not rerun; data represents results from initial runs for the post primary vaccination persistence stage.FHbp=factor H binding protein; hSBA=serum bactericidal assay with human complement; LLOQ=lower limit of quantitation.

Conclusions

A booster dose given 4 years after a licensed 2- or 3-dose MenB-FHbp schedule can be used to elicit robust anamnestic immune responses, providing broad protection for at least 2 additional years to a large proportion of recipients reaching college age who are at continued risk of meningococcal disease.

Clinical Trial Registration (Please input N/A if not registered)

NCT01543087. Funded by Pfizer.

ESPID19-0198
Science Track

ESPID Symposium 16 - Infections in paediatric oncology and HSCT patients

Pharmacokinetic results of a prospective, open-label study: anidulafungin in children aged 1 month-<2 years with invasive candidiasis (ic), including candidemia, or high risk for ic

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Background

An open-label, non-comparative, international study investigated the use of intravenous (IV) anidulafungin in patients aged 1 month-<18 years with (or at high risk for) IC, including candidemia. We present results from the pharmacokinetic (PK) sub-study and a polysorbate 80 (PS80, a solubilising agent for IV anidulafungin) analysis in patients aged 1 month-<2 years.

Methods

The first 6 patients aged 1 month-<2 years with IC were included in the PK sub-study. Patients received IV anidulafungin (3.0 mg/kg loading dose [LD]; 1.5 mg/kg/day maintenance dose) for 10−35 days. Serial blood samples for anidulafungin PK were collected on Days (D)1 and 2. Sparse blood samples for PS80 were collected between D1-D9 from a subset of patients aged 1 month-<2 years (with, or at high risk for, IC [including candidemia]), for analysis by high-performance liquid chromatography/tandem mass spectrometry.

Results

Of 20 patients aged 1 month-<2 years who were enrolled, 6 were included in the PK sub-study, and another 8 (same age group) had PK samples analysed for PS80. Anidulafungin PK (Table 1) was generally comparable to steady-state values reported for adults receiving the approved adult dose (200 mg LD; 100 mg/day): maximum anidulafungin concentration, 7 mg/L; average steady-state area under the concentration−time curve: 110 mg.h/L.PS80 concentrations were below the lower limit of quantification (5.0 mg/L) in all patients except one 20-month old (5.3 mg/L, 5-h post-dose on D1). Anidulafungin was

generally well-tolerated in patients aged 1 month-<2 years.

Table 1. PK parameters of anidulafungin in the PK sub-study population aged 1 month-<2 years

	AUC_{24} (mg.h/L)[a] (N=6)	C_{max} (mg/L)[b] (N=6)	T_{max} (h) (N=6)	T_{last} (h) (N=6)
Geometric mean (CV%)	66.4 (28)	5.96 (29)	NA	NA
Median (range)	70.2 (42.9–87.7)	6.77 (3.91–7.72)	0.39 (0.17–2.25)	24.0 (23.7–24.4)

[a]AUC was calculated based on observed concentration data using the trapezoidal rule without any extrapolation. Where T_{last} was <24 h, actual AUC_{24} was slightly higher than the reported value.

[b]C_{max} was determined without extrapolation. True peak concentration may not be reflected as flexible PK sampling was allowed.

AUC_{24}, area under the plasma concentration–time profile from time 0 to T_{last}; C_{max}, maximum observed concentration; CV%, percent coefficient of variation; NA, not available; PK, pharmacokinetic; T_{last}, time of last quantifiable concentration; T_{max}, time at which C_{max} was observed.

Conclusions

The anidulafungin and PS80 results from these PK sub-studies support the dose regimen of anidulafungin 3.0 mg/kg LD and 1.5 mg/kg/day maintenance dose, in patients aged 1 month-<2 years with, or at high risk for, IC.

Clinical Trial Registration (Please input N/A if not registered)

NCT00761267

ESPID19-0661
Science Track

ESPID Symposium 16 - Infections in paediatric oncology and HSCT patients

Blood stream infections (bsi) caused by candida spp in a reference center for pediatric oncology in latin america: epidemiology and associated factors

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Background and Aims:

Invasive Fungal Disease (IFD) is an important cause of morbidity and mortality in hospitalized and immunosuppressed children, with blood stream infection (BSI) by *Candida spp* being the most prevalent infection. Our aim was to characterize the BSI caused by *Candida spp* in a reference center for pediatric oncology.

Methods:

A retrospective cohort study was carried out through the evaluation of data from medical records patients aged 0 to 18 years, followed-up at the Institute of Pediatric Oncology, São Paulo, Brazil, who presented at least one positive blood culture for *Candida spp* from January 2004 to December 2016.

Results:

Ninety episodes of candidemia were analyzed. The median age was 4.5 years, with a predominance of males (57.8%) and solid tumors (54.5%). The most common *Candida* species were *C. albicans* (35.5%), *C. parapsilosis* (30.0%) and *C. tropicalis* (16.7%). BSI by *C. tropicalis* was positively associated with neutropenia ($p<0.001$) and chemotherapy ($p=0.006$) and inversely associated with presence of CVC ($p=0.009$) when compared to the other species. The majority of patients had fever (87.8%) and patients with *C. tropicalis* had more skin lesions ($p=0.001$). Polyenes were used as first therapeutic option in 68.9% of episodes and in 35.5% antifungal replacement was needed. Therapeutic success was achieved in 63.3% of episodes, with advanced age ($p=0.002$) and thrombocytopenia ($p=0.049$) related to therapeutic failure. Death in 30 days was 24.4%, with advanced age a predictive factor for death ($p=0.008$).

Conclusions:

C. albicans was the most common species isolated and *C. tropicalis* was more related to neutropenia, chemotherapy and development of skin lesions when compared to other species. Death rate was significant, with advanced age associated to a worse prognosis.

Systematic Review Registration:

N/A

ESPID19-0214
Science Track

ESPID Symposium 16 - Infections in paediatric oncology and HSCT patients

New method of differential diagnosis of infectious etiology in febrile pediatric hematology/oncology patients using infrared spectroscopy of peripheral blood

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Background

The objective of this study was to evaluate the potential of the mid infrared spectroscopic method for rapid and reliable identification of bacterial and viral infections based on peripheral blood samples. Fourier transform infrared (FTIR) spectroscopy has been found useful for monitoring the effectiveness of antibiotic treatment in cancer patients with bacterial infections and has been used to distinguish between bacterial and viral etiology, based on an analysis of the blood components.

Methods

Hundred and sixteen events of pediatric hematology oncology admissions were evaluated. White blood cells (WBC) and plasma were isolated from peripheral blood. WBC and plasma from patients with confirmed viral or bacterial infections were evaluated with FTIR spectroscopy. FTIR spectra were analyzed for biomarkers and classified by support vector machine (SVM).

Spectroscopy of diagnostic markers were used for monitoring the biochemical changes in WBCs and plasma during treatment. The obtained spectra were analyzed by multivariate analysis: principal component analysis, followed by linear discriminate analysis, in a time span of approximately one hour after the collection of the blood sample. Each confirmed result was then used to develop and refine an algorithm for prediction of the etiology.

Results

With regular methods (cultures and DNA analysis for viral etiology) 60 samples revealed a bacterial infection and 56 a viral infection. By employing the FTIR spectroscopy of feature extraction with Fisher linear discriminate analysis in order to identify the infectious type, a sensitivity of ~95% and an accuracy of ~81% for an infection type diagnosis were achieved.

Conclusions

The present preliminary study suggests that FTIR spectroscopy of WBCs is a rapid potentially feasible tool for the diagnosis of an infection etiology.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0622
Science Track

ESPID Symposium 17 - Infection or inflammation?

Inflammatory responses of children exposed to m. Tuberculosis but who remain uninfected identify a novel role for eicosanoids in protective mycobacterial immunity

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[4]University of Ghana, Department of Biochemistry- Cell and Molecular Biology, Accra, Ghana
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Background

LTBI is a paradigm of the fine balance between successful host immunity and infection. Children with latent tuberculosis (LTBI) are at high risk of developing active disease. However, the majority of children exposed to *Mycobacterium tuberculosis* (MTB) neither have positive immunological tests for LTBI, nor develop tuberculosis. Understanding this “protective” response may help guide vaccine development.

Methods

Pairs of children with discordant tuberculin skin test results but matched exposure to the same smear-positive tuberculosis index case were recruited from households in The Gambia. Whole blood from these Exposed Infected (EI) and Exposed but Uninfected (EU) children was incubated with a recombinant strain of BCG and supernatants were collected. A targeted mass-spectrometry assay quantified eicosanoids in the supernatants. Mixed effects modelling was used to identify eicosanoid levels that differed between EI and EU children. RNA sequencing data from the same EI and EU children were examined to corroborate the identified pathways of interest. Functional relevance was tested through addition of pharmacologic agonists to *in vitro* THP1 human cell line cultures with pathogenic mycobacteria.

Results

Supernatants from EU children had significantly higher levels of a key eicosanoid metabolite than those from EI children at baseline and in response to BCG at 24 hours. RNA transcripts of two eicosanoid receptors were also increased in whole blood at baseline in EU children compared to EI children. Addition of an FDA-licensed agonist that acts upon these receptors enhanced THP1 killing of *M. abscessus* and MTB *in vitro*.

Conclusions

A novel role for eicosanoid inflammatory responses in effective host control of MTB has been identified and provides opportunities for adjunctive immunotherapy and improved vaccine design.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0043
Science Track

ESPID Symposium 17 - Infection or inflammation?

The diagnostic value of fdg-pet/ct in the assessment of infection or inflammatory disease in children

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Background and Aims:

Fever of unknown origin (FUO) and infection or inflammation of unknown origin (IUO) can be difficult medical situations in paediatrics for which conventional diagnostic workup does not always lead to a final diagnosis. The purpose of this study is to assess the value of FDG-PET/CT in the diagnostic process and follow-up in case of a suspected infection or inflammation in children.

Methods:

In this observational retrospective multicentre study, FDG-PET/CT scans in paediatric patients (0-18 years) from 5 different hospitals in the Netherlands, performed between January 2016 and September 2017 for the indication infection or inflammation, were analysed. The diagnostic value was determined by confirmation of the final diagnosis or exclusion of focal pathology.

Results:

Seventy-one scans from 60 patients were collected (59 diagnostic and 12 follow-up scans). In the diagnostic FDG-PET/CT scans, a final diagnosis was obtained in 44 (75%) patients, where the FDG-PET/CT contributed to the final diagnosis in 29 FDG-PET/CT scans (49%). Of those, 16 scans showed new information compared to previous performed diagnostics. Twenty scans (34%) were helpful in excluding focal pathology. In total, 49 (83%) of the diagnostic FDG-PET/CT scans were clinically helpful. In the follow-up FDG-PET/CT scans, 9 (75%) scans were clinically helpful in mapping disease activity e.g. localisation and or extend of disease. In addition, elevated C-reactive protein (with an optimal cut-off of >54 mg/L) was a positive predictor for a true positive scan result.

Conclusions:

This study showed that FDG-PET/CT is a sensitive and non-invasive method for assessing various infectious and inflammatory diseases when previous diagnostic tools did not lead to a final diagnosis with FDG-PET/CT adding clinical relevant information in 83% of the scans.

Systematic Review Registration:

NA

ESPID19-1199
Science Track

ESPID Symposium 17 - Infection or inflammation?

Comparison of henoch schonlein purpura and kawasaki disease using whole blood gene expression profiling

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Background

Henoch-Schonlein Purpura (HSP) and Kawasaki Disease (KD) are acute multi-system vasculitides with unclear aetiologies, which differ in clinical features and organ involvement. An important difference is involvement of the coronary arteries in KD. We used microarray data to identify significantly differentially expressed (SDE) genes, in order to understand common and distinct biological pathways, and we compared this overlap in KD patients with and without coronary artery aneurysms (CAA)s.

Methods

We compared Illumina microarray gene expression data from children with acute KD (n=78) and HSP (n=17) to healthy children (convalescent KD patients, n=9) recruited in the UK and USA. We compared SDE genes found in HSP and KD, to identify unique and overlapping transcripts. Findings were correlated with the clinical phenotype based on presence of CAA. The biological function of the differentially expressed genes was interrogated using pathway analysis in R studio (tmod) and Ingenuity Pathways Analysis.

Results

There were 462 and 9584 SDE genes when acute KD and HSP were compared to healthy children, respectively. There was strong overlap, with Xx of 250 transcripts SDE in HSP also found in acute KD. Of 8 transcripts not concordantly regulated, 2 showed orthogonal expression. KD children with CAAs had less overlap with HSP, and pathway analysis identified that the discordant genes were enriched for nuclear pore pathways.

Conclusions

KD and HSP showed strong differences in the extent of transcript regulation. However, SDE transcripts in HSP were largely shared with KD, which may reflect a common vasculitis core signature. KD children with CAA had less overlap with HSP. Transcripts associated with nuclear pore transport were downregulated in HSP and KD, but not in those with CAAs.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESPID19-0562
Science Track

ESWI/ESPID Joint symposium 06 - Influenza prevention and children: current issues and developments

Immunogenicity and safety of mf59-adjuvanted quadrivalent influenza vaccine in children after revaccination

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[4]Seqirus Netherlands BV, Clinical Science and Strategy, Amsterdam, The Netherlands
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Background

Higher efficacy, enhanced immunogenicity and an acceptable safety profile of MF59-adjuvanted influenza vaccines in unprimed young children were demonstrated in several clinical studies. However, immunogenicity and safety of revaccination with adjuvanted quadrivalent influenza vaccine (aQIV) in children have not been evaluated extensively. We performed this study to assess immunogenicity and safety of repeated administration of aQIV in children primed with aQIV in a previous season.

Methods

In total, 1601 children,18 to 87 months of age, who received aQIV or QIV in a previous study (Vesikari T, Lancet Resp. Med. 2018) were enrolled and randomly assigned to receive, in a 1:1 ratio, a dose of the same or the alternate vaccine. The vaccine-specific immune response was assessed at baseline, 21 and 180 days after vaccination using hemagglutinininhibition (HI), microneutralization, and anti-neuraminidase assays. Reactogenicity (7-day) and safety (12-month) were assessed in all subjects.

Results

At baseline, HI GMTs were higher across all strains in subjects who received aQIV vs. QIV in the parent study. In aQIV primed subjects, Days 22 and 181 HI antibody responses demonstrated immunological superiority of aQIV over QIV for 3 of 4 homologous strains (A/H1N1 and both B strains). Superior HI immune response of aQIV vs. repeated administration of QIV was demonstrated for the same homologous strains.

The proportion of subjects who had solicited AEs, in particular, systemic AEs, was generally higher with aQIV than QIV, regardless of treatment assignment (aQIV vs. QIV) in the parent study. The frequency and severity of solicited AEs were similar in both studies.

Conclusions

This study demonstrates immunological benefit and an acceptable safety profile of revaccination with aQIV in young children primed with aQIV and supports the use of aQIV for annual vaccination.

Clinical Trial Registration (Please input N/A if not registered)

NCT01964989

ESPID19-0660
Science Track

ISTM/ESPID Joint symposium 07 - Children on the move - practical aspects on travel medicine and migrant health

Screening for infection in unaccompanied asylum seeking children - a clinical audit across two paediatric infectious disease clinics in london, uk.

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Background and Aims:

There has been a significant increase in unaccompanied asylum seeking children (UASC) arriving in Europe in recent years. Many originate from countries with high rates of infections, often treatable in the asymptomatic stage preventing progression to severe disease and transmission to others. In the UK, referral to specialist clinics for TB testing is recommended, providing an opportunity to screen for other infections.

Methods:

We carried out an audit across two hospitals to determine if UASC infection screening was offered as recommended by national guidance and to assess infection rates. Data were anonymously extracted from patient records into an Excel database for patients seen between January 2016 and December 2018.

Results:

252 individuals from 19 countries were included, 88% were male, median age was 17 years (range 11-18). 55 were from Afghanistan, 51 from Eritrea. 94% (238) were tested for TB, of whom 23% were positive (including 3 with active TB). 211 were tested for Hepatitis B, C and HIV, of whom 4.8% were positive for Hepatitis B, 0.5% for Hepatitis C and none for HIV. Of the 127 tested, 8.6% had giardia and 7% tapeworm. 14% of those tested were positive for schistosomiasis. Median time between arriving in the UK and infection screening was 6 months (range 1-60 months, data available on 197 children).

Conclusions:

We demonstrate clinically significant rates of treatable infections. Patients were offered testing recommended by national guidance but delay in screening could delay treatment and lead to symptomatic disease and increased risk of transmission. Work is underway to reduce delays to appointment Our data suggest benefit in timely screening for infectious diseases for all UASC. More data are needed to inform formal guidance.

Systematic Review Registration:

ESPID19-0912
Science Track

ISTM/ESPID Joint symposium 07 - Children on the move - practical aspects on travel medicine and migrant health

Infectious diseases among refugee children at a tertiary care children's hospital in greece

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Background and Aims:

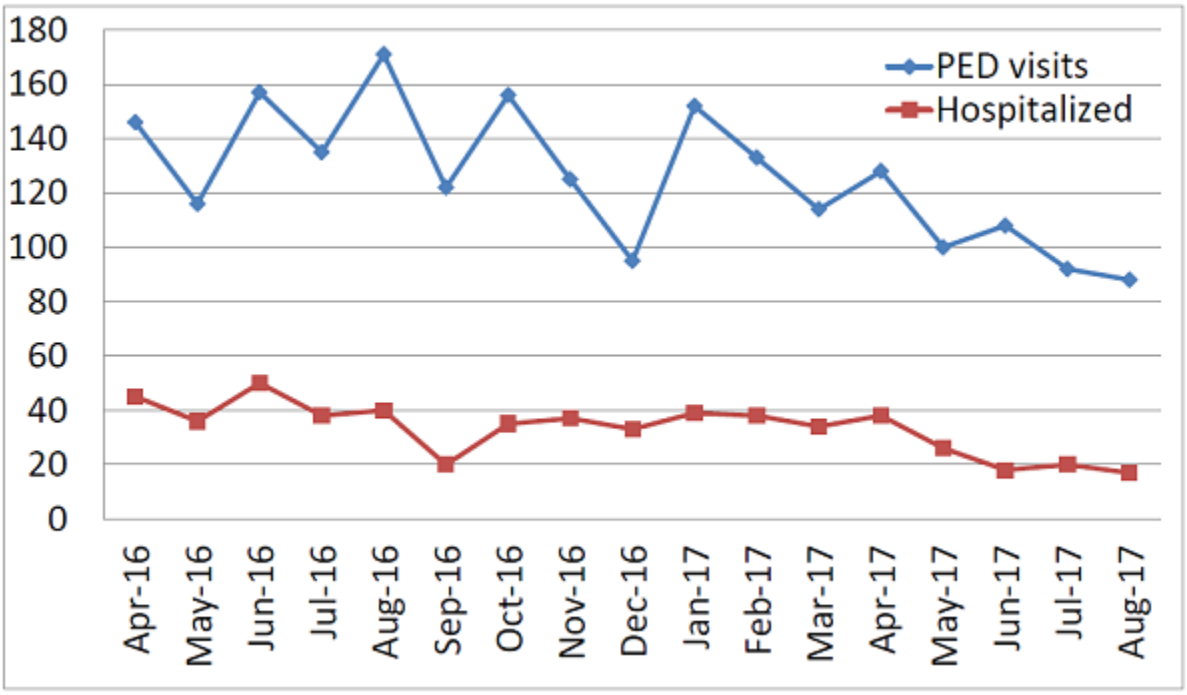
Concerns about emerging and re-emerging infectious diseases(IDs) in refugees have been raised due to the high influx in Europe in the past few years. Greece is the country of first arrival in Europe, as more than 200.000 refugees arrived during 2016-2017, 32% being children. Data on IDs among these children are limited.

Methods:

The aim of this study was to describe the burden of IDs among refugee children presenting at a tertiary care children's hospital in Athens, Greece. We retrospectively recorded and evaluated children(0-16 years) that presented to the Emergency Department(ED) and admitted το the general Paediatric wards during an 18-month period(03/2016-08/2017).

Results:

A total of 2.200 children(57% males) visited our ED. Median age was 2 years old(range:6 days-16 years). The main countries of origin were Syria(52%) and Afghanistan(26%). The highest admission rate per month was recorded in 08/2016(n=171children) while the lowest was in 08/2017(n=88children). Most of the visits were due to infectious diseases(71%) and the main reason for admission was fever(45%). The commonest site of infection among non-hospitalized children was the respiratory tract(67.3%), followed by the gastrointestinal tract(17%). Hospitalization rate was 26.6%(n=584 children). Median age of hospitalized children was 22 months(range:6 days-15 years) and the commonest reason for hospitalization was upper and lower respiratory tract infections(73.5%). A case of active tuberculosis and 5 cases of cutaneous leishmaniasis were diagnosed. As long as vaccine preventable diseases are concerned, 32 cases of varicella and 12 cases of hepatitis A were recorded. All children recovered well and were discharged from the hospital.



Conclusions:

The most important health issue that refugee children face are common and often vaccine preventable IDs. The risk importation of rare and serious infectious diseases in Europe appears to be very low.

Systematic Review Registration:

ESPID19-0832
Science Track

ISTM/ESPID Joint symposium 07 - Children on the move - practical aspects on travel medicine and migrant health

Evaluation of immigrant children referred for a positive tst with an interferon gamma release assay (igra): a 4-year experience at a tuberculosis referral center.

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Background and Aims:

With waves of refugees crossing country borders, public health systems in Europe have raised concerns over transmission of diseases such as Tuberculosis (TB). Tuberculin skin test (TST) has been widely used as screening tool when refugees arrive in the European borders. In this study, we examined the specificity of TST in the diagnosis of TB among refugee children

Methods:

This was a prospective study of refugee children referred to our clinic with positive TST between 2014-2018. Positive TST was defined as an induration ≥10mm regardless of BCG vaccination status. Demographic, epidemiological and socioeconomic data, prior BCG vaccination and history of contact with an adult index case were recorded. All subjects underwent further investigation with CXR and QuantiFERON-TB Gold In-Tube test (QFT-GIT).

Results:

Overall, 128 children were referred for evaluation of positive TST [mean age 8y (range 1mo-17y)]. Of them, 77(60%) tested negative with QFT-GIT and 32/77 (41,5%) had no evidence of prior BCG vaccination. Latent TB infection was diagnosed in 42/128 subjects (32.8%) and TB disease in 9/128 cases (7%). The majority of refugees originated from Afganistan, Syria, Pakistan, India and Iraq. Median TST size for QFT-GIT(-) subjects was 13mm (range:10-25mm) while for latent TB infection or active TB was 17mm .

Conclusions:

Almost half of refugee children referred with positive TST and no history of prior BCG vaccination were found to have negative QFT-GIT. Refugees originating from countries with high disease burden need to be tested with IGRAs along with TST in order to confirm the diagnosis and avoid unnecessary treatment for latent TB.

Systematic Review Registration:

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ESPID19-0247
Science Track

ISTM/ESPID Joint symposium 07 - Children on the move - practical aspects on travel medicine and migrant health

A single dose of diphtheria-tetanus-pertussis vaccination is sufficient to generate long-term protection in most migrant

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Background and Aims:

Worldwide infant immunization coverage for 3 doses of Diphtheria-Tetanus-Pertussis is high. Therefore, despite the lack of written evidence of past vaccinations, most children do not require complete revaccination, as it's proposed in some protocols. Our primary objective is to describe vaccine protection against tetanus among migrant children after a single booster dose. Our secondary objective is to identify potential determinants of vaccine response.

Methods:

Newly arrived migrant children were prospectively enrolled between October 2014 and August 2017 at the Lausanne University Hospital. Patient aged 1 to 18 years were approached for inclusion if they had no proof of past vaccinations and accepted a single dose of Tetanus-Toxoid-containing vaccine (TTCV). Anti-tetanus toxoid antibodies (anti-TT) was performed after 4 to 6 weeks. Anti-TT ≥1IU/mL were considered as evidence of a booster-type response. Patients with anti-TT <1IU/mL received additional dose(s) of TTCV. Potential determinants of vaccine response were identified using univariate and multivariate linear regression analyses.

Results:

Two hundred and eight children were available for analysis. Mean age was 9.0 years (SD 4.5), and 100 (48%) were female. The majority (n=129, 62%) came from the eastern Mediterranean WHO region. Two hundred and five children (98.6%) had a booster-type response. A Syrian origin ($p<0.001$) and a direct arrival in Switzerland (without transiting through other European countries) ($p=0.029$) were statistically significantly associated with a higher anti-TT level, in a multivariate regression model (multiple $r2=0.210$).

Conclusions:

A single dose of Diphtheria-Tetanus-Pertussis vaccination is sufficient to generate long-term protection in most migrant children. Determinants associated with a higher antibody response might be associated with a higher number of previous vaccine doses. No systematic revaccination protocol is needed. Post-vaccine serology should be used to determine the indication for additional doses.

Systematic Review Registration:

257/14

ESPID19-0350
Science Track

MSF/ESPID Joint Symposium 04 - Paediatric infectious disease in unstable settings

Migrant infections were a problem but not the cause of resurgence of measles epidemics in 2013-2014 in southern china

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Background and Aims:

In Guangdong, the largest province in Southern China, the 2009 province-wide and 2010 nation-wide supplementary immunization activities (SIAs) have greatly reduced the measles prevalence. However, a resurgence of measles epidemics started in 2013 with a high prevalence persisted for years. Officials specifically points out non-vaccinated migrants as one of the main causes. In this study, we examined the association between migrant infections and the resurgence of epidemics in 2013-2014.

Methods:

A total of 22,362 clinically and laboratory confirmed measles cases from 2009 to 2014 were extracted from the National Infectious Disease Monitoring Information System by the Centers for Disease Control and Prevention of Guangdong Province. The epidemiological characteristics of the migrant infections were compared between two periods of 2009-2012 to 2013-2014.

Results:

We found migrant infections were not significantly associated with the resurgence of measles epidemic in 2013-2014. Nevertheless, we found substantial increases in the proportions of infections from children aged <8 months and from the unvaccinated population in both local and migrant infections (p<0.0001). In general, migrant infections were more from individuals aged 16 to 30 years or unvaccinated when comparing with the local infections in two different periods.

Conclusions:

Migrant infections were probably not the major cause to the resurgence of measles epidemic in 2013-2014. Rather, the resurgence was likely due to the infections from children aged <8 months and from the unvaccinated population in both local and migrant individuals. The results thus advise officials prioritizing the control measures such as SIAs on particular age groups.

Systematic Review Registration:

NA

ESPID19-1046
Science Track

PIDS/ESPID Joint Plenary Symposium 01 - The future of vaccines (is now)

Phase 3 PREPARE study: efficacy and safety of an RSV vaccine administered to pregnant women

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Background

Respiratory syncytial virus (RSV) is the leading cause of infant lower respiratory tract infection (LRTI) hospitalization worldwide; the burden of severe RSV LRTI is greatest in infants ≤4 months old. The objective of the ongoing PREPARE trial is to assess the efficacy and safety of maternal immunization with RSV F nanoparticle vaccine in protecting young infants against RSV-positive, medically significant LRTI through the first 90-180 days of life.

Methods

PREPARE is a randomized, observer-blinded, placebo-controlled, phase 3 trial conducted over 3.5 years in 11 countries. Healthy women 18-40 years of age with low-risk, singleton pregnancies were injected with a single dose of RSV F nanoparticle vaccine or placebo between 28 and 36 weeks' gestation. Maternal immune responses, and transfer and persistence of RSV-specific antibodies in infants, were evaluated. Infants were monitored via active and passive surveillance for RSV LRTI during their first RSV season through 6 months of age. The primary efficacy endpoint is the proportion of infants with medically significant RSV LRTI, defined by physician examination and objective measures of hypoxemia or tachypnea, occurring from delivery through 90, 120, 150, and 180 days of life. Key secondary and exploratory endpoints include RSV-related hospitalization, presence of severe hypoxemia, and symptomatic maternal RSV infections. Safety is monitored in mothers through 9 months after treatment and infants through 12 months after delivery.

Results

A total of 4636 pregnant women were enrolled. Preliminary efficacy and safety data from PREPARE will be available Q1 2019.

Conclusions

Passive protection of infants via maternal immunization with the RSV F nanoparticle vaccine was well tolerated and may protect against medically significant RSV-associated LRTI and hospitalization in the first 6 months of life.

Clinical Trial Registration (Please input N/A if not registered)

NCT02624947

ESPID19-1071
Science Track

WHO/ECDC/ESPID Joint symposium 15 - Big issues for vaccination in Europe and beyond

Reasons of delayed vaccination against measles

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Background and Aims:

Background: Measles has re-emerged during the previous two years in Europe, including Greece, showing that, despite the presence of a safe and effective vaccine, elimination of the disease has not yet been achieved.

Aim: In this study we describe the reasons of delayed vaccination in the pediatric population in Crete.

Methods:

In collaboration with the regional state health and education authorities, we checked immunization records of all children attending primary school. Families of children with missing doses were called by telephone, asked for the reasons of delayed vaccination and advised on the importance of and the practicalities of fulfilling the vaccination schedule. A second telephone contact was followed six months later to assess the outcome of the intervention.

Results:

Starting from November 2016, 27,020 vaccination records have been checked from children attending all primary schools in Crete. 2 doses of measles vaccine were documented in 25,111 (91.6%), 1 dose in 1,476 (5.53%) and no doses in only 103 (0.39%) children. A total of 1,369 (86.7%) families were advised on the missing doses. Medical contra-indication was perceived in 18 cases and vaccine hesitancy in 9. In 11 cases parents asked for more information by an Infectious Disease expert. In 34 cases, families have not yet proceeded to vaccination because of medical insurance issues. In all other cases, the cause of delayed of vaccination was carelessness. The assessment of the outcome of these interventions with the second telephone contact showed great response to our advice for immediate vaccination due to the current outbreak (81.2% of the families reached).

Conclusions:

The delayed immunization of the children is often a matter of omission rather than true vaccine hesitancy. Intensive prevention policies may work well in vaccine-preventable diseases.

Systematic Review Registration:

ESPID19-0968
Science Track

WHO/ECDC/ESPID Joint symposium 15 - Big issues for vaccination in Europe and beyond

The associations between mandatory vaccination in europe and incidence of measles and pertussis and vaccination rates

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Background and Aims:

Examine associations between vaccination mandate policies and subsequent vaccination coverage and measles and pertussis incidence in 29 European countries.

Methods:

We conducted a longitudinal analysis of country-level vaccine coverage and measles and pertussis incidence in 29 European countries included in the Vaccine European New Integrated Collaboration Effort. The primary outcomes of interest were measles and pertussis incidence and vaccine coverage in countries with mandatory vaccination versus countries without mandatory vaccination.

Results:

Mandatory vaccination was associated with 3.00 (95% Confidence Interval: 0.35 to 5.64) percentage points higher prevalence of measles vaccination and 2.14 (0.13 to 4.15) percentage points higher of pertussis vaccination when compared to countries that did not have mandatory vaccination. Mandatory vaccination was associated with decreased measles incidence, but only for countries without non-medical exemptions (adjusted Incidence Rate Ratio =0.14, 95% Confidence Interval: 0.05 to 0.36). We did not find a significant association between mandatory vaccination and pertussis incidence. Among countries that impose a monetary fine for non-compliance, every €500 increase in the maximum possible penalty was associated with an increase of 0.8 (0.50 to 1.15) percentage points for measles vaccination coverage and an increase of 1.1 (0.95 to 1.30) percentage points for pertussis vaccination coverage. The presence of a fine was associated with lower incidence rates of measles (adjusted Incidence Rate Ratio = 0·14, 95% Confidence Interval: 0.05 to 0.39) and pertussis (adjusted Incidence Rate Ratio=0.42, 95% Confidence Interval: 0.18 to 0.98).

Conclusions:

Mandatory vaccination and the magnitude of fines were associated with higher vaccination coverage. Moreover, mandatory vaccination was associated with lower measles incidence for countries with mandatory vaccination without non-medical exemptions. These findings can inform legislative policies aimed at increasing vaccination coverage.

Systematic Review Registration:

N/A

ESPID19-0537
Science Track

WHO/ECDC/ESPID Joint symposium 15 - Big issues for vaccination in Europe and beyond

Impact of mandatory vaccination extension on infant vaccine coverages in france

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[8]Institut des Mamans, Na, Issy-les-Moulineaux, France
[9]Université de Lille, Santé publique : épidémiologie et qualité des soins, Lille, France

Background and Aims:

In France, infant vaccines protecting against 11 diseases have changed from a recommended to a mandatory status for all children born on or after January 1, 2018. Using the Vaccinoscopie survey, we measured the impact of this new vaccination policy on perception of mothers towards vaccination and on vaccine coverage rates (VCRs) of infants in their first year of life.

Methods:

Vaccinoscopie is a French annual survey conducted by the Institut des Mamans on behalf of GSK manufacturer since 2008. It is an online standardized questionnaire survey including 1000 mothers of 0 to 11-month-old infants interviewed on their opinion and attitude towards vaccination. They also report all the vaccines recorded in their child's health record.

Results:

Mothers were more favorable to mandatory vaccination and better informed on vaccination in 2018. VCRs for at least one dose at 6 months of age strongly progressed for diseases that previously did not meet Public Health objectives (in 2017 and 2018, from 88.7 to 96.8% for Hepatitis B (HepB) and from 43.0 to 74.2% for Meningococcal C). For the complete primovaccination at 6 months of age (2 doses), HepB VCR increased from 86.3 to 95.5%. VCRs for the other diseases were already very high and did not significantly increase.

Conclusions:

These first results showed that the extension of mandatory vaccination associated with the communication strategy implemented by the French Authorities had a positive impact on both mothers' opinion regarding vaccination and on infant VCRs. The 2019 Vaccinoscopie survey will help further evaluate the impact of mandatory vaccination on infant VCRs.

Systematic Review Registration:

N/A

ESPID19-0827
Science Track

WHO/ECDC/ESPID Joint symposium 15 - Big issues for vaccination in Europe and beyond

Building resilient public trust in vaccination: the international pediatric association (ipa) vaccine hesitancy master trainer program

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Background and Objective

Vaccine hesitancy is an existential threat to immunisation programs: the World Health Organisation recently identified it as one of the 10 threats to Global Health in 2019. The WHO defines vaccine hesitancy as "*a delay in acceptance or refusal of vaccines despite availability of vaccination services*". Vaccine hesitancy may lead to a spectrum of behaviours ranging from cautious acceptance, to a delay of one or more vaccinations, or active refusal. Socio-psychological research has identified myriad possible demographic or socio-psychological root causes, which may change with context and over time. However, one determinant of vaccine acceptance that is consistently shown to correlate with vaccination behavior is a recommendation from a healthcare provider (HCP), who are almost always the most trusted voice on vaccines.

Methods

Any national strategy to address vaccine hesitancy should effectively empower, equip and galvanise HCPs to recommend and discuss vaccination.

Learning Points Discussion

The IPA is currently leading a global initiative to develop master trainers in multiple training modules on vaccine confidence. The objective of this initiative is to develop Master Trainers who will return to their countries to train other HCPs to: (i) Have more effective conversations with patients on vaccination (and healthy preventative behaviors) using the AIMS methodology; (ii) empower national pediatrics societies & paediatricians to advocate the need for effective vaccination programs; (iii) become media go-to experts on vaccination; and (iv) become influencers in the social media conversation on vaccines. Pilot workshops in Delhi & Panama have trained over 70 pediatricians from 30 countries. We are currently determining how to build a sustainable training program and network of trainers to support countries to instill a resilient HCP & public confidence in vaccination.