Invited Speaker Abstracts

ESPID-1134
ESPID ORGANISED SYMPOSIUM 1: GLOBAL PERSPECTIVES ON ARTHROPOD-BORNE INFECTIONS

LYME DISEASE

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Lyme borreliosis (LB) is the most common tick-borne disease in Europe and North America. It affects children and adults; its incidence is increasing in many countries. The disease is caused by spirochaetes of the *Borrelia burgdorferi* sensu lato complex, in Europe predominantly by *Borrelia afzelii* and *Borrelia garinii*, rarely by *Borrelia burgdorferi* and only exceptionally by other *Borrelia* species, whereas in North America *B. burgdorferi* is the only causative agent. In LB involvement of several tissues/organs can occur. The most common clinical manifestation is erythema migrans, a skin lesion that develops at the site of an infected tick bite, which eventually resolves, even without antibiotic treatment. Nevertheless, *Borreliae* can spread from skin to other tissues/organs, resulting in additional manifestations. A complete clinical presentation, in which a skin lesion develops at the site of a tick bite, and is followed by hearth and nervous system involvement, and later by arthritis, is rare. For a reliable diagnosis of LB clinical signs should be present and laboratory evidence of infection with *Borreliae* is needed. The only sign that enables a trustworthy clinical diagnosis of LB is erythema migrans. Earlobe lymphocytoma, meningoradiculoneuritis (Bannwarth's syndrome), and acrodermatitis chronica atrophicans are also of diagnostic significance, while diagnostic value of several other signs and especially symptoms is low. After 2-4 weeks treatment with antibiotics most patients make an uneventful recovery, however therapy is most successful early in the course of the illness. Prevention relies mainly on protection against tick bites. No vaccine is available for human beings.

ESPID-1105
ESPID ORGANISED SYMPOSIUM 2: VACCINE DEVELOPMENTS UNDER DEBATE

VARICELLA AND ZOSTER VACCINATION

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Varicella is frequently believed to be a mild childhood disease. However, disease complications are meaningful in terms of frequency and severity, leading to hospitalization and significant morbidity including long term sequelae and death. Accordingly, several countries have introduced immunization programs to reduce the burden of this disease not only in primary healthy individuals but also to achieve indirect protection of individuals with increased risk for complications, as is the case for immunosuppressed patients. Success and challenges of such immunization programs will be discussed. Moreover, an outlook on zoster vaccination will be given.

ESPID-1142
ESPID ORGANISED SYMPOSIUM 2: VACCINE DEVELOPMENTS UNDER DEBATE

ACCELERATING CLINICAL TRIALS FOR NEW VACCINE DEVELOPMENT

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In August 2014 the escalating Ebola virus disease outbreak in West Africa led to efforts to undertake an unprecedented accelerated vaccine development programme. This aimed to initiate a phase I first-in-human trial within weeks and move to a large phase III efficacy trial in West Africa in four months. This was achieved with considerable efforts from many collaborating parties. A chimpanzee adenovirus vectored vaccine moved from a phase I trial in Oxford and a phase Ib trial in Mali to an efficacy trial which started in January 2015.

This very unusual experience of compressing a clinical trial programme as part of an emergency response provides some insight into how the general process might be accelerated. I suggest opportunities for streamlining clinical development and biomanufacturing and associated review processes that could not just accelerate the development of new vaccines but might considerably reduce the excessive costs of vaccine and drug development.

ESPID-1092
ESPID ORGANISED SYMPOSIUM 2: VACCINE DEVELOPMENTS UNDER DEBATE

VACCINES OF THE FUTURE

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Vaccination has been the most effective medical intervention in the history of mankind. Infectious diseases that used to kill or cause disability in millions of people annually such as diphtheria, tetanus, smallpox, polio, measles, mumps, and rubella were conquered during the last century with the first wave of vaccines. The second wave of vaccination started during the 1980s and consisted of vaccines that were made possible by the new technologies such as recombinant DNA, conjugation, genomics, that allowed the development of vaccines against Hepatitis B, papillomavirus, Haemophilus influenzae, penumococcus, and meningococcus. Thanks to the advances in understanding of the structure of the antigens and their epitopes and how they interact with the human immune system we are now entering the third wave of vaccine development, characterized by optimal design antigens, adjuvants, and delivery systems. This new phase is expected to tackle disease such as tuberculosis, malaria, and HIV that have, so far, been refractory to vaccine development, to boost the field of therapeutic vaccination and to optimize the response against infectious disease that are not yet controlled by vaccination such as influenza and respiratory syncytial virus.

ESPID-1113
ESPID ORGANISED SYMPOSIUM 3: SKIN INFECTIONS

ATOPIC ECZEMA AND THE MICROBIOME

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The skin in atopic dermatitis is highly colonised by Staphylococcus aureus and other staphylococcal species which exist on dry skin zones in mild, as well as in severe disease manifestations. The role of staphylococci has been elusive until now. However, the current hypothesis is that Staphyloccoccal antigens are thought to act as super-antigens causing non-specific symptom exacerbation. Therefore, increased staphylococci colonization/infection could be responsible for flares. Reducing bacterial load will result in clinical improvement.

The human microbiome (from the Greek micro "small" and bios "life") is a "living organism" existing on various bodily surfaces. The cutaneous microbiome is an ecosystem composed of trillions of microorganisms (bacteria, yeast, viruses, fungi etc.) which colonise the stratum corneum. Recently, it was shown that the microbiome or biofilm differs from normal skin in atopic dermatitis, and psoriasis. Staphylococci form a biofilm thus playing a dominant role in the occluding sweat ducts, leading to inflammation and pruritus.

This may also explain why regular baths of diluted bleach (sodium hypochlorite) and intranasal application of mupirocin ointment reduces the disease severity in both children and adults, in particular with secondarily infected eczema. Severe childhood atopic dermatitis has been show to be successfully treated with wet wraps (‘wet pyjama”) and diluted corticosteroids but also with antiseptics and therefore indirectly supporting the role of the microbiome.

A next step will be the development of emollients with antibacterial effects, that will result into a balanced microbiome in the damaged involved and non-involved atopic skin and restore a normal skin microbiome.

ESPID-1114
ESPID ORGANISED SYMPOSIUM 3: SKIN INFECTIONS

SKIN INFECTIONS THROUGH PETS

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Animals kept as pets have evolved alongside humans. As companions they have proven health benefits. With increasing urbanisation and densification of housing, there is a trend towards pocket-pets and the importation of exotic species, some from the wildlife pool. There are some infection risks, especially to children, of living close to and closely with pets, not least because of contamination of the environment around such animals. This session will focus on skin infections associated with pets. Examples will be given of the skin manifestations of zoonotic infections in humans acquired from the bites, scratches and exoparasites of pets as well as from their fur, skin and scales.

ESPID-1103
ESPID ORGANISED SYMPOSIUM 4: HOSPITAL ACQUIRED INFECTIONS

Manipulating the Microbiome to Prevent HAIs

A. Milstone[1]
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Healthcare associated infections (HAIs) lead to morbidity and mortality among vulnerable children. HAIs due to multidrug-resistant organisms (MDROs) occur with increasing frequency. MDROs and other members of the microbiome colonize hospitalized children, and these endogenous organisms often cause HAIs. To prevent infections, strategies have emerged to manipulate the microbiome. These measures include reduction in bioburden, targeted eradication (decolonization), and repopulation or replacement. Studies have found that manipulating the microbiome may reduce MDRO transmission and prevent HAIs. Additional studies on altering the host microbiome are needed to evaluate the efficacy in preventing infections and to monitor for unintended consequences that may result.

ESPID-1139
ESPID ORGANISED SYMPOSIUM 4: HOSPITAL ACQUIRED INFECTIONS

BUNDLE APPROACHES IN THE PREVENTION OF NOSOCOMIAL INFECTIONS IN CHILDREN

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INICC apply following strategy in NICUs and PICUs worldwide: Before-after prospective surveillance study. During Baseline Phase we performed just active surveillance, and during Intervention Phase the INICC multidimensional infection control approach include the following practices: (1) HAI care bundle, (2) education, (3) outcome surveillance, (4) process surveillance, (5) feedback of HAI rates, and (6) performance feedback of infection control practices. We compared HAI rates obtained during both phases. We calculate rates, and, using random-effects Poisson regression to allow for clustering by ICU, we calculate the incidence rate ratio (IRR) for each follow-up time period compared with the 3-month baseline. Following are 5 examples of INICC strategy:

Infect Control Hosp Epidemiol. 2012 Jul;33(7):704-10. VAP reduction in NICUs of Argentina, Colombia, El Salvador, India, Mexico, Morocco, Peru, Philippines, Tunisia, and Turkey. Baseline Phase: 3,153 MV-days (17.8 VAP per 1000-MV-days). Intervention Phase: 15,981 MV-days (17.8 per 1,000-MV-days). RR=0.67 [95%CI=0.50-0.91].

Am J Infect Control. 2012 Aug;40(6):497-501. VAP reduction in PICUs. Baseline Phase: 5,212 MV-days (11.7 VAP per 1,000-MV-days). Intervention Phase: 9,894 MV-days (8.1 per 1,000-MV-days). RR=0.69; 95%CI=0.5-0.96; P=0.02.

Infect Control Hosp Epidemiol. 2013 Mar;34(3):229-37. CLAB reduction in NICUs of El Salvador, Mexico, Philippines, and Tunisia. Baseline Phase: 21.4 CLAB per 1,000-CL-days. Intervention Phase: 9.7 per 1,000-CL-days. (RR=0.45 [95%CI=0.33-0.63]).

Infection. 2012 Aug;40(4):415-23. CLAB reduction in PICUs of Colombia, India, Mexico, Philippines, and Turkey. Baseline Phase: 1,029 CL-days (10.7 CLAB per 1,000-CL-days). Intervention Phase: 3,861 CL-days (5.2 per 1,000-CL-days). RR=0.48, 95%CI=0.29-0.94, P=0.02).

Infect Control Hosp Epidemiol. 2012 Jul;33(7):696-703. CLAUTI reduction in PICUs of Colombia, El Salvador, India, Mexico, Philippines, and Turkey. Baseline Phase: 1,513 UC-days (5.9 CAUTI per 1,000-UC-days). Intervention Phase: 7,000 UC-days (2.6 per 1,000-UC-days). RR=0.43 [95%CI=0.21-1.0])

ESPID-1129
ESPID ORGANISED SYMPOSIUM 5: CHANGING FACES OF NON TUBERCULOUS MYCOBACTERIAL (NTM) INFECTIONS

GENETIC AND CLINICAL ASPECTS OF NTM INFECTIONS

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Non-tuberculous mycobacteria (NTM) are emerging pathogens with respect to the frequency of isolation from usually sterile sites, and occurence of novel phenotypes. Association of NTM with diseases other than self-limiting lymphadenitis is always suspicious of (specific) immunodeficiency, yet in many cases even detailed immunophenotyping does not reveal a defined underlying disease. Accordingly, despite advances in microbiological and immunological diagnostics, we are far from fully understanding the spectrum of NTM infections both regarding the virulence of the organism, and the quality of the specific host response.

ESPID-1141
ESPID ORGANISED SYMPOSIUM 5: CHANGING FACES OF NON TUBERCULOUS MYCOBACTERIAL (NTM) INFECTIONS

INTERFERON-GAMMA RELEASE ASSAYS FOR THE DIAGNOSIS OF TUBERCULOUS AND NON-TUBERCULOUS MYCOBACTERIAL INFECTIONS

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Interferon-gamma release assays (IGRAs) were licensed for use in the routine clinical diagnostic setting more than a decade ago and yet there are many unanswered questions remaining. This talk will focus on the performance of IGRAs in both tuberculosis (TB) and disease caused by non-tuberculous mycobacteria in children. In particular, during this talk the limitations of IGRAs in both settings will be discussed, including their suboptimal performance in active TB, the issues surrounding indeterminate assay results and the discordance with tuberculin skin test results. Finally, novel immune-based diagnostic approaches will also be discussed briefly.

ESPID-1128
ESPID ORGANISED SYMPOSIUM 6: CURRENT PROBLEMS IN PEDIATRIC INFECTIOUS DISEASES

CLOSTRIDIUM DIFFICILE -ASSOCIATED DISEASE IN CHILDREN

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Clostridium difficile is the most common cause of health care–associated diarrhea among adults and is associated with significant morbidity and mortality. During the past decade, the epidemiology of C difficile infection (CDI) has changed, including a rise in the rate and severity of infection related to the emergence of a hypervirulent strain as well as an increase in disease among outpatients in community settings. Although less is known about CDI among pediatric patients, C difficile is increasingly recognized as an important pathogen among children. recent updates in the incidence and epidemiology of CDI among children, including risk factors for infection, and highlight the importance of CDI in special populations of children, particularly those with inflammatory bowel disease or cancer will be presented. In addition, we review current knowledge in the areas of diagnosis and management of CDI among children and highlight future areas for research.

ESPID-1086
ESPID ORGANISED SYMPOSIUM 6: CURRENT PROBLEMS IN PEDIATRIC INFECTIOUS DISEASES

TREATMENT OF MDR-PATHOGENS IN CHILDREN

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Due to both biologic evolution and misuse of antibimicrobial agents, antimicrobial resistance of bacteria causing pediatric infections has escalated, being more common and complicated in recent years. Although formerly confined to hospital settings, multi-drug resistant (MDR) bacteria currently cause also community-acquired infections. Very frequent travel and economic globalization have led to the rapid and extensive spread of MDR bacteria that are sometimes resistant to all currently available antibiotic agents.

Treatment of infections caused by resistant pathogens is difficult, necessitating thinking both inside and outside the box. Determination of the precise minimal inhibitory concentration (MIC) is often crucial for selecting the most appropriate antibiotics, their doses, and utilization of the prolonged infusion method. For some MDR bacteria, off-label use of antibiotics, sometimes without evidence of controlled studies ("salvage therapy"), is unavoidable.

The definition and impact of MDR bacteria will be defined. Current recommended treatment of resistant organisms, such as methicillin-resistant *Staphylococcus aureus*, extended spectrum beta lactamase-producing and carbapenem-resistant Enterobacteriaceae, will be discussed.

ESPID-1101
ESPID ORGANISED SYMPOSIUM 7: UPDATE IN DIAGNOSTICS AND TREATMENT OF HEPATITIS B AND C

HEPATITIS B

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Due to vaccination programs in many countries the prevalence in children is comparably low and the dominating route of infection in industrialized countries is vertical transmission. Despite of a rather benign spontaneous course of the disease during early life there is a considerable life time risk of progressive liver disease, which may eventually reduce life expectancy. We differentiate two HBeAg positive phases, the immune tolerant with normal and the immune reactive phase with elevated aminotransferases. Seroconversion to anti-HBe may occur at any time, which means a dramatic decline of viral load and normalization of aminotransferases. Anti-HBe seroconversion is considered as the main endpoint of current treatment.
For children two treatment options are available: interferon based immune stimulation or nucleos(t)ide analogue based suppression of viral replication. For Europe both entecavir and tenofovir have been approved. Currently no peg-interferon drug has been licensed by authorities; however, two clinical trials with peg-interferon-alpha2a are in progress, the first one in children with immune active chronic hepatitis B and the second one in combination with lamivudine and in patients during the immune tolerant phase. The anti-HBe seroconversion rate in patients treated with a nucleos(t)ide analogue ranges between 20% and 25% during the first two years, exceeded by an interferon based treatment regimen by roughly 10%.
In conclusion, the treatment situation remains dissatisfying. Normally, in the vast majority of patients the cure of the disease is not possible and seroconversion to anti-HBe occurs in less than one third of treated subjects according to current treatment guidelines.

ESPID-1090
ESPID ORGANISED SYMPOSIUM 7: UPDATE IN DIAGNOSTICS AND TREATMENT OF HEPATITIS B AND C

HEPATITIS C

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Pegylated interferon α-2a or 2b in combination with ribavirin is the standard treatment for chronic hepatitis C for children aged 3 years and older. In recent years, a number of direct-acting antiviral agents are under development for treatment of chronic hepatitis C virus (HCV) infection. These agents block viral replication inhibiting directly one of several steps of the HCV lifecycle. Direct-acting antiviral agents are classified into several categories, based on their molecular target: HCV NS3/4A protease inhibitors, HCV NS5B polymerase inhibitors and HCV NS5A inhibitors. Other promising compounds are Cyclophillin A inhibitors, mi-RNA122 and interferon λ.

Several new drugs associations will be developed in the near future starting from the actual standard of care. Interferon-based and interferon-free regimens are being studied in adults. In this constantly evolving scenario new drug regimens targeted and suitable for children would be possible in the next future. Especially for children, it is crucial to identify the right combination of drugs with the highest potency, barrier to resistance and the best safety profile.

ESPID-1130
ESPID ORGANISED SYMPOSIUM 8: SEPSIS AND MENINGITIS

EVIDENCE BASED TREATMENT FOR SEPSIS IN NEONATES

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Children's Hospital at Westmead and University of Sydney, Sydney, Australia

This talk will review the evidence on choice and duration of of antibiotics in suspected and proven neonatal sepsis. The evidence suggests it is safe to stop empiric antibiotics after 2-3 days if blood cultures are negative and the baby is well, and measuring the serum C-reactive protein or other acute phase reactants leads to increased antibiotic use without benefit to the babies. The evidence also suggests prolonged antibiotics in the face of negative cultures significantly increase the risk of death in very preterm infants.

ESPID-1106
ESPID ORGANISED SYMPOSIUM 8: SEPSIS AND MENINGITIS

Evidence of adjuvant therapies in bacterial meningitis

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Bacterial meningitis remains a main threat to children worldwide. Despite improvement of general management, antibiotic therapy and increased vaccine availabilities bacterial meningitis is still associated with a high morbidity and mortality. Treatment options to improve long-term outcome are warranted. The cerebral injury that occurs in bacterial meningitis is largely due to a host-mediated inflammatory response. This process is triggered by the release of bacterial toxins and other virulence factors of the bacteria and may be exacerbated by antibiotic treatment. For several inflammatory diseases of the CNS, including meningitis, the treatment includes glucocorticoids as dexamethasone. The use of dexamethasone in patients with proven or suspected meningitis has been studied extensively in both animal models and human trials. Moreover the potential benefit other adjuvant therapies such as glycerol have been studied *in vitro* and in humans. An overview of the current evidence of adjuvant therapies in bacterial meningitis will be given.

ESPID-1112
ESPID ORGANISED INVITED LECTURE 2: NEONATAL VACCINATION: A ONCE IN A LIFETIME OPPORTUNITY

Predictors of Vaccine Response in Children

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Globally newborn and infant immunization programs are highly effective in providing protection from infection and/or disease and rightfully represent major triumphs of preventive medicine and public health (Objective 1). However, existing predictors of host responses to childhood vaccines are exclusively based on descriptive associations, with little to no insight into underlying cellular and molecular mechanisms (Objective 2). Systems biological approaches have recently been applied to vaccinology (systems vaccinology) and have provided unprecedented insight into functional cause-effect relationships (Objective 3). These promising tools have so far not been applied to the youngest (under 6 months of age), despite the fact that this age group is most at risk to suffer from infection and also the one in receipt of most vaccines (both in terms of type of vaccine and number of doses). A careful review of the rapid and radical changes of immune development in early life coupled with the galvanizing tools of systems vaccinology, will likely reveal relevant predictors of vaccine responses in early life (Objective 4). This will greatly improve our understanding of the underlying molecular drivers of early life immunity, which is prerequisite to optimise interventions such as vaccines. Together, these efforts have the potential to transform a window of vulnerability to infections early in life into one of opportunity towards life-long homeostasis and health.

ESPID-1138
ESPID/ESID JOINT SYMPOSIUM SESSION: INFECTIOUS CLUES TO PRIMARY IMMUNODEFICIENCY

PID REVEALED BY EBV INFECTION

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Epstein-Barr Virus (EBV) infection is one of the most powerful viral trigger of the immune system in humans. After the age of 35 years, the incidence of the infection in the general population is more than 90 %. The primary infection occurs in infancy and adolescence and it is largely asymptomatic. However, in some immunocompetent individuals EBV causes infectious mononucleosis (IM), a self-limiting lymphoproliferative disease characterized by a massive and sustained expansion of CD8+ T cells and infected B cells reflecting a strong immune response to the virus. In immunocomprised individuals, the persistence of EBV infected is associated with virus-associated hemophagocytic syndrome (VAHS), malignant and non-malignant lymphoproliferative disorders and nasopharyngeal carcinomas. There are several known pediatric inherited immunodeficiencies leading to a susceptibility to EBV infection. These natural mutants represent unique models to study the immune response to EBV. However, there are still patients presenting a high susceptibility to EBV in whom the genetic basis of their disease is not known. We recently reported that CTPS1 deficiency in humans caused a severe combined immunodeficiency characterized by a high susceptibility to EBV infection. We provided the evidence that CTPS1 is required for sustained proliferation of activated T lymphocytes during EBV infection. More generally CTPS1 appears to be a key factor of adaptive immunity.

ESPID-1099
ESPID/ESID JOINT SYMPOSIUM SESSION: INFECTIOUS CLUES TO PRIMARY IMMUNODEFICIENCY

OTHER INFECTIOUS CLUES SUGGESTING PID

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Great North Children's Hospital, Newcastle upon Tyne, United Kingdom

Severe, frequent or unusual infectious suggest PID. Persistent RSV or PIV bronchiolitis suggests SCID, as does interstitial pneumonitis due to PCP but also CD40 Ligand deficiency or ICF syndrome; Aspergillus, CGD, CMV a T cell PID. S.aureus Pneumatocoeles are pathognomonic of Hyper IgE syndrome. Recurrent pneumonia with S.pneumoniae, S.aureus and Pseudomonas species is seen in antibody deficiency. Pneumonia extending into bone and soft tissue is highly suggestive of Aspergillus infection and CGD. Gastrointestinal infection is common in PID. Cryptosporidium in CD40 Ligand and CD40 deficiencies and MHC II before, whist Giardia occurs in antibody deficiencies. Chronic viral enteritis strongly suggests a severe T cell immune deficiency.

Persistent superficial candida infection is the hallmark of APECED.

Staphylococcal and Pseudomona are seen in neutrophil and antibody deficiency; and innate deficiency such as IRAK4 and NEMO defects; suppurative Staphylococcal lymphadenitis suggests CGD. Recurrent Streptococcal pneumoniae and Haemophilus influenzae infections are seen in defects of the early components of the classical complement pathway, recurrent meningococcal disease in defects of the alternate and late pathways. Disseminated BCG suggests SCID, whereas non-tuberculous Mycobacterial infection in older children suggests a defect in the IL-12 / IFNg pathogen or a NEMO defect.

Human Herpes virus infections are difficult to control and persistent or severe infections uncover a further group of PIDs; HSV1 in Unc deficiency, VZV in CHH, EBV in XLP or XIAP, HHV6 in other CIDs, often with CD4 lymphopenia. Severe molluscus or warts – DOCK8 deficiency.

ESPID-1087
ESPID/PIDS JOINT SYMPOSIUM SESSION: INFECTIONS IN THE PEDIATRIC TRANSPLANT PATIENT

UPDATE ON CURRENT DIAGNOSIS, TREATMENT AND MANAGEMENT OF INVASIVE FUNGAL INFECTIONS IN TRANSPLANT PATIENTS

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The optimal diagnosis and treatment of invasive fungal infections is rapidly changing. New molecular technologies are introducing new algorithms for best diagnostic strategies, and newer antifungals and dosing are required for preferred outcomes. In addition, the epidemiology of fungal resistance is always changing, including newer species found and resistance patterns increasing. This talk will focus on infections due to Candida and Aspergillus, as the major invasive fungal infections seen at most centers, but also cover principles useful for management of rare yeasts and molds. Special emphasis will be on the diagnostics and treatments tested in children, including the often unique dosing patterns required in pediatric patients.

ESPID-1089
ESPID/PIDS JOINT SYMPOSIUM SESSION: INFECTIONS IN THE PEDIATRIC TRANSPLANT PATIENT

NEW ANTIVIRAL THERAPIES IN DEVELOPMENT FOR THE TREATMENT OF ADENOVIRUS, CMV, RSV, PIV INFECTIONS IN TRANSPLANT PATIENTS

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Viral infections may have serious consequences in the immunocompromised pediatric transplant recipient. Advances in the rapid detection and quantitation of viruses have resulted in improved recognition, diagnosis, and evaluation of viral infections. The introduction of international standards for the quantitation of DNA viruses such as CMV and EBV has enabled the reporting of reslts that are now comparable among clinical laboratories. New developments in antiviral therapy have resulted in therapies that are now being evaluated in human trials. The experimental agent brincidofovir (CMX001;Chimerix, Inc, Durham, NC, USA) has been used successfully for the prevention and treatment of adenovirus disease in pediatric and adult clinical trials. This oral antiviral also has activity against other double-stranded DNA viruses including CMV and BK viruses, and is undergoing further clinical trials in diverse populations for the prophylaxis and/or treatment of multiple viruses. Maribavir was studied for the prevention of CMV in adult hematopoietic stem cell transplant patients (HSCT) without demonstration of benefit, the revaluation of this drug following the disappointing prophylaxis clinical trials is ongoing. New fusion inhibitors for RSV are under development with one oral fusion inhibitor (GS5806; Gilead Sciences, Foster City, CA, USA) showing efficacy in adult challenge studies and now undergoing clinical trials in adult HSCT recipients. An antiviral drug against parainfluenza viruses administered with an inhaler (DAS181, ParaDase; Ansun Biopharma, San Diego, CA, USA) has also been evaluated in pediatric and adult immunocompromied patients in uncontrolled case series and is now undergoing clinical trials in adult HSCT. Clniical trials are needed in pediatric patients, who have high rates of viral infection and may suffer serious sequelae following these viral infections.

ESPID-1126
ESPID/PIDS JOINT SYMPOSIUM SESSION: INFECTIONS IN THE PEDIATRIC TRANSPLANT PATIENT

EBV: PREVENTION AND TREATMENT OF EPSTEIN BARR VIRUS AND POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)

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University of Pittsburgh School of Medicine Children's Hospital of Pittsburgh, Pittsburgh, USA

Epstein Barr Virus (EBV) infections and post-transplant lymphoproliferative disorders (PTLD) are important potential causes of morbidity and mortality following solid organ and stem cell transplantation in children. Despite the absence of data derived from prospective, randomized trials, analysis of ongoing experiences in the diagnosis, management and prevention of EBV infection and PTLD in children undergoing transplantation has led to improved outcomes in these patients. The use of EBV viral load has allowed for earlier identification of EBV and creates the possibliity of preemptive interventions at the point of subclinical infection to prevent progression to EBV disease/PTLD though issues with the specificity require attention. The use of a stepwise approach to the treatment of EBV disease using reduction of immune suppression as a first step has been associated with markedly improved outcomes for those patients who develop EBV disease/PTLD. This presentation will review the pathogenesis and epidemiology of EBV and provide an overview of essential information relating to the diagnosis, management and prevention of EBV/PTLD in both solid organ and stem cell recipients.

ESPID-1125
LITERATURE REVIEW SESSION

VIRAL INFECTIONS

G. Ferwerda[1]
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The development of molecular techniques in virology has led to novel insight in epidemiology, pathophysiology, treatment and prevention of pediatric viral infections. This has sometimes direct implications for our daily clinical practice or policy making. In this literature review on viral infections I will discuss the most recent publications on this topic with special emphasis molecular epidemiology, viral co-infections, virome sequencing and diagnostic developments.

ESPID-1094
LITERATURE REVIEW SESSION

VACCINES

A.J. Pollard[1]
[1]*Department of Paediatrics, University of Oxford, Oxford, United Kingdom*

Recent key papers on vaccines for children will be reviewed and discussed

ESPID-1131
LITERATURE REVIEW SESSION

IMMUNO-DEFICIENCIES

A. Fasth[1]
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Primary Immunodeficiencies – Progress During the Last Years

The progress in four areas will be discussed: 1. The number of primary immunodeficiencies (PID) genetically defined is now around 260. This is an increase with more than 50 PID between the last two biannual meetings of the European Society for Immunodeficiency (ESID). Comments will be given on some of the new forms, progress in hematopoietic stem cell transplantation and in immunoglobulin substitution. 2. An update on the progress on neonatal screening for severe combined immunodeficiency in Europe will be given. 3. The progress regarding autoinflammatory disorders will be commented upon. Many more monogeneic forms have been reported and some of the new disorders overlap with classical PID with not only inflammatory symptoms but also infections. This gives new insight into the interaction between the innate and adaptive immune system. 4. The progress in gene therapy with new safer vector will be commented upon. Also the new fascinating technique of CRISP-Cas9, developed from the adaptive immune system of bacteria will be mentioned.

ESPID-1110
MEET THE PROFESSOR SESSION 1: MSSA AND MRSA INFECTIONS

MSSA AND MRSA INFECTIONS

A. Mueller[1]
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Staphylococcus aureus is one of the most important pathogen in human and especially in children. Methicillin-susceptible *S. aureus* (MSSA) is the most common cause of pyogenic skin infections (e.g. folliculitis, impetigo, necrotizing fasciitis) but also other organ infection (e.g. pneumonia, meningitis, endocarditis), sepsis and catheter associated infections. Typical *S. aureus* toxin associated manifestations were described as toxic shock syndrome, scalded skin syndrome especially in neonates and food poisoning.

Microbial diagnosis from clinical specimens is usually done with culture methods and colonies should be tested for antibiotic susceptibility. However, molecular techniques play an increasing role especially in rapid detection of antibiotic resistant strains (e.g. *mecA* gene).

In the last decade the methicillin-resistant *S. aureus* (MRSA) has been increasing as one of the most important causes of antimicrobial-resistant healthcare- associated infections (HA-MRSA) but also emerging as community- associated MRSA (CA-MRSA). MRSA represent a rare but significant cause of nosocomial infections (pneumonia, bacteremia) and outbreaks in hospitalized children with comorbidities (HA-MRSA).

CA-MRSA prevalence is very variable in different European countries, from less than 2% in some northern European countries to up to 40% in Greece. In recent years the increases of severity of S. aureus infections have been associated to the increase of CA-MRSA. But severe S. aureus infections have also been caused by CA-MSSA so other virulence factors are being studied. Panton-Valentine Leukocidin (PVL) is being studied as a possible virulence factor related to severity.

Treatment of *S. aureus* infections is depending on underlying conditions and risk factors of the patient, infection site, virulence factors and antibiotic resistance.

ESPID-1111
MEET THE PROFESSOR SESSION 1: MSSA AND MRSA INFECTIONS

MSSA AND MRSA INFECTIONS

P. Rojo[1]
[1]*Pediatric Infectious Diseases, Hospital 12 de Octubre, Madrid, Spain*

MSSA and MRSA infections

Staphylococcus aureus is one of the most important pathogen in human and especially in children. Methicillin-susceptible *S. aureus* (MSSA) is the most common cause of pyogenic skin infections (e.g. folliculitis, impetigo, necrotizing fasciitis) but also other organ infection (e.g. pneumonia, meningitis, endocarditis), sepsis and catheter associated infections. Typical *S. aureus* toxin associated manifestations were described as toxic shock syndrome, scalded skin syndrome especially in neonates and food poisoning.

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Treatment of *S. aureus* infections is depending on underlying conditions and risk factors of the patient, infection site, virulence factors and antibiotic resistance.

ESPID-1098
MEET THE PROFESSOR SESSION 6: DIAGNOSIS OF LOWER RESPIRATORY TRACT INFECTIONS

DIAGNOSIS OF LOWER RESPIRATORY TRACT INFECTIONS

S. Esposito[1], *S. Bianchini*[1], *N. Principi*[1]
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Lower respiratory tract infections (LRTIs) are among the most common infections of infants and children in developing and industrialised countries. Given the clinical, social and economic importance of LRTIs for the pediatric age, there is general agreement that a prompt and adequate diagnostic and therapeutic approach is essential in order to reduce the impact of the disease. However, there are various issues that make it difficult to establish a rational management of pediatric LRTIs, including difficulty in identifying the etiology of the disease, the emergence of resistance of the most frequent bacterial pathogens to commonly used antibiotics, and the lack of certain information about the possible role of new biomarkers. The etiology of LRTIs is much more difficult to identify in children than in adults, because lower airway secretions can rarely be obtained and invasive diagnostic methods cannot routinely be used. In addition, as is the case in adults, cultures of upper respiratory tract secretions are not useful because normal flora frequently includes the bacteria commonly responsible for pneumonia. Moreover, diagnosing CAP in children with mild signs and symptoms remains a difficult problem, and it is possible that a considerable number of patients without CAP (particularly those that are seen and treated in the community) may be treated in the same way as those with the disease (including unnecessary antibiotic administration). More research is required in many areas, including the etiologic agents associated with LRTIs complications, the absence of a pediatric LRTI severity score, a better definition of second-line antibiotic therapies, how to follow-up on patients with LRTIs, and the cost effectiveness of vaccines against respiratory pathogens.

ESPID-1115
MEET THE PROFESSOR SESSION 7: MANAGEMENT OF INVASIVE INFECTIONS AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION

MANAGEMENT OF INVASIVE INFECTIONS AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION

N. Klein[1], T. Lehrnbecher[2]
[1]Infection and immunity, Institute of Child Health, London, United Kingdom
[2]Hematology and Oncology, Johann Wolfgang Goethe-University, Frankfurt, Germany

Patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT) are at high risk for invasive infections due to the complex and time-dependent impairment of the immune system. Neutropenia and mucositis characterize the first period after HSCT until engraftment (recovery of the absolute neutrophil count >500/µl), which usually occurs until 30 days after HSCT. At this time, patients are at high risk for infections from bacteria, herpes viruses and fungal infections. Following engraftment, continued impairment of cellular and humoral immunity renders the patients highly susceptible to viruses such as cytomegalovirus, adenovirus and varicella-zoster virus, as well as fungi such as Aspergillus spp. In this session, risk factors, diagnostic considerations and prophylactic and therapeutic strategies of various invasive infections in HSCT recipients will be discussed.

ESPID-1123
MEET THE PROFESSOR SESSION 7: MANAGEMENT OF INVASIVE INFECTIONS AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION

MANAGEMENT OF INVASIVE INFECTIONS AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION

T. Lehrnbecher[1], *N. Klein*[2]
[1]*Hematology and Oncology, Johann Wolfgang Goethe-University, Frankfurt, Germany*
[2]*Infection and immunity, Institute of Child Health, London, Germany*

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ESPID-1121
MEET THE PROFESSOR SESSION 8: OSTEOMYELITIS AND SEPTIC ARTHRITIS

OSTEOMYELITIS AND SEPTIC ARTHRITIS

H. Girschick[1]
[1]*Pediatrics, Department of Pediatrics Childrens Hospital in the Friedrichshain, Berlin, Germany*

Infectious an other inflammatory bone conditionsin Childhood-

From osteomyelitis to hypophosphatasia

If a child is presented to a doctor with limping,localized bone or joint pain, in addition to swelling and redness of a part ofthe extremities one usually would consider bacterial osteomyelitis to bepresent. Suspicion is very high especially when fever is present. Mostly thiskind of osteomyelitis would be of bacterial origin leading to high inflammationlocally and systemically. However differential diagnosis is more complex whenfever is absent and signs of inflammation are limited. Thus, osteomyelitis inchildhood includes a multitude of differential diagnoses. The clinical pictureof **bacterial osteomyelitis** can be ofacute or subacute onset, but also chronic courses are possible. Septicarthritis is defined as a bacterial infection of the joint, which often is asequel of an osteomyelitis adjacent to the joint space. In contrast to thesedisease entities driven by bacterial agents, chronic **non-bacterial osteomyelitis** is not directly triggered by a localpathogen. However, indirect chronic stimulation of the immune system by aninfectious agent has not been ruled out completely. **Osteonecrosis** can either be ofidiopathic origin or a therapeutic side effect of steroid or cytotoxicmedication. Often this diagnosis is confused with the diagnosis ofosteomyelitis, because it can also show signs of inflammation like effusions injoints next to the necrotic bone. The best example would be perthes disease,which often manifests with effusions in the hip joint. **Bone tumors** are major differential diagnoses.

The seminar will focus atfirst on osteomyelitis driven by an infectious pathogen, at second chronicinflammatory (chronic nonbacterial osteomyelitis) and metabolic conditions (hypophosphatasia)will be addressed.

ESPID-1118
MEET THE PROFESSOR SESSION 8: OSTEOMYELITIS AND SEPTIC ARTHRITIS

OSTEOMYELITIS AND SEPTIC ARTHRITIS

***J. Saavedra*[1]**
[1]Pediatrics, Greorio Marañon Hospital, Madrid, Spain

Bone and joint infection, although not a very frequent infection in children, causes important morbidity and, sometimes, mortality in pediatrics. Bones in children are in continuous growth and any injury that affects this development may have important sequelae such as limb asymmetry and limping. Furthermore, when the joint is involved the consequence may be chronic pain or decrease in joint mobility. Therefore, it is very important to have an appropriate diagnostic approach and management of these infections to avoid complications and major future problems. In this seminar we will provide some concepts about epidemiology and etiological agents, since understanding the incidence of different types of bone and joint infections, most common microorganisms and, especially, resistance may be very important for the management of these infections. We will try to give some guidance for the most suitable diagnostic tools, such as whether magnetic resonance may better than bone scan or if a plain x-ray should always be performed initially. Finally, we will discuss the best treatment options. Should we always tap the joint upon a suspected septic arthritis? Which way of draining a joint is better? Do we always need to obtain a bone sample to orient the antibiotic therapy? Which is the best antibiotic as empirical treatment? Recently published Spanish guidelines will help us better understand these concepts. Finally, a multicenter, national survey of bone and joint infection in children conducted in Spain will be presented to open the final discussion. Several practical cases will be presented within the seminar.

ESPID-1135

MEET THE PROFESSOR SESSION 9: VACCINES IN CHILDREN WITH CHRONIC CONDITIONS AND CATCH UP VACCINATION IN CASE OF DELAYED IMMUNIZATION

VACCINES IN CHILDREN WITH CHRONIC CONDITIONS AND CATCH UP VACCINATION IN CASE OF DELAYED IMMUNIZATION

M. Knuf[1]

[1]*Children's Hospital, Dr. Horst Schmidt Klinik, Wiesbaden, Germany*

Prevention of severe infections is a very important component of care and an important determinant of clinical outcomes in a diverse population of people with chronic illness or in a population of immunocompromized hosts. At risk cohorts include the elderly, preterm infants and neonates, pregnant woman, recipients of haematopoietic stem cell or solid organ transplants, HIV-infected children and adolescents, recipients of chemotherapies or biologic therapies. In addition individuals suffering from cormorbid conditions with immunosuppression as a consequence of an underlying disease like diabetes mellitus, end-stage organ failure, autoimmune dieases and others are at specific risk for a fatal outcome of vaccine-preventable infectious diseases. Vaccination represents a fundamental preventive strategy. According to the diversity of underlying diseases or conditions at risk, it is not possible to follow an universal recommendation. Multiple factors contribute to vaccine effectiveness and risk of vaccination. In these situations, carefully choosen vaccines or special vaccination schedules are indicated or vaccines should be postponed or even forbidden. In general, toxoid or inactivated vaccines can be used, considering the possibility of insufficient immune response. For immunsuppressed patients, in accordance with type of immunosuppression, live virus vaccines should be avoided, because of the risk of vaccine agent spread. The immunization strategy should not only the patient, but the social surrounding and contacts as well.

ESPID-1107
MEET THE PROFESSOR SESSION 9: VACCINES IN CHILDREN WITH CHRONIC CONDITIONS AND CATCH UP VACCINATION IN CASE OF DELAYED IMMUNIZATION

VACCINES IN CHILDREN WITH CHRONIC CONDITIONS AND CATCH UP VACCINATION IN CASE OF DELAYED IMMUNIZATION

P. van Damme[1], *H. Theeten*[1]
[1]*Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium*

Catch-up vaccination in case of delayed immunization

Optimal immune response to a vaccine depends on several factors, including the type of vaccine, age of the recipient, the adequate and complete schedule and immune status of the recipient. Recommendations for the age at which vaccines are administered are influenced by age-specific exposure and risks to vaccine-preventable diseases, age-specific risks for complications, age-specific responses to vaccination, and potential interference with the immune response by passively transferred maternal antibodies.

Non-attenuated vaccines require >2 doses to elicit an adequate antibody response. For some vaccines booster doses are required to maintain protective antibody concentrations. Attenuated vaccines usually require 2 doses for an optimal immune response. All the above mentioned principles need to be taken into consideration to start an individual catch-up immunization program.

In Belgium 4 basic principles will be respected to decide on an individual catch-up program:

- consider someone as non-vaccinated if previous vaccination cannot be documented

- a vaccine series does not need to be restarted, regardless of the time that has elapsed between doses.

- the quality of the induced immunity depends on the minimal age at first immunization, on the required minimal interval between doses and the number of doses

- the use of combination vaccines eases the correct implementation of a catch-up schedule and requires less injections.

We will illustrate the application of these principles with a number of catch-up immunization scenarios.

ESPID-1133

MEET THE PROFESSOR SESSION 10: ADVANCES IN PATHOPHYSIOLOGY AND MANAGEMENT OF PERIODIC FEVER SYNDROMES

ADVANCES IN PATHOPHYSIOLOGY AND MANAGEMENT OF PERIODIC FEVER SYNDROMES

H.J. Laws[1]

[1]*Department of Pediatric Oncology Hematology and clinical Immunology, University Hospital Duesseldorf, Düsseldorf, Germany*

Autoinflammatory diseases (AIDs) represent a spectrum of genetic and non-genetic inflammatory diseases characterized by recurrent episodes of fever and systemic inflammation affecting the eyes, joints, skin, and serosal surfaces. Several of them are monogenetic diseases with an early onset in childhood. Because of recurrent fever, these diseases were summarized as "periodic fever syndromes." Physicians need to consider AIDs in children with recurrent, unexplained fevers, when infectious and malignant causes have been discarded. Included in this spectrum are familial Mediterranean fever (FMF), mevalonate kinase deficiency (Hyper IgD), cryopyrin-associated periodic syndrome (CAPS) and tumor necrosis factor receptor-associated disease (TRAPS). In autoinflammatory diseases, the monocyte-macrophages are often involved in immune-dysregulation. Therapeutic effects are seen after colchicine and to biologic agents, who modulateT- and B-cell functions, including anti-TNF, anti-IL -1 or 6 receptor antibodies.In our session we will present some cases and discus the pathophysiology and therapeutic management with the audience.

ESPID-1093
MEET THE PROFESSOR SESSION 11: PRE- AND PROBIOTICS IN PEDIATRIC INFECTIOUS DISEASES

PRE- AND PROBIOTICS IN PEDIATRIC INFECTIOUS DISEASES

V. Wahn[1], *T. Zaoutis*[2]
[1]*Pediatric Pulmonology and Immunology, Charité University Hospital, Berlin, Germany*
[2]*Division of Infectious Diseases, The Children's Hospital of Philadelphia, Philadelphia, USA*

Prebiotics, probiotics, and synbiotics have been extensively studied for several potential indications. In this MTP seminar we try to summarize a couple of aspects:

1. Definition of pre-, pro-, and synbiotics

2. Not all probiotics are the same. What are the microbiological differences?

3. How could probiotics influence local infections in the gut?

4. How could probiotics reduce airway infections?

On this basis we will try to present our current knowledge coming from clinical studies. Some of the studies had a preventive design, others aimed for for treatment of established infections. For a few "indications" metaanalyses are available.

Finally, we will try to cover aspects of novel applications other than gut or airway infections which might play a role in the future.

ESPID-1091
MEET THE PROFESSOR SESSION 12: HEPATITIS A

HEPATITIS A

G. Indolfi[1]
[1]*Paediatric and Liver Unit, Meyer Children's University Hospital of Florence, Firenze, Italy*

Hepatitis A is an acute infection transmitted through the fecal-oral route. The incidence of the infection, which is endemic in developing countries, has declined since hepatitis A vaccine was licensed in 1995. Following vaccine introduction, despite a shift in age-specific rates with a more rapid decline among children than among adults, most people are still infected during the first decade of life.

Symptoms of hepatitis A virus (HAV) infection, when present, are often nonspecific (fever, malaise, anorexia and nausea). Jaundice and liver failure are more common in older children (>6 years of age). Extrahepatic manifestations are rare. Hepatitis A is usually a benign disease although a possible severe course of the infection is possible also in children.

ESPID-1122
MEET THE PROFESSOR SESSION 13: PRACTICAL ASPECTS OF HOSPITAL HYGIENE MEASURES

PRACTICAL ASPECTS OF HOSPITAL HYGIENE MEASURES

A. Simon[1], K. Butler[2]
[1]Paediatric Oncology Haematology and Infectious Diseases, University Children's Hospital, 66421 Homburg Saar, Germany
[2]Consultant Paediatrician & Paediatric Infectious Diseases Specialist, Our Lady's Children's Hospital, Crumlin Dublin 12, Ireland

Public awareness of health care associated infections (HCAI) and their negative impact on patient outcome is increasing. The potential to prevent HCAI remains underexploited. Important key interventions have been identified (environment control, hand hygiene, personal protective equipment, and asepsis) but must be applied in an integrated trans-disciplinary fashion, respecting the unique challenges for the individual patient, if best outcome is to be achieved. Challenges particular to a children's hospital include the frequency of transmissible pathogens, prolonged asymptomatic shedding of some (e.g. RSV, rotavirus, enterovirus etc), children's incomplete (age dependent) ability to follow standard hygiene precautions. Additionally, children are generally accompanied by family members, for whom infection control intervention may be also necessary (e.g. child hospitalised with TB). Importantly, the safety and quality of their medical treatment when in isolation must be guaranteed and the potential negative consequences of prolonged isolation considered. Unique risk groups include patients in NICU, in haematology/oncology wards, and those with congenital diseases (e.g. congenital heart disease), severe neuromuscular impairment and cystic fibrosis. The prevalence of multidrug-resistant bacteria (MDRs like MRSA, VRE, MRGN) is lower in the paediatric setting but colonisation can persist for months, potentially fostering risk of subsequent infection and inappropriate or inadequate empirical treatment. Colonised children can act as a reservoir for transmission to adult high-risk groups (e.g. grandparents). The role of *C. difficile* (CD) as nosocomial pathogen in children has been questioned because of high rates of toxin-positive healthy infants; today CD is accepted as a relevant gastrointestinal pathogen in the in- and outpatient paediatric setting. This session addresses important practical issues covering at least some of those current challenges of hospital hygiene and infection prevention in the paediatric setting.

ESPID-1124
MEET THE PROFESSOR SESSION 13: PRACTICAL ASPECTS OF HOSPITAL HYGIENE MEASURES

PRACTICAL ASPECTS OF HOSPITAL HYGIENE MEASURES

K. Butler[1], A.R.N.E. Simon[2]
[1]Consultant Paediatrician & Paediatric Infectious Diseases Specialist, Our Lady's Children's Hospital, Dublin, Ireland
[2]Paediatric Oncology Haematology and Infectious Diseases, University Children's Hospital, Homburg, Germany

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ESPID-1116
MEET THE PROFESSOR SESSION 14: INFECTIONS BY PETS AND REPTILES

INFECTIONS BY PETS AND REPTILES

D. Nadal[1], *W. Handrick*[2]
[1]*Infectious Diseases, Childrens University Hospital, Zürich, Switzerland*
[2]*Infectious Diseases, Childrens University Hospital, Leipzig, Germany*

The overall goal of this session is to give an overview on the variety of zoonoses that can be transmitted by pets including reptiles that are increasingly regarded as pets within a household. The transmission of the zoonoses can be bite-associated or non-bite-associated. The management of bite-associated infections and non-bite associated infections may considerably differ, as the latter infections may have potential implications for the behavior of primarily non-affected household or family members. Illustrative cases will be presented to ignite fruitful discussions on the possible patient management options. Thus, the benefit for attendees of this session will be a thorough summary of current knowledge including epidemiology aspects and practical issues related to diagnosis establishment, treatment and prophylaxis of infections by pets and reptiles.

ESPID-1136
MEET THE PROFESSOR SESSION 15: FUNGAL INFECTIONS

FUNGAL INFECTIONS

E. Roilides[1]
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Neonates are especially vulnerable to invasive *Candida* infections (ICI), partly because of their young age and immunoimmaturity and partly because of the invasive procedures commonly used in intensive care units. Central vascular catheters, parenteral nutrition, mechanical ventilation and extensive use of antimicrobial agents enhance the risk of ICI. *Candida albicans* continues to be the most prevalent isolate. However, an increasing role of non-*C. albicans* spp., some of which (i.e. *Candida glabrata* and *krusei* are intrinsically or potentially resistant to antifungal agents, has been observed. Others, like *Candida parapsilosis* may have higher MIC's to echinocandins. *Candida parapsilosis* and *tropicalis,* account for a large number of ICI in the NICU.
Many NICU's administer fluconazole prophylaxis to a substantial number of neonates based to international guidelines. Breakthrough candidemia may occur in the neonates.

Early diagnosis is an effective way of pre-emptively treating neonates with ICI. Molecular methods, potential detection of beta-glucan and high index of clinical suspicion help in early starting antifungal therapy. Prompt removal of lines and initiation of antifungal treatment are the milestones of management. Conventional amphotericin B remains a commonly used antifungal agent, whereas its lipid formulations and fluconazole are also used frequently. However, when fluconazole prophylaxis is practised, therapy with fluconazole is not recommended. Echinocandins (caspofungin, micafungin and anidulafungin), exhibit potential as alternative agents in neonates with ICI. Although response rates are still far from satisfactory, improved understanding of risk factors, preventive strategies and new treatment options promise a better future outcome.

ESPID-1100
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

IS NEC AN INFECTIOUS DISEASE?

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Necrotizing enterocolitis (NEC) is a devastating disease of the immature bowel characterized by mucosal necrosis, focal ischaemia and haemorrhage, a major cause of death in premature infants.

Clearly multifactorial - requiring an immature gut exposed to enteral feeds, but recognising that breast milk has protective properties - several lines of evidence implicate bacteria in the pathway to disease. NEC cannot be induced in animals born and raised under sterile conditions, and antimicrobials modulate risk, both adversely (an association with early empirical use of broad-spectrum agents) and beneficially (modest efficacy of empirical antibiotic cocktails in arresting progression in early cases). However, no specific pathogen has been consistently identified, and it is increasingly recognised that abnormal bacterial colonization of the gastrointestinal (GI) tract plays a role in pathogenesis. This has fed enthusiasm for the use of probiotics (strains of *Bifidobacterium* or *Lactobacillus*, prominent in the healthy breast-fed infant GI microbiome) in attempts to modulate the premature GI microbiome in a beneficial manner, a strategy attended with inconstant success in preventing NEC.

Recent research has revealed a pivotal role for Toll-like receptor 4 (TLR4) and its regulators. Rather than an infectious disease, NEC can be considered the catastrophic outcome of exposure of the developmentally-directed pro-inflammatory gut epithelium of the pre-term infant, expressing TLR4 at high level, to bacteria that by rights should never have been there. Strategies aimed at reducing activation of GI mucosal TLR4 or reversing the downstream effects of signalling hold considerable promise for prevention or treatment of this terrible disease.

ESPID-1132
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

WHOLE GENOME SEQUENCING IN THE NICU

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[2]Center for Pediatric Genomic Medicine, Children's Mercy Hospital, Kansas City, USA

Monogenic diseases are frequent causes of neonatal morbidity and mortality, and disease presentations are often undifferentiated at birth. More than 3,500 monogenic diseases have been characterized, but clinical testing is available for a minority of them. Furthermore, many feature clinical and genetic heterogeneity that further complicates diagnosis. Hence, an immense unmet need exists for improved molecular diagnosis of ill infants. Because disease progression is extremely rapid, albeit heterogeneous, in newborns, molecular diagnoses must occur quickly to be relevant for clinical decision-making. We have demonstrated the feasibility of conducting rapid, whole-genome sequencing (WGS) with automated bioinformatic analysis to obtain a molecular differential diagnosis of genetic disorders in infants in neonatal intensive care units (NICUs). The entire process can be completed in less than 50 hours. A notable application of rapid, WGS in NICUs is the potential for early diagnosis, management, and treatment of primary immunodeficiencies, which may prevent life-threatening infections.

ESPID-1120
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

INFECTIONS BY PENICILLIUM MARNEFFEI

P. Lee[1], W.L. Yang[1], K.W. Chan[1], M.H.K. Ho[1], Y.L. Lau[1]
[1]Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong, Hong Kong China

Penicillium marneffei infection is indigenous to Southeast Asia. Most cases occur in patients with AIDS and secondary immunodeficiencies. The fact that penicilliosis is an AIDS-defining illness affecting patients with CD4+ count <100 cells/mm3 suggests that individuals who are HIV negative and without secondary immunodeficiencies may have primary immune defects, especially those with disseminated disease. However, information on the spectrum of primary immunodeficiencies (PIDs) and genetic susceptibility associated with penicilliosis is lacking. Our previous systemic review on penicilliosis occurring in HIV-negative children revealed that many of them had underlying immunodeficiencies, including severe combined immunodeficiency, hyper-IgM syndrome, common variable immunodeficiency, Kostmann syndromme and hypogammaglobulinemia. Our further work on 4 patients with penicilliosis and chronic mucocutaneous candidiasis identified a genetic defect in STAT1 in all of them. Two mutations were located in the coiled-coil domain and two in the DNA-binding domain. All of them recovered from penicilliosis, but one eventually died of aspergillosis. The percentage of pSTAT1-positive PBMCs induced by interferon-alpha and interferon-gamma was significantly higher in all 4 patients than normal controls, indicating that they had gain-of-function mutations. PBMCs from these patients displayed defective interferon-gamma and interleukin-17 production towards PMA and PMA plus ionomycin, respectively. Interferon-gamma production induced by C. albicans and P. marneffei in the patients was significantly lower than normal controls. For the first time, we demonstrated STAT1 gain-of-function mutation as an important genetic etiology of invasive mycosis including penicilliosis and aspergillosis. Penicilliosis should be regarded as an indicator disease for PIDs in children without HIV infection unless proven otherwise

ESPID-1140
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

SEVERE VIRAL RESPIRATORY INFECTIONS – DO CO-INFECTIONS PLAY A ROLE?

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The clinical severity of virus co-infection remains unclear. Some respiratory viruses are likely to be found among children with single viral infections whereas other respiratory viruses are mainly reported among children with viral co-infections. In the 1990´s, a non-systematic review reported increased hospitalization rates among patients with viral co-infections. Therefore, increased severity was attributed to them. However, shortcomings were recognized like heterogeneous patient-populations and diverse laboratory methods. A recent (2014) systematic review evaluated the association of viral co-infections detected by molecular assays with severity of disease in hospitalized patients with ARI. Overall, 21 cohort studies were included-19 (90%) evaluated children aged <18 years. No significant differences in length of hospital stay, frequency of admission to Intensive Care Unit, need for mechanical ventilation or oxygen requirement were documented. Among preschool children, mortality was higher in cases with viral co-infections. Heterogenity was high in all outcomes. Papers published more recently have shown that: children with rhinovirus-enterovirus (HRV-ENT) alone were more likely to be admitted to the hospital compared to those co-infected with HRV-ENT and at least another virus; significantly longer hospital stays were associated with Respiratory Syncytial Virus(RSV) co-infections compared with RSV single infection; severity was significantly higher among children with single RSV infection in comparison with children with RSV-HRV co-infection. The role of viral co-infections remains to be debated. It is possible that different pathogenic mechanisms may be triggered by different viruses, which may potentiate or inhibit each other´s effect.

ESPID-1104
ESPID ORGANISED PLENARY SESSION 1: ADDRESSING THE NEEDS OF THE MANY: VACCINES TO PREVENT COLONIZATION

ADDRESSING THE NEEDS OF THE MANY: VACCINES TO PREVENT COLONIZATION

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The successes of polysaccharide conjugate vaccines, first directed against *Haemophilus influenzae* type b, followed by *Streptococcus pneumoniae* and *Neisseria meningitidis*, have provided abundant confirmation that antibodies directed against the polysaccharide capsule of different pathogens are highly effective in preventing disease in the individual. What is even more impressive, however, is the growing realization that the efficacy of these vaccines in generating herd protection is even more important than the effect on the individual recipients of the vaccine. Such herd protective effects with conjugates were first noted in the case of Hib, but made abundantly clear in epidemiological studies of pneumococcal pneumonia in the elderly in the US, which estimated that two thirds of the disease reduction by pneumococcal conjugates could be attributed to an indirect effect. More recently, advances in immunology and vaccinology have revealed a new form of T cell-based mucosal immunity that appears particularly effective at targeting colonization by extracellular pathogens. The generation of memory CD4+ Th17 cells for example has been associated with significantly reduced density and duration of carriage in animal models. These pathogen-specific Th17 cells, which recognize specific bacterial antigens and activate innate immune responses that facilitate clearance, are readily detected in humans. These developments lead logically to the question as to whether vaccines that target colonization and aim primarily to generate herd protection can be developed and licensed. This presentation will describe the underlying immunologic mechanisms and provide examples of vaccine efforts targeting colonization, with a particular focus on *S. pneumoniae*.

ESPID-1095
ESPID ORGANISED PLENARY SESSION 2: PAEDIATRIC VACCINES TODAY AND TOMORROW

PAEDIATRIC VACCINES TODAY AND TOMORROW

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Immunisation is the most important global programme for child health and continues to reduce mortality and morbidity in the first 5 years of life. There are major challenges today for maintaining the incredible impact of our immunisation programmes whether it is delivery of vaccines to remote villages in Africa, responding to the Ebola outbreak, closing the polio story, or maintaining confidence in measles vaccine to prevent outbreaks, such as the ongoing transmission across the US. While these are immense remaining challenges for the global heatlh providers and funders, immunisation has transformed our society and perhaps our greatest challenge today is about access and communication.
The success of vaccines used thus far provides a strong argument for new vaccine development with the aim of further reducing morbidity and mortality. There important developments in vaccines for RSV, the leading cause of infant hospitalisation in industrialised countries and one of the leading causes of infant mortality globally. Vaccines for the primary cause of neonatal meningitis, group B streptococcus, are within sight and many vaccines with potential against nosocomial pathogens or for use in specific populations could be available in the decade ahead. One of the main issues that will be faced for many new vaccines, in the context of a limited health budget, are policy questions over the balance between spending on rare severe diseases and common mild diseases, which may have a similar financial burden for health services. Addressing and communicating the value of vaccines as tools for sustaining and improving child health has never been more pressing.

ESPID-1096
ESPID ORGANISED PLENARY LECTURE 3: ANTIMICROBIAL RESISTANCE - ALL YOU NEED TO KNOW

MECHANISMS OF ANTIMICROBIAL RESISTANCE

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In a vote to determine the focus of a new research effort funded by the UK government, the British public named antibiotic resistance as one of the most pressing challenges of modern times. This level of knowledge is fruit of the continuous information dealt by the infectious diseases community.Indeed, antibacterial resistance has for decades been a growing threat to the effective treatment. Until know, practically all clinically important bacteria have developed resistance against majority of antibacterial compounds. Countless amounts of resistance mechanisms have been identified.The clinicians need knowledge of bacterial resistance mechanisms in planning the most effective treatment options. Without studying the resistance mechanisms, surveillance of resistant bacteria is not well understood. In addition, mechanisms behind resistance have also to be known to find best ways to tackle spread of resistant bacteria. Lord Kelvin said wisely: “If you cannot measure it, you cannot improve it.” In the second week of this year 2015, Nature published an article of a new antibiotic teixobactin. The authors conclude: “The properties of this compound suggest a path towards developing antibiotics that are likely to avoid development of resistance.” I have heard this sentence several times in 1970’ies and again in 1980’ies. Is there finally light in the tunnel?

ESPID-1097
ESPID ORGANISED PLENARY LECTURE 4: ANTIMICROBIAL RESISTANCE - ALL YOU NEED TO KNOW

PREVENTION OF ANTIMICROBIAL RESISTANCE IN THE CLINIC

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Antimicrobial resistance is rapidly increasing all around the world. Especially the increase of carbapenemase producing Enterobacteriaceae (CPE) is worrisome. Recent estimates predict that by 2050 more people will die from infections with antimicrobial resistant organisms than from cancer and the associated costs will be enormous.

There are many variants of CPE with different incidences in the European community. In general the spread is more extensive in the South of Europe and almost absent in The Northern part. Control strategies depend on reliable and rapid detection with subsequent aggressive control measures.

Some examples of outbreak control with variable success will be presented. It will show that a delayed response is associated with exponential efforts to regain control, if achievable at all. Also it is important to change the concept of individual patient care in independent health care organizations to a systematic approach based on patient movements and spread of microorganisms.

In The Netherlands a regional network approach is proposed based on a network of microbiological laboratories with high-level expertise in microbiology, infectious diseases and infection control attached to it. This network will cover public health, general practitioners, hospitals and nursing homes in a region defined by patient-movements. It should provide a better system for early detection and rapid response. Thereby, it will ensure an optimal system for patient safety now and in the future.

ESPID-1102
ESPID OPENING SYMPOSIUM: EMERGING INFECTIOUS DISEASES OUTBREAKS

Emerging infectious diseases between reality and perception

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Our globalised environment, supports the unprecented spread of pathogens, including pathogens emerging from the animal reservoir. Global movement of infected people or animals cause continuous outbreaks of emerging infectious diseases that may be very distant from the index case. Prompt identification and subsequent management of these outbreaks is essential. Initiatives to support sharing of diagnostic reagents, virus strains and sequences in a timely manner will enable the scientific community to advance its understanding more efficiently , but their success is dependant on the willingness of scientists to contribute their tools and data.
Another essential issue is the optimisation of communication between scientific community and stakeholders. In particular, it is essential that communication between scientists and politicians is fostered, if operational change is to be achieved in disease management at the global level. However, politicians do not base their decisions on the same dataset as health professionals and this causes a misalignment with the priorities of the scientific community.
It would beneficial for the scientific community to engage in a more targeted communication effort with the political environment and be proactive in rejecting journalistic inaccuracies or non-scientific conspiracy or hoax accusations. Doing so, would bring added value and would enable the medical research community to improve the outcome of their efforts, with positive consequences for public health as a whole.

ESPID-1137
WALTER MARGET EDUCATIONAL WORKSHOP

Managing Severe Infections in the Immunocompromised

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Children who have an underlying immunodeficiency are at high risk of suffering from serious infections. These infections are usually caused by bacteria, viruses and fungi, although protozoans such as Cryptosporidium can also be problematic. The specific defects within the immune system can influence the aetiology as well as the severity and frequency of infections. Whatever the cause, there are some basic principles that govern our approach to managing these infections. In this session, the risk factors, diagnostic considerations and therapeutic strategies for managing patients with an underlying immunodeficiency will be discussed.

Oral Presentations

ESPID-0636
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

CLINICAL FEATURES OF CHILDHOOD ADENOVIRUS INFECTIONS IN AN OUTBREAK IN TAIWAN, 2011

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Background

We studied pediatric patients with adenovirus infection in the 2011 outbreak in northern Taiwan to define clinical features of serotype 2 (ad2), 3 (ad3) and 7 (ad7) infections in children.

Methods

Between January 2011 and December 2011, 637 patients aged less than 19 years with culture-confirmed adenovirus infection and specimens available for serotype determination, by an in-house PCR method, in Chang Gung Memorial hospital were enrolled. Clinical data were retrospectively collected.

Result

Excluding 5 cases with multiple serotypes, a total of 632 cases were included for analysis. Three serotypes were identified, including ad3 (67.6%), ad7 (22.6%) and ad2 (9.8%). Median age was 4.58 years (range: 2 to 216 months); children infected with ad3 were significantly older (82.9% > 3 years, $p<0.001$). Of the 621 inpatients, 97.6% had fever, all had respiratory symptoms, 75 patients (12.1%) had lower RTI, 20 patients (3.2%) required intensive care (ad2: 1, ad3: 8, ad7: 11) and three patients died (all ad7-infected). Ad3-infected patients were significantly more likely to have upper respiratory symptoms, while leukocytosis (WBC>15,000/mm^3) was more common in ad2-infected (p=0.007). Ad7-infected patients were significantly associated with a longer duration of fever, leukopenia (WBC<5,000/mm^3), thrombocytopenia (Platelet <150000 /mm^3), high serum C-reactive protein level >100 mg/L, lower RTI, a longer length of hospital stay, and requiring intensive care (all p < .001).

Conclusion

Childhood ad2, ad3 and ad7 infections may have different clinical manifestations. Although ad3 was the most prevalent serotype in 2011 Taiwan outbreak, ad7 caused more severe disease entities.

ESPID-0176
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

OUTCOMES OF INFANTS RECEIVING PALIVIZUMAB PROPHYLAXIS FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) IN CANADA AND ITALY: A PROSPECTIVE, COHORT STUDY

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Background/Aims: Severe RSV infection results in hospitalization (RSVH) with accompanying morbidity/mortality. Palivizumab has been available for prophylaxis for 15 years. We examined the outcomes of palivizumab recipients within the Canadian (CARESS) and the Torino-Verona Italian Registries.

Methods: Infants were recruited during the 2002-2014 RSV seasons, and RSVHs captured. Premature infants (≤35 completed weeks gestational age [GA]; Group 1) were compared to infants who received palivizumab for serious medical disorders (BPD, Hemodynamically significant congenital heart disease (HSCHD), Neuromuscular and Pulmonary disorders, Airway anomalies, Cystic fibrosis, Down syndrome; Group 2). Data were analyzed by Fisher's exact test, Relative Risk [95%CI] and logistic regression.

Results: 14,468 patients were enrolled (Group 1; n=9,612; Group 2; n=4,856). RSVH was significantly more frequent in neonates with underlying conditions (211/4856, 4.34%) than in preterms (216/9612 [2.22%]; RR 1.93; 95% C.I. 1.60-2.33; p<0.0001). Among Group 2, RSVH occurred more significantly in BPD (4.73%; R.R.1.70; 95% C.I. 1.29-2.23; p=0.0003) and HSCHD infants (4.10%; R.R.1.45; 95% C.I. 1.10-1.90; p<0.0008). After multivariable logistic regression controlling for age at first palivizumab injection, GA, birth weight, HSCHD, BPD, and gender, only HSCHD (RR 1.74; 95%C.I. 1.26-2.40; p=0.001) and BPD (RR 1.75; 95%C.I. 1.30-2.37; p=0.000) significantly predicted RSVH in palivizumab-treated infants

Conclusions: Our data provide international, multicenter, prospective evidence that RSVH rates are higher in infants given palivizumab for reasons other than prematurity. Further research is warranted to assess whether the findings relate to the current palivizumab dosing protocols, or on a specific increased risk for RSVH inherent in these "special" populations

ESPID-0591
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

VIRAL RESPIRATORY INFECTION AND SEPSIS AMONG BCG VACCINATED AND UNVACCINATED CHILDREN IN SPAIN

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Background: *Bacille Calmette-Guerin (BCG) vaccination has been shown to have non-specific beneficial effects in children from Africa.*

Objective: *To assess the heterologous protective effects of BCG vaccination against viral respiratory infection (VRI) and sepsis in Spain.*

Methods: *Retrospective epidemiological study, using data from the Official Spanish Registry of hospitalizations (CMBD-HA) to identify difference of hospitalization rates (HR) in Basque Country (BC) (where neonatal BCG is part of the immunization schedule) as compared to the rest of Spain (where BCG is not administered).*

Results: *A total of 464,611 hospitalization episodes from 1997 to 2011 were analyzed. The HR due to VRI in BCG vaccinated children (BCG immunization coverage of 100%) was significant lower compared to BCG unvaccinated children for all age groups with a total preventive fraction (PF) of 41.4% (95%CI: 40,3-42,5; P-value>0.001) [children <1 year old PF: 32.4% (95%CI: 30.9 - 33.9; P-value<0.001); children 1-4 years old PF: 60.1% (95% CI: 58.5 – 60.1; P-value<0.001); children 5-9 years old PF:66.6% (95% CI: 62.8 – 70.3; P-value<0.001) and children 10-14 years old PF:69.6% (95% CI: 63,3 – 75.0; p<0.001). The HR due to sepsis in BCG vaccinated children was also significant lower for children <1 year old with a PF of 52.8% (95% CI: 43.8 – 60.7: p<0.001).*

Conclusions: BCG vaccination at birth may decrease the hospitalizations in children due to VRI and sepsis not related to Tb through heterologous protection in a developed country.

ESPID-0956
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

ANTIBIOTIC RESISTANCE IN NEONATAL AND PAEDIATRIC BLOOD STREAM INFECTION: DATA FROM THE ANTIBIOTIC RESISTANCE AND PRESCRIBING AMONG EUROPEAN CHILDREN (ARPEC)PROJECT

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Background and aims

The aim of the ARPEC project was to develop and evaluate surveillance methodologies to monitor antimicrobial use and resistance among European neonates and children.

Methods

Blood culture isolate data were submitted by 19 collaborating hospitals in 12 countries for children <18 years of age between 1 January 2011 and 31 December 2012. Percent resistant and rate resistant isolates per 1000 occupied bed days (OBD) were calculated for selected pathogen/antibiotic pairs. OBD were estimated using country level bed occupancy data from the 2012 European Antimicrobial Resistance Surveillance Network (EARS-Net) report and mean Organization for Economic Co-operation and Development (OECD) bed occupancy for 2011.

Results

Table 1. Percent resistant blood stream isolates for all isolates tested for each selected pathogen/antibiotic combination (95% confidence interval), ARPEC data 2011-2013

Pathogen	Antibiotic															
	AMP		3GC		AMG		FQU		CPM		APP		GPD		MCO	
	N	C	N	C	N	C	N	C	N	C	N	C	N	C	N	C
E. coli	65.0% (.57-.73)	70.9% (.64-.77)	7.9% (.04-.12)	15.5% (.11-.20)	12.1% (.07-.17)	15.2% (.10-.20)	7.2% (.03-.11)	17.1% (.12-.22)	0.0% (-)	0.9% (-.00-.02)	13.2% (.07-.19)	17.7% (.12-.23)	-	-	-	-
K. pneumoniae	-	-	35.7% (.23-.49)	30.4% (.22-.39)	32.1% (.20-.45)	31.0% (.23-.39)	16.1% (.06-.26)	18.6% (.12-.25)	3.6% (-.01-.09)	7.3% (.03-.12)	30.4% (.17-.44)	27.3% (.19-.36)	-	-	-	-
P. aeruginosa	-	-	8.3% (-.04-.20)	28.3% (.20-.37)	20.8% (.03-.38)	27.4% (.19-.36)	20.8% (.03-.38)	23.9% (.16-.32)	31.8% (.11-.53)	32.2% (.23-.41)	10.0% (-.04-.24)	40.4% (.31-.50)	-	-	-	-
E. cloacae	-	-	34.9% (.20-.50)	35.9% (.25-.47)	9.3% (.00-.18)	12.8% (.05-.20)	2.3% (-.02-.07)	3.9% (-.01-.08)	0.0% (-)	5.2% (.00-.10)	35.9% (.20-.52)	37.8% (.27-.49)	-	-	-	-
E. faecalis	4.0% (-.01-.08)	8.3% (.02-.14)	-	-	-	-	-	-	-	-	-	-	0.0% (-)	0.0% (-)	-	-
E. faecium	79.0% (.59-.99)	87.9% (.80-.96)	-	-	-	-	-	-	-	-	-	-	10.5% (-.05-.26)	9.2% (.02-.16)	-	-
S. aureus	-	-	-	-	-	-	4.7% (.01-.08)	8.2% (.05-.11)	-	-	-	-	0.0% (-)	0.0% (-)	12.4% (.06-.19)	16.1% (.12-.20)

AMP-ampicillin/amoxicillin; 3GC-3rd generation cephalosporins; AMG-aminoglycosides; FQU-fluoroquinolones; CPM-carbapenems; APP-antipseudomonal penicillins; GPD-glycopeptides; MCO-methicillin, cefoxitin, or oxacillin

Table 2. Rates of resistant blood stream isolates per 1000 occupied bed days by selected pathogen/antibiotic combinations, ARPEC data 2011-2013

Pathogen	Antibiotic															
	AMP		3GC		AMG		FQU		CPM		APP		GPD		MCO	
	N	C	N	C	N	C	N	C	N	C	N	C	N	C	N	C
E. coli	14.6	4.4	2.6	0.8	3.5	1.5	1.5	0.5	0.0	0.0	3.6	2.0	-	-	-	-
K. pneumoniae	-	-	6.0	1.0	5.3	1.0	2.5	0.9	0.7	0.1	4.0	1.3	-	-	-	-
P. aeruginosa	-	-	0.7	0.7	1.0	0.9	0.9	0.3	1.2	0.3	0.7	1.1	-	-	-	-
E. cloacae	-	-	3.9	0.5	1.7	0.1	0.4	0.0	0.0	0.7	2.9	0.4	-	-	-	-
E. faecalis	1.0	0.1	-	-	-	-	-	-	-	-	-	-	0.0	0.0	-	-
E. faecium	3.9	2.1	-	-	-	-	-	-	-	-	-	-	0.2	0.4	-	-
S. aureus	-	-	-	-	-	-	1.5	0.7	-	-	-	-	0.0	0.0	3.1	0.7

AMP-ampicillin/amoxicillin; 3GC-3rd generation cephalosporins; AMG-aminoglycosides; FQU-fluoroquinolones; CPM-carbapenems; APP-antipseudomonal penicillins; GPD-glycopeptides; MCO-methicillin, cefoxitin, or oxacillin

Higher percentages of isolates from children were resistant to selected antibiotic/pathogen pairs, except for 3rd generation cephalosporins, aminoglycosides, and antipseudomonal penicillins and *K. pneumoniae* and glycopeptides and *E. faecium*, which exhibited higher resistance percentages among neonates. However, rates of resistant infections for each selected antibiotic/pathogen pair per 1000 OBD were consistently higher among neonates, with the exception of carbapenem-resistant *E. cloacae*, antipseudomonal penicillin-resistant *P. aeruginosa*, and glycopeptide-resistant *E. faecium*.

Conclusions

While the percentage of resistant isolates is generally higher among children, neonates experience a higher burden of resistant disease. This is important for allocating resources to address blood stream infection and antibiotic resistance among neonates and children, and highlights the need to monitor and treat these groups separately.

ESPID-0102
ORAL PRESENTATION SESSION 1: NEONATAL INFECTIONS AND SELECTED TOP ABSTRACTS

HEME OXYGENASE-1 RELATED IMPAIRMENT OF NEUTROPHIL OXIDATIVE BURST IN CHILDREN WITH SICKLE CELL DISEASE.

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Background and aims: Induction of heme oxygenase-1 (HO-1) in sickle cell disease (SCD) protects against heme toxicity. However HO-1 induction during granulopoiesis impairs neutrophil oxidative burst activity and increases susceptibility to bacterial infection in malarial hemolysis. In this study, we aimed to determine whether neutrophil function was impaired in children with SCD, and the relationship with hemolysis and HO-1.

Methods: We compared neutrophil oxidative burst and degranulation, hemolysis, and HO-1 activity in 26 children with SCD and 26 matched control subjects. We also examined HO-1 expression in blood neutrophils and bone marrow. We assessed the effect of HO-1 induction during neutrophil maturation using a promyelocytic cell line (HL-60).

Results: Subjects with SCD had lower oxidative burst activity than control subjects. The severity of impairment was related to HO-1 activity and the mobilisation of neutrophils from bone marrow. HO-1 was not expressed in circulating neutrophils, but was upregulated in neutrophil precursors in SCD bone marrow. Incubation of HL-60 cells with hemin during neutrophilic differentiation increased HO-1 expression and impaired oxidative burst activity, an effect partially reversed by treatment with a competitive HO inhibitor.

Conclusions: Neutrophil oxidative burst is impaired in SCD, related to HO-1 induction during granulopoiesis. This could contribute to the increased susceptibility of patients with SCD to infections. This finding may assist stratification of risk of infection in patients with SCD, and modulation of HO-1 expression may play a role in treatment of patients with SCD.

ESPID-1022
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

CLINICAL AND CELLULAR PHENOTYPE OF HETEROZYGOUS STAT1 GAIN-OF-FUNCTION MUTATIONS: AN INTERNATIONAL SURVEY

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[18]Study performed in collaboration with 24 countries, from 5 continents, X, France

Background and aims

Since their discovery in patients with autosomal dominant (AD) chronic mucocutaneous candidiasis (CMC) in 2011, heterozygous *STAT1* gain-of-function (GOF) mutations have been quickly identified in a growing number of patients worldwide. The full range of clinical features have however never been reported in a large series of patients.

Methods
We enrolled 223 patients heterozygous for *STAT1* GOF mutations, originating from 133 kindreds in 30 countries from 5 continents. Demographic data, infectious and non-infectious diseases, immunological parameters, treatment and outcome were recorded.

Results
The median age of the 223 included patients was 23 years (range, 6 months - 70 years). CMC, mainly caused by *Candida albicans*, was found in 97% of patients with a median age of onset of one year (range, 0-24 yrs). Most patients also displayed bacterial skin and respiratory tract (76%), or viral skin (42%) infections. The main pathogens involved were *Staphylococcus aureus* and herpes viruses. Fewer patients displayed invasive fungal infections (10%) or mycobacterial disease (6%). Almost half (43%) of the patients had a wide range of auto-immune manifestations, mainly hypothyroidism. Cerebral aneurysms (8%) and cutaneous or gastrointestinal malignancies (5%) were associated with a poor outcome (mortality rate 37%). Lymphocyte cell count was abnormally low for 40% of the patients. Anti-fungal prophylaxis was commonly used (74%); CMC however persisted in 39% of the treated patients.

Conclusions
STAT1 GOF mutations are almost invariably associated with CMC. The range of clinical manifestations is broader than initially thought. Cerebral aneurysms and malignancies confer a poor prognosis.

ESPID-0686
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

INDICATIONS OF LONG-TERM IMPAIRED GROWTH IN IN UTERO EXPOSED CHILDREN TO TENOFOVIR: THE NEED FOR RAPID FURTHER STUDIES

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BACKGROUND: Tenofovir disoproxil fumarate (TDF) is increasingly used in pregnancy to prevent mother-to-child- transmission (MTCT) of HIV. However, there are concerns regarding its potential harmful effect on infant growth.

METHODS:The study population included HIV-exposed-infants of mothers using combined antiretroviral therapy (cART)born at the Academic Medical Center in the Netherlands between 2001-2007. A potential effect of exposure to TDF was assessed in uni- and multivariate linear regression models with Z-scores for weight-for-age (WFA) or Z-scores for height-for-age (HFA) up to the age of 40 months in and adjusted for potential confounders such as maternal HIV parameters and exposure other antiretroviral compounds.

RESULTS: 74 infants were included with 500 clinical visits. Nine (13%) infants were exposed to TDF. Children exposed in utero to TDF had significantly lower WFA z-scores (Coefficient=-0.72, P= 0.028) and HFA (Coefficient=0.87, P=0.02) during follow-up compared to children with no intrauterine exposure to TDF in multivariate analyses . Although the data became more scarce after 20 months, TDF exposed children seemed to show catch-up growth of weight at the age of 20 months, however not for height. In utero exposure to other antiretrovirals did not have a significant effect on either weight or height.

CONCLUSION: *In utero* exposure to TDF has a significant negative effect on both WFA and HFA in HIV-exposed children. As WHO MTCT guidelines currently advise a TDF containing regimen, our data warrant rapid further evaluation in larger longitudinal cohort studies.

ESPID-0498
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

EPIDEMIOLOGICAL, CLINICAL, GENOTYPIC AND PHENOTYPIC CHARACTERISTICS OF AN EMERGING MENINGOCOCCAL SEROGROUP B CLONE IN QUEBEC.

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Background: In the province of Quebec, Canada, the incidence of Serogroup B meningococcal disease has increased steadily from 0.27/100,000 in 1998 to 0.86/100,000 in 2011, and this was caused by the emergence of a new clone.

Objective: To describe the epidemiological, clinical, genotypic and phenotypic characteristics of the emerging clone.

Methods: MenB cases identified by the provincial reference laboratory and characterized by the national reference laboratory in 2003-2010 were analysed.

Results: The new ST-269 clone belonging to the ST-269 complex was first detected in 2003, and spread throughout the province without any intelligible geographical pattern. The age-group 15-21 years was disproportionally affected, especially in the first years. Persons in disadvantaged social groups were at increased risk. The frequency of major acute complications (40.4 % vs 31.0 %), fatality (6.6% vs 3.6%) and sequelae in survivors (26.9% vs 25.9%) was substantial but not significantly higher among ST-269 cases as compared with other clonal complexes. ST-269 strains are not expressing the PorA P1.4 antigen and the gene coding the NadA protein included in the 4-component meningococcal B vaccine is not present. Nevertheless, this vaccine had the potential to cover 95% of cases belonging to the ST-269 clone thanks to the expression of the fHbp and NHBA antigens.

Conclusion: The recent trend in MenB in Quebec prompted public health authorities to launch a mass immunization campaign in May 2014, targeting approximately 56,000 persons 2 months to 20 years of age in the region with the highest and persistent incidence rate (Saguenay-Lac-St-Jean).

ESPID-0379
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

SAFETY AND EFFICACY OF DAPTOMYCIN IN CHILDREN WITH COMPLICATED SKIN AND SKIN STRUCTURE INFECTIONS (CSSSI) CAUSED BY GRAM-POSITIVE PATHOGENS

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Background and aims: Daptomycin is approved for treatment of cSSSI and bacteremia in adults. This study evaluated the safety and efficacy of daptomycin in children 1-17 years of age with cSSSI.

Methods: This multicenter, prospective, evaluator-blinded, randomized, IRB-approved phase 3 clinical trial compared daptomycin to standard of care (SOC). Age-adjusted daptomycin doses (12-17 years, 5 mg/kg; 7-11 years, 7 mg/kg; 2-6 years, 9 mg/kg; 1-

Results: 263 and 133 patients were randomized to daptomycin and SOC (clindamycin 50.4%; vancomycin 42.1%), respectively; 80.6% had a confirmed Gram-positive infection. Clinical success rates for daptomycin (88.3%) and SOC (86.3%) were comparable. More patients in the daptomycin arm received

Conclusions: Daptomycin given at age-appropriate doses is efficacious, safe, and generally well tolerated for treatment of cSSSI in children. Both daptomycin and SOC exhibited comparably high success rates, with daptomycin patients requiring fewer days of IV therapy.

ESPID-0175
ORAL PRESENTATION SESSION 2: SEVERE INFECTIONS AND SELECTED TOP ABSTRACTS

EPIDEMIOLOGY OF 377 PAEDIATRIC OSTEOARTICULAR INFECTIONS AND EVALUATION OF MANAGEMENT PROTOCOL

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Background: The epidemiology of pediatric acute osteoarticular infections (OAI) has changed. *Kingella kingae* became the first bacterial species responsible for septic arthritis in children < 3 years, due to the improvement of microbiological diagnosis. In 2009, we developed a protocol allowing improved diagnostic, bacteriological documentation and reduction of antibiotic treatments.

Aim: To review the clinical presentation, epidemiology and clinical management of paediatric OAI and to evaluate current French antibiotic guidelines.

Methods: We conducted a retrospective study and two successive series were compared, before and after institution of the protocol. All children suspected of community acquired OAI were included and followed-up for 2 years. We compared clinical, biological, and radiological data; duration of antibiotic and hospital stay; complications and sequelae.

Results: From 1rst of January 2006 to September 2012, 377 children with suspected OAI were included (190 septic arthritis, 133 osteomyelitis, 32 osteoarthritis and 22 spondylodiscitis). Bacteriological identification improved from 32% to 44%. The main pathogens found were *Staphylococcus aureus* (52,5%), *K. Kingae* (17%), *Streptococcus pyogenes* (15%) and *Streptococcus pneumoniae* (7,5%). Mean duration of intravenous antibiotic therapy (11 days *versus* 6 days), mean duration of total antibiotic therapy (45 days *versus* 32 days) and mean length of hospital stay (13 days *versus* 7 days) were significatively improved. After institution of the protocol, all patients recovered entirely.

Conclusions: Improvement in bacteriological diagnostic and shorter antibiotic therapy lead to shorter hospital stay with no supplementary morbidity. A simplification of the protocol and a better diffusion would permit an efficient treatment of OAI.

Table 1. Isolated organisms in the 120 children with proven osteoarticular infection

	Septic arthritis		Osteomyelitis		Spondylodiscitis		Total	
	< 4years	≥ 4years	< 4years	≥ 4years	< 4years	≥ 4years	*n*	%
Staphylococcus aureus	6	13	5	37	0	2	63	52,5
Kingella kingae	16	1	2		1	0	20	17
Streptococcus pyogenes	7	8	2	1	0	0	18	15
Streptococcus pneumoniae	9	0	0	0	0	0	9	7,5
Neisseria meningitidis	1	2	0	0	0	0	3	2
Salmonella	-	1	-	1	-	-	2	1,5
Acinetobacter baumanii	-	-	-	1	-	-	1	0,8
Bartonella henselae	-	-	-	-	-	1	1	0,8
Brahamella catarrhalis	-	1	-	-	-		1	0,8
Enterococcus faecalis	-	-	1	-	-	-	1	0,8
Streptococcus mitis	1	-	-	-	-	-	1	0,8
Total	40	26	10	40	1	3	120	100

Table 2. Population analysis before and after institution of the protocol

	Total	Before	After	p
Sexe Ratio	1,39	1,47	1,3	0,60
Median age, *years*(IQR)	2,3 (5,6)	2,2 (6,2)	2,35 (5,2)	0,50
First symptoms, *mediane days*	4 (5)	4 (5)	4 (5,75)	0,90
Fever, *median °C* (IQR)	38,4 (2)	38,3 (2)	38,4 (2)	0,56
Anti-inflammatory taken, *n(%)*	83 (22)	40 (21,6)	43 (22,3)	0,64
Previous antibiotic therapy, *n(%)*	36 (9,5)	18(9,7)	18 (9,4)	0,90
Type of infection				
Septic arthritis, *n(%)*	190 (50)	97 (52)	93 (48)	0,50
Osteomyelitis, *n(%)*	165 (44)	75 (40)	90 (47)	0,25
Spondylodicitis, *n(%)*	22 (6)	13 (7)	9 (5)	0,33
Biology				
CRP, *median mg/l* (IQ)	40 (63)	36 (61)	44 (64)	0,72
GB, *median /mm3* (IQ)	11850 (6470)	12200 (6725)	11400 (6200)	0,20
PNN, *median /mm3* (IQ)	6400 (4988)	6930 (5710)	5800 (4040)	0,03
Patelets, *median/mm3* (IQ)	365000	383000	335000	0,02
Identified organisms	120	59	61	0,57
Staphylococcus aureus, *n*	63	32	31	
Streptococcus pyogenes, *n*	18	9	9	
Kingella kingae, *n*	20	9	11	
Streptococcus pneumoniae, *n*	9	6	3	0,32
Others, *n*	10	3	7	
Site from which agent cultured,	120	59	61	
joint or bone, *n*(%)	90(75)	49(83)	41(67)	
joint or bone and blood, *n*(%)	16(13)	7(12)	9(15)	
Only blood, *n*(%)	14(12)	3(5)	11(18)	
Surgical procedure, *n*	289	162	127	<0,001
Arthrotomy, *n*(%)	33(12)	20(12)	13(10)	
Bone biopsy, *n*(%)	94(32)	65(40)	29(23)	
Antimicrobials given (days),				
Intravenous administration	9 (8)	11 (9)	6 (4)	<0 ,001
Total course	41 (16)	45 (9,5)	32 (14)	<0,001

Short Oral Presentations

ESPID-0682
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

STREPTOCOCCUS PNEUMONIAE AND STAPHYLOCOCCUS AUREUS CARRIAGE IN HEALTHY SCHOOL-AGE CHILDREN AND ADOLESCENTS

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Background and aims: Understanding the relationship between *Streptococcus pneumoniae* and *Staphylococcus aureus*, including their potential for mutual interference, is needed to evaluate the epidemiology of the diseases they cause, the factors that condition acquisition and carriage, and the impact of related preventative measures.

Methods: We obtained oropharyngeal and nasal swabs from 497 healthy subjects aged 6 to 17 years. *S. pneumoniae* detection and serotyping were performed using a real-time polymerase chain reaction, and *S. aureus* detection was performed using the RIDAGENE MRSA system.

Results: We found that 136 (27.3%) of the children were carriers of both species, 121 (24.3%) of the children carried *S. pneumoniae* alone, and 128 (25.7%) of the children carried *S. aureus* alone. *S. aureus* carriage was similar between children who carried *S. pneumoniae* (136/257, 52.9 %, 95 % confidence interval [CI]: 46.8% - 58.9%) vs. those who did not (128/240, 53.3 %, 95 % CI: 47.0 % - 59.5 %) and was independent of age and vaccination with 7-valent pneumococcal conjugate vaccine (PCV7). Vaccination with PCV7 did not affect *S. aureus* carriage (*S. pneumoniae*: 84/143 (58.7%, 95% CI: 50.5% - 66.5%) vaccinated children *vs* 171/351 (48.7%, 95% CI: 43.5% - 53.9%) unvaccinated children; S. *aureus*: 67/143 (46.9%, 95% CI: 38.9% - 55.0%) vaccinated children *vs* 195/351 (55.6%, 95% CI: 50.3% - 60.7%) unvaccinated children). Pneumococcal serotype did not affect *S. aureus* carriage.

Conclusions: The carriage of *S. pneumoniae* does not affect that of *S. aureus* in older children and adolescents, regardless of age, PCV7 vaccination, and pneumococcal serotype.

ESPID-0710
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

PERTUSSIS SEASONALITY EVIDENT IN PCR AND SEROLOGICAL TESTING DATA, QUEENSLAND AUSTRALIA

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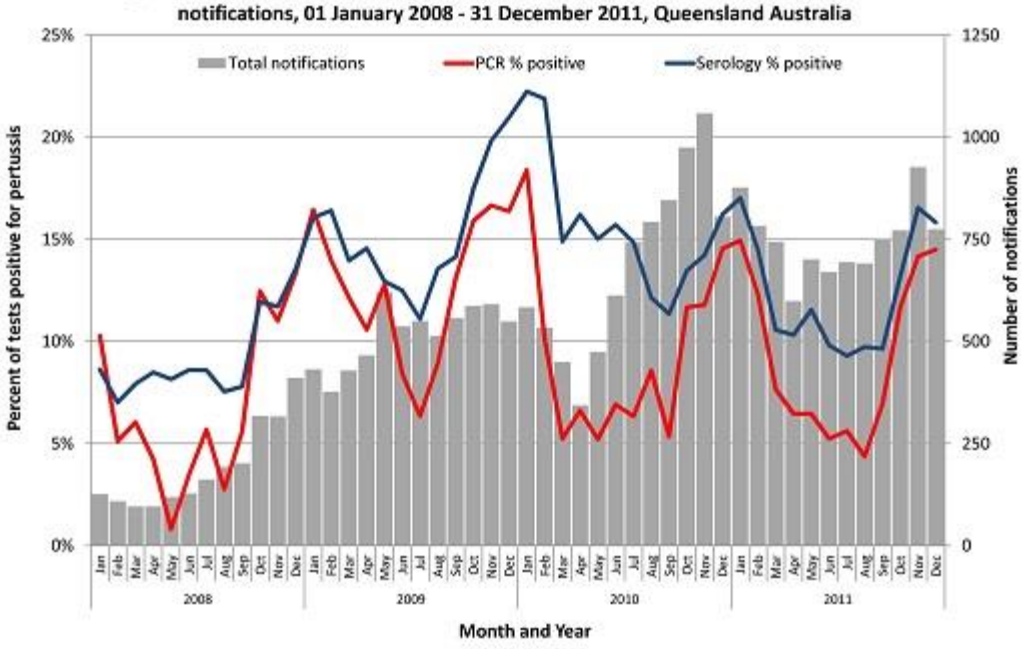
Background: Many infectious diseases show clear seasonal patterns in both temperate and tropical climates, and seasonality has been particularly well documented for viral, respiratory infections. The seasonality of pertussis is less clear and the cause of debate.

Methods: In Queensland, Australia, a tropical and sub-tropical region, two diagnostic laboratory providers provided data on pertussis diagnostic tests (PCR and serology) performed between 01 January 2008 and 31 December 2011. Data for all confirmed pertussis cases reported in Queensland over the same time period were obtained. Using the laboratory data, we calculated the proportion of tests positive for pertussis, and compared these with counts of Queensland pertussis cases.

Results: The two laboratories conducted 48,578 pertussis PCR tests and 79,505 pertussis serology tests between 01 January 2008 and 31 December 2011, of which 4,574 (9.4%) and 10,465 (13.2%) were positive, respectively. The proportion of tests positive peaked primarily in summer months at 15-18% for PCR and 16-22% for serology, decreasing between March and September to lows of approximately 5% for PCR and 10% for serology (Figure). Over the study period there were 25,688 pertussis cases notified, however seasonal trends were less evident in Queensland notification data (Figure).

Conclusion: Pertussis seasonality may not be obvious if absolute counts of case notifications are the sole source of information. By calculating the proportion of tests positive, we were able to clearly demonstrate the summer seasonality of pertussis in Queensland Australia.

Figure: Proportion of tests positive for pertussis (by diagnostic test type) and pertussis notifications, 01 January 2008 - 31 December 2011, Queensland Australia



ESPID-0753
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

TRANSIENT BUT NO SUSTAINED EFFECT OF FIRST-YEAR DAYCARE ON GP-DIAGNOSED ACUTE GASTROENTERITIS INCIDENCE; THE WHISTLER BIRTH-COHORT STUDY.

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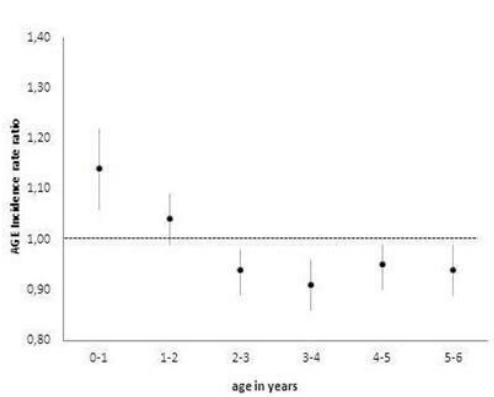
Background: Daycare attendance has been associated with increased acute gastroenteritis (AGE) incidence in young children, but long-term effects are generally unknown. This study investigated effects of first-year daycare attendance on AGE incidence and GP-contact rate up to age six years.

Methods: In the WHeezing Illnesses STudy LEidsche-Rijn (WHISTLER), a birth-cohort study conducted in the Netherlands, daycare attendance during first year of life was recorded monthly through questionnaires. Data on GP-diagnosed AGE episodes and number of GP-contacts per episode were collected from electronic health records. Children followed from birth up to age six years were included for analysis by generalized estimating equations to assess associations between first-year daycare and AGE incidence or GP-contact rate.

Results: 1563 children were included in the analysis, 82% attended daycare before age one year. Overall, the 6-year AGE incidence rate (IR) among first-year daycare attendees and non-attendees was comparable (IR: 12.4/100 vs. 11.8/100 child-years, IR ratio: 0.955; 95%CI: 0.76-1.21), after adjustment for important confounders. However, the effect of daycare was age-dependent (test for interaction $p<0.001$), with significantly higher AGE incidence during the first year and lower incidence during third to sixth year of age among daycare attendees compared to non-attendees (Figure 1). A similar pattern was observed for GP-contact rate per AGE episode.

Conclusion:
A biphasic, but overall null effect of first-year daycare attendance on AGE-incidence and GP-contact rate exists with increased incidence during the first, and decreased

incidence during later childhood years among daycare attendees.



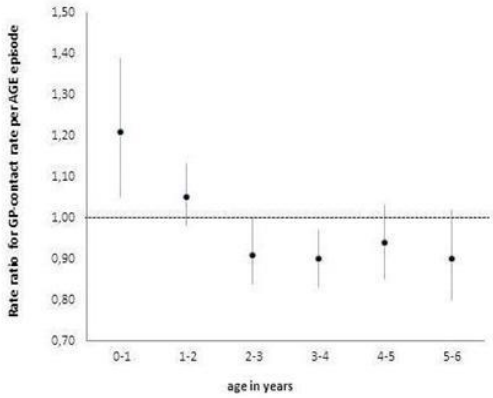


Figure 1.

A. *AGE Incidence rate ratios per one-year age categories for daycare attendance in the first year of life, adjusted for gender, parental education level, older siblings and duration of exclusive breastfeeding*

B. *Rate ratios for GP-contact rate per AGE episode and per one-year age categories for daycare attendance in the first year of life, adjusted for gender, parental education level, older siblings and duration of exclusive breastfeeding .*

ESPID-0705
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

THE CONTRIBUTION OF PCR TESTING TO INFLUENZA AND PERTUSSIS NOTIFICATIONS IN AUSTRALIA

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Background: Influenza and pertussis are the two most common vaccine-preventable infections notified in Australia. The role of improved availability of PCR testing has been hypothesised to have led to improved case ascertainment and detection of disease activity. We assessed the role of PCR diagnosis among notified influenza and pertussis cases in Australia.

Methods: Pertussis and influenza notifications were obtained from the Australian National Notifiable Diseases Surveillance System (NNDSS). We compared notifications in the pre-PCR era (≤2006) to those in the PCR-era (≥2007).

Results: There were a total of 210,786 notified influenza cases (2001-2013) and 255,866 notified pertussis cases (1991-2013), of which 183,186 (92.5%) and 141,412 (73.9%), respectively, occurred in the PCR-era. From 2001, there was a gradual increase in the proportion of PCR-based notifications, and by 2013, PCR-based notifications had largely replaced all other diagnostic methods for influenza and pertussis (Figures 1 and 2), other than among pertussis cases in adults which remained primarily serology-based.

Conclusion: In Australia by 2013, the majority of influenza and pertussis notifications were PCR-based. PCR has changed the understanding of pertussis and influenza epidemiology in Australia, and as PCR testing is expanded to other pathogens, such as those that cause gastrointestinal infections, changes to their epidemiology are likely to be observed. When relying on a laboratory-based surveillance system, any changes in disease epidemiology need to be interpreted in conjunction with knowledge of underlying testing patterns.

Figure 1: Influenza notifications by diagnostic test method and time period, 01 January 2001 to 31 December 2013, Australia

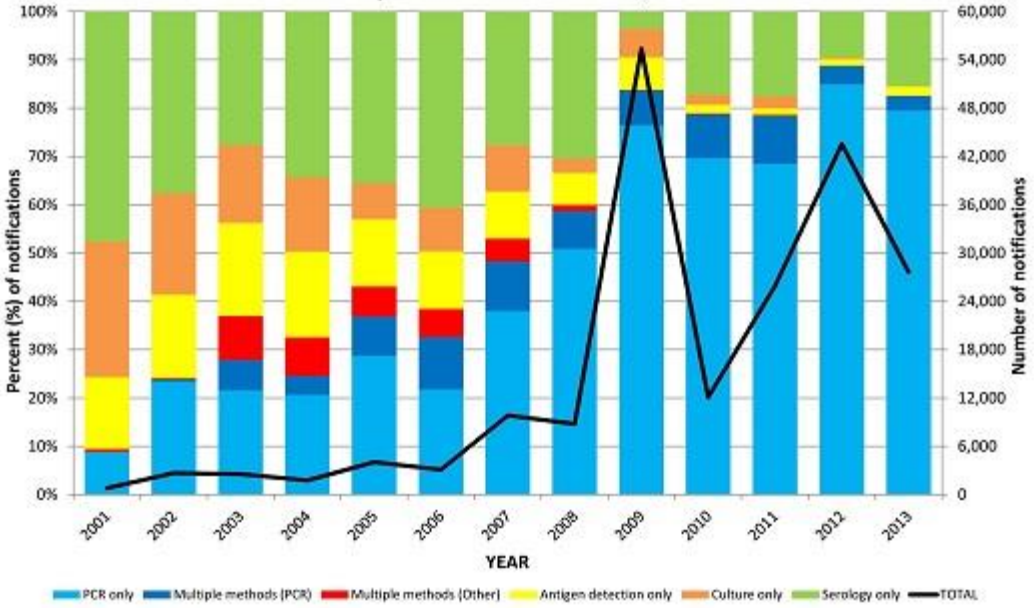
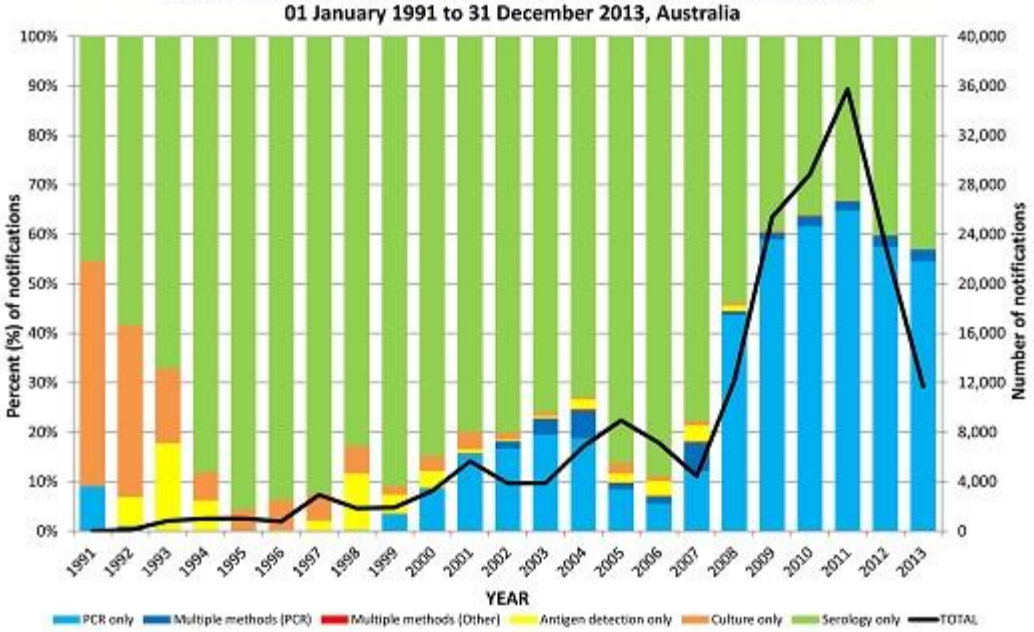


Figure 2: Pertussis notifications by diagnostic test method and time period, 01 January 1991 to 31 December 2013, Australia



ESPID-0166
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

SERIOUS ADVERSE EVENTS (SAES) IN CANADIAN CHILDREN RECEIVING PALIVIZUMAB FOR THE PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION

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Background: RSV prevention with palivizumab was deemed safe in clinical trials without major SAEs. The objective is to evaluate the safety and tolerability of palivizumab in high-risk Canadian children.

Methods: Subjects were recruited into a prospective registry (CARESS) with monthly follow-up during the 2008-2013 RSV seasons. SAEs involving death, life-threatening events, hospitalization, significant incapacity, or medical intervention were assessed for severity and relationship to palivizumab. Possibly or probably related SAEs were also assessed for severity: mild, transient events; moderate, SAEs interrupting usual activities; severe, life-threatening events. Data were analyzed by standard descriptive methods, Chi-square or Fisher Exact Tests.

Results: 13,025 infants, <2 years were enrolled and received 57,392 injections: preterms ≤35 weeks GA (n=8224; 63.1%), chronic lung disease (n=978; 7.5%), significant heart disease (n=1442; 11.1%) other medical disorders (n=2381; 18.3%). 915 patients were hospitalized for respiratory illness (RIH rate: 7.03%); 196 tested RSV-positive (RSVH rate: 1.76%). All RIHs were not or probably not related to palivizumab. 62 single or multiple SAEs occurred in 52 infants. Fourteen events in 6 patients were hypersensitivity reactions (moderate: 11; mild: 3).These were possibly (n=10) or probably (n=4) related to palivizumab (rate: 0.00028 events per patient-month). The remaining 48 SAEs in 46 patients were not related (n=39), probably not related (n=5), or unclassifiable (n=4).

Conclusions: A very small proportion of infants in the CARESS registry experienced SAEs that had a clear relationship with palivizumab and the events appeared idiosyncratic. Palivizumab appears to be a safe and well-tolerated antibody for RSV prophylaxis in high-risk children.

ESPID-0981
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

MEASLES OUTBREAKS IN HEALTH CARE SETTINGS IN THE EU: TIME FOR MONITORING PROOF OF MMR VACCINATION AND IMMUNITY AMONG HEALTHCARE WORKERS?

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Background

Measles cases are highly infective and can cause healthcare associated outbreaks that are costly and time-consuming to control, particularly when diagnosis and isolation of the patient is delayed and healthcare workers become infected. Children too young to have been vaccinated, pregnant women and immunocompromised patients are most at increased risk of complications if infected with measles.

Methods

ECDC monitors measles outbreaks through epidemic intelligence, provides secure communication platforms to exchange information, and can assist national authorities with outbreak investigations. We analysed data on healthcare associated measles outbreaks from January 2010 to December 2014. We also reviewed data on vaccination uptake and measles immunity among healthcare workers.

Results

We identified 8 measles outbreaks over the period 2010 to 2014. A total of 719 measles cases were reported. Out of these 205 (28%) were healthcare workers and staff involved in the care of patients who were either index cases or part of the transmission chain. The age ranged from 22-48 years across outbreaks. Almost all were unvaccinated or unable to show proof of immunity.

Conclusion

Healthcare associated outbreaks can be reduced with better monitoring of immunity against measles among healthcare staff and stronger promotion of MMR vaccination. Healthcare workers do not tend to be better protected against measles and rubella than people who do not work in healthcare settings. The case for regulated controls on measles and rubella immunity and free-of-charge MMR vaccinations for healthcare workers who lack immunity or documentation of MMR vaccination as standard practice throughout the EU should be considered.

ESPID-0467
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

INVASIVE PNEUMOCOCCAL DISEASE (IPD) AND PNEUMOCOCCAL CONJUGATE VACCINE (PCV) COVERAGE IN CHILDREN FROM SOUTHERN EUROPE: WHAT IS THE STATUS?

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Background and aims: Extended PCVs were licensed from 2009; similar worldwide clinical effectiveness data have since been acquired for both PCVs in routine use.[1] Despite a proven clinical need, PCV use in Southern Europe remains suboptimal, and various barriers are observed (national recommendations, costs, political will). Portugal has not introduced PCV in its national immunisation programme (NIP); Madrid (Spain) has removed PCV from its programme. PCV is included in Italian and Greek NIPs, but austerity measures in Greece may have contributed to parents postponing paediatrician visits, potentially impacting vaccination coverage.

Methods: We assessed literature and surveillance data on IPD in Southern Europe in light of national immunisation calendars and PCV coverage data.

Results: Coverage in the Portuguese private market peaked around 2008 at 75% but declined to 63% in 2012.[2] In Madrid, coverage was 95% in children [3] In Italy, coverage for the complete PCV schedule in different regions was 44.7%–98.5% (2011; children ≤2 years).[4] In Athens (Greece), 77.1% of assessed children aged 6 months received ≥1 dose (2009–2011).[5] IPD rates have decreased since vaccine introduction in each country except for Greece (Table).

Conclusions: Implementation of PCVs has impacted IPD in Southern European children. IPD surveillance is needed to assess the consequences of decreasing vaccination coverage, as vaccine serotypes remain important causes of IPD in Portugal and Greece.[2,6]

Funding: GlaxoSmithKline Biologicals SA

Table. PCV coverage and overall IPD in children in Southern European countries

Portugal PCV coverage:[2] 75% (2008) – 63% (2012)				**Spain** (Community of Madrid) PCV coverage:[3] 95% (2007–June 2012) – 60% (from July 2012)			**Italy** PCV coverage:[4] 44.7%–98.5% (2011)			**Greece** PCV coverage:[5] 77.1% (2009–2011)	
Number of overall IPD cases[2]				**Number of overall IPD cases (incidence per 100.000)**[7]			**Number of overall IPD cases (incidence per 100.000)**[a 8,9]			**Pneumococcal meningitis cases (incidence per 100.000)**[6]	
	<1y	*1–<2y*	*2–4y*		*<1y*	*1–2y*		*0y*	*1–4y*		*<1–4y*
2008–2009	54	32	36	**2007–2010**	107 (47.62)	89 (40.24)	**2009**	34	51	**2009**	8 (1.54)
2009–2010	38	27	33				**2010**	29	56	**2010**	10 (1.98)
2010–2011	23	21	16	**2011–2012**	20 (27.20)	11 (14.63)	**2011**	15 (6.16)	40 (4.00)	**2011**	9 (1.73)
2011–2012	24	16	22				**2012**	16 (6.88)	31 (3.18)	**2012**	9 (1.73)
							2013	11 (4.79)	31 (3.18)	**2013**	11 (2.11)

IPD, invasive pneumococcal disease; PCV, pneumococcal conjugate vaccine; y, years
[a]Regions: Piedmont, PA Trento, Bolzano PA , Lombardy, Veneto, Friuli-Venezia Giulia and Emilia-Romagna

[1]Hausdorff et al, Expert Review of Vaccines 2014

[2]Aguiar et al, Eurosurveillance 2014

[3]Recomendaciones de calendario de vacunación infantil para Iberoamérica
http://vacunasaep.org/sites/vacunasaep.org/files/Recomendaciones_Calendario_Vacunacion_Infantil_Iberoamericano.pdf

[4]Dati e evidenze disponibili per l'utilizzo dei vaccini anti-pneumococcici nei soggetti a rischio di qualsiasi età e per l'eventuale ampliamento dell'offerta ai soggetti anziani
http://www.epicentro.iss.it/temi/vaccinazioni/pdf/Dati%20e%20evidenze%20vaccini%20antipneumococcici.pdf

[5]Papaevangelou et al, BMC Public Health 2014

[6] Tzanakaki G. et al, National Meningitis Reference Laboratory Data 1993–2013
http://www.nsph.gr/files/001_Dimosias_Dioikitikis_Ygieinis/EKAM/ApologismoiEKAM/EKAM_Apologismos_2013.pdf

[7]Picazo et al, Clinical and Vaccine Immunology 2013

[8]Dati di sorveglianza delle malattie batteriche invasive 2007–2010
http://www.iss.it/binary/mabi/cont/Report_MBI2_2007_2010.pdf

[9]Dati di sorveglianza delle malattie batteriche invasive aggiornati al 30 maggio 2014
http://www.iss.it/binary/mabi/cont/Report_MBI_20140919.pdf

(Online references last accessed 18 December 2014)

ESPID-0481
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

LONG-TERM PROTECTION AGAINST DIPHTHERIA IN THE NETHERLANDS AFTER 50 YEARS OF VACCINATION: RESULTS FROM A SEROEPIDEMIOLOGICAL STUDY

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Background and aims

To evaluate the National Immunisation Programme (NIP) we assessed diphtheria antibody levels in the general population in the Netherlands and among orthodox Protestant individuals refusing vaccination based on religious grounds.

Methods

In 2006/2007 a national serum bank was established. Blood samples were tested on diphtheria antibodies using a Multiplex Immunoassay for 6383 participants from the national sample (NS) and for 1518 participants from municipalities with low vaccination coverage (LVC) where many orthodox Protestant individuals live. A cut-off $\geq$ 0.01 IU/ml was used for protection.

Results

In the NS 91% of the population had protective antibody levels against diphtheria. Geometric mean concentrations were lower among females compared to males (0.09 vs. 0.13, $p<0.0001$). On average, 21% of individuals from the NS born before introduction of diphtheria vaccination in the NIP (i.e. $\geq$ 55 years) and 54% of orthodox Protestants living in LVC areas had antibody levels below the protective cut-off. Linear regression analysis among fully immunized individuals (six vaccinations) without evidence of revaccination showed a decline in antibodies of -0.046 ln IU/ml per year estimating that the protective cut-off would be reached at the age of 85 years.

Conclusions

The NIP provides long-term protection against diphtheria. However, as result of waning immunity, a substantial proportion of individuals born before introduction of diphtheria vaccination lack adequate levels of diphtheria antibodies. Susceptibility due to lack of vaccination is high among strictly orthodox Protestants. The potential of introducing diphtheria in the Netherlands has not yet disappeared, despite long-term high vaccination coverage.

ESPID-0503
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

THE HEALTH ECONOMIC CAULIFLOWER TOOLBOX: A METHOD TO ASSESS THE TOTAL VALUE OF NEW VACCINES

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Many vaccines are introduced in the health care market with a health economic (HE) assessment that mimics cost-effectiveness analysis for therapeutic intervention. However, vaccines are part of an active medical prevention strategy against infectious diseases that should be positioned as a public health offer. They create more value than just quality-adjusted survival gain in vaccinees. Because there is no systematic structure available that helps identifying where additional values could be recognised, we developed a tool to facilitate that task.

The HE cauliflower toolbox is an instrument composed of many different florets along 3 essential axes of economic evaluation: vaccine effect, individual benefit, and cost. Each of the 3 axes is explored assessing different layers/florets of evaluation. For example, the benefit axis evaluates first the individual subject floret, then the care-giver floret, the employer floret, the third party payer floret, and finally the societal floret. In each floret, we can assess a change in cost or effect when introducing the new vaccine.

We applied the toolbox on rotavirus vaccination and evaluated 10 different florets going from direct and indirect effect, over to indirect cost, portfolio management, carbon foot evaluation, quality of care (QoC), and others. We discovered that two domains we often miss to assess in detail are highly impacted: the employer (indirect cost) and unexpectedly the hospital (QoC).

The HE cauliflower toolbox could help evaluating the economic benefit of a new vaccine in a more systematic approach, and thus prevent to overlook some key components of its total value package.

ESPID-0627
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

YOUNG CHILDREN, THEIR WORKING PARENTS AND PRIMARY CARE ARE BEARING THE BURDEN FOR SEASONAL INFLUENZA-LIKE ILLNESS

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Background and aims

The seasonal variation of influenza-like illness (ILI) is well known. This Swedish regional healthcare register study aimed to calculate the overall disease burden of ILI for children, including direct and indirect costs.

Methods

Seasonal variation and associated costs of influenza-related healthcare visits (primary and hospital care settings) were examined for seven-years (2005-2012) for all children aged 2-17 years in open cohorts in a defined Swedish region. ILI was defined as ICD-10: J00-J06; J09-J15, J20; H65-H67.

Results

During the 10-week influenza season peak, ILI-visits in primary care for children increased compared to pre-influenza season by OR 1.64 [95%CI 1.61-1.68]. The visits almost doubled for children 2–4 years, OR 1.96 [95% CI 1.89–2.04] **(Figure 1)**. On average, 20% of all healthcare visits, 10% of total healthcare costs and 29% of costs in primary care for children in these ages were attributable to seasonal influenza. Temporary parental employment benefits for caring of ill children mirrored the pattern of seasonal ILI visits **(Figure 2)**. Work absenteeism was estimated to generate annual indirect costs in loss of production of € 2.5 – 3.3 million vs. the direct cost of € 0.4 million per 10,000 children per year.

Conclusions

Increased direct and indirect costs during influenza season were found predominantly for the youngest children and in primary care settings. The major part of the societal ILI-costs was due to parental work absenteeism.

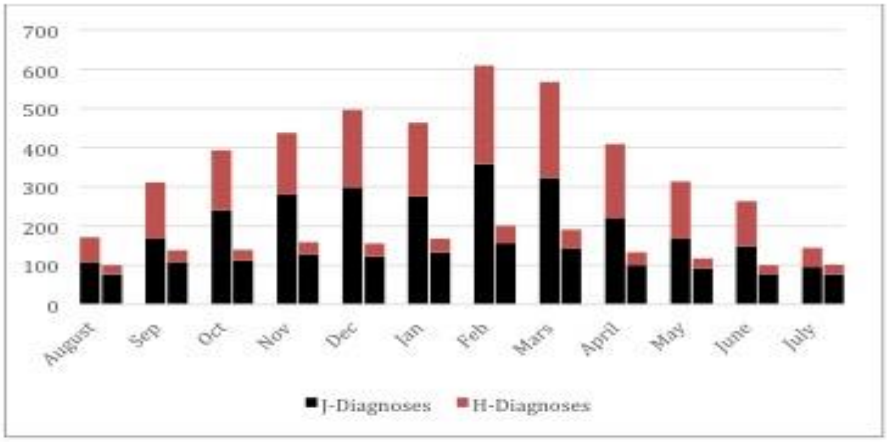

Figure 1. Average number of ILI visits to a physician in primary care per 10 000 person years across months and age-groups. The youngest children 2-4 years have a more pronounced increase and decrease of visits across the months compared to the older group of children (aged 5-17 years). The youngest children are represented with the first (and left) bar each month.

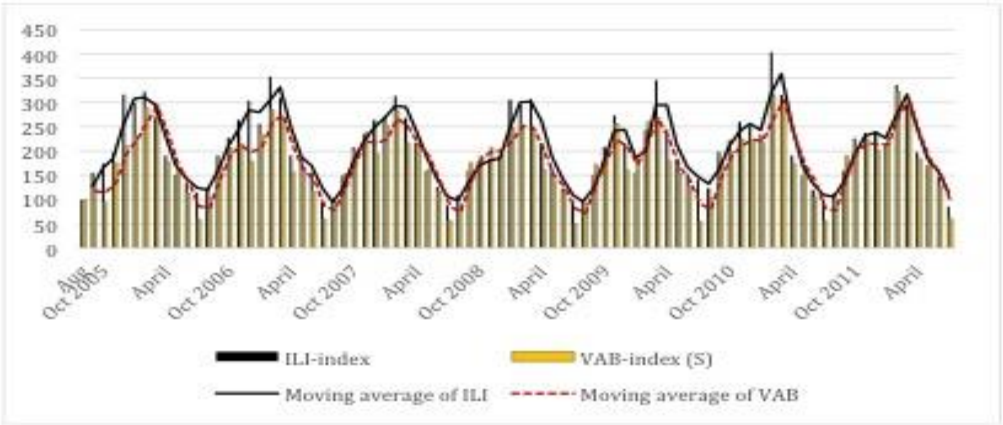

Figure 2. Seasonal variation of ILI visits in the studied county (ILI index) and the national number of reimbursed days for parental care of their sick children in Sweden (VAB index) during the seven-year study period.

ESPID-0755
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

INFLUENZA CIRCULATION IN SÃO PAULO STATE (SP), BRAZIL: REVIEW OF 2 SEASONS (2013-2014).

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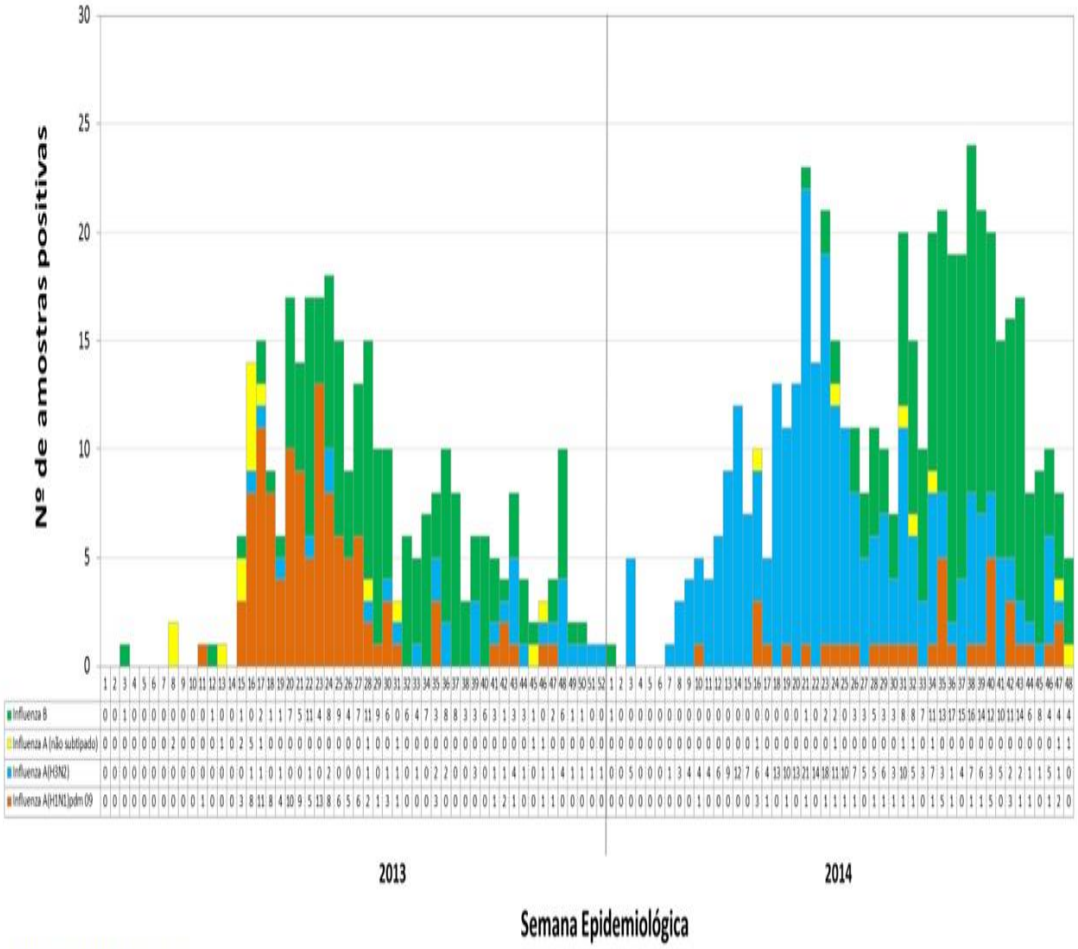
Background: Information on circulating influenza strains is essential to update vaccines. Limited information about influenza B is available in Brazil, and the aim of this study is to review the influenza B burden and lineages identified in the last 2 seasons.

Methods: SIVEP – Gripe and Institute Adolfo Lutz data on influenza strains identified in influenza like illness cases (ILI) registered in São Paulo State from January/2013 until December/2014, broken down by type, subtype and lineage B were reviewed.

Results: A total of 836 influenza strains were isolated from 7,133 samples collected from people with ILI (11.7%); from these, 362 (43.3%) were influenza B; 301 (36.0%) A(H3N2); 151 (18.1%) A(H1N1) and 22 (2.6%) A subtyping not performed. Most strains were confirmed using RT-PCR technique (95.5%), and the majority of cases were detected in São Paulo capital. Both influenza B lineages were detected in SP in 2013 and 2014.

Conclusion: Influenza B was detected in > 40% of ILI cases in São Paulo State in 2013 and 2014. Mismatch with the lineage B included in the trivalent influenza vaccine used in São Paulo was observed in both seasons. It is expected that the introduction of new quadrivalent influenza vaccines be more effective in reducing the burden of disease.

Figure 1 - Influenza A and B virus detected in São Paulo State, by epidemiologic week, 2013-2014.



Source: SIVEP - Gripe

Figure 2 - Distribution of 71 influenza B strains identified in ILI and SARI cases by year according to the lineage

Year	B/Victoria N	%	B/Yamagata N	%	Total N	%
2013 (Yamagata) *	16	88.9	2	11.1	18	100.0
2014 (Yamagata) *	4	7.5	49	92.5	53	100.0
Total	20	28.2	51	71.8	71	100.0

* Influenza B lineage recommended by WHO for the trivalent vaccine used in Southern Hemisphere.

Source: Institute Adolfo Lutz

ESPID-0237
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

EPIDEMIOLOGY OF PERTUSSIS IN ESTONIAN INFANTS OVER THE LAST 25 YEARS

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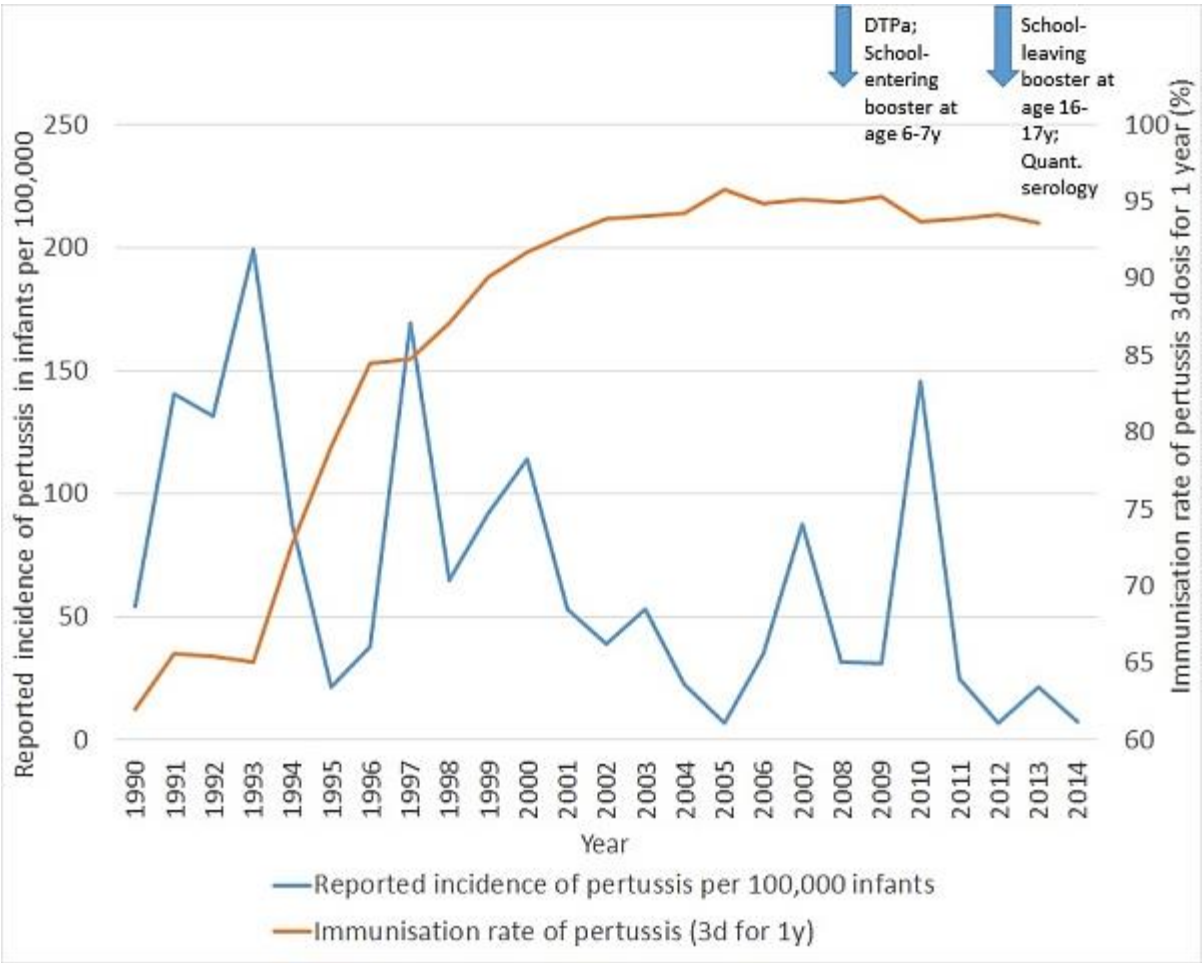
Background and aim: In recent years an increase in the incidence of pertussis related to the use of acellular vaccines has been reported in several countries. In Estonia DTPa was introduced in 2008 for primovaccination, with school-entry and school-leaving boosters added in 2008 and 2012, respectively. Pertussis immunisation rates in Estonian infants have been >90% since 1999. Qualitative serology was replaced with the more specific PT-antibodies based quantitative tests in 2012.

We aim to analyse reported pertussis incidence among children

Methods: Pertussis cases and immunisation rates reported between 01.01.1990 and 31.12.2014 were retrieved from the databases of the Health Board of Estonia.

Results: Altogether 263 cases and one pertussis-related death (in 2007) were reported. During the study period several incidence peaks occurred, the last in 2010 (145/100,000). After introduction of the school-leaving booster and quantitative serology, pertussis incidence fell to ≤21/100,000 (1-3 cases per annum) (Figure). Since 2012 PCR confirmed pertussis was diagnosed in four

Figure: Pertussis incidence per 100,000, immunisation rate and changes in immunisation strategies



Conclusion: Pertussis incidence in Estonian infants decreased to single figures annually after the implementation of new immunisation and testing strategies. The need for maternal immunisation should be decided upon after a longer observational period.

(Funded by Estonian Science Foundation, grant 9259)

ESPID-0241
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

THE EPIDEMIOLOGY OF PAEDIATRIC BONE AND JOINT INFECTIONS IN THE NORTHERN TERRITORY, AUSTRALIA

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Background:

Acute haematogenous osteomyelitis and septic arthritis are the most common presentations of bone and joint infections in childhood. Our clinical workload as infectious diseases paediatricians in Northern Australia is dominated by complicated bone and joint infections in Indigenous children. We reviewed the clinical presentation, management and outcomes of children presenting to Royal Darwin Hospital with bone and joint infections, and aimed to compare severity and incidence with other populations worldwide.

Methods:

A retrospective audit was performed on children aged 0-18 years admitted to Royal Darwin Hospital between 1 January 2010 and 31 December 2013. ICD-10 discharge codes of osteomyelitis or septic arthritis were utilised.

Results:

Seventy-nine patients were identified, of whom 72% had osteomyelitis +/- associated septic arthritis and 28% septic arthritis alone. 76% were Indigenous Australians. The incidence rate of osteomyelitis for Indigenous children was 88.6/100 000. 72% had a positive microbiological diagnosis, of which 30% were methicillin-resistant *Staphylococcus aureus* (MRSA). Mean length of stay was 23 days and average length of IV antibiotics was 17.4 days. 71% required at least one surgical procedure. Relapse within 12 months was documented in 15%.

Conclusions:

We report three key findings: osteomyelitis incidence in Indigenous children of Northern Australia is amongst the highest reported in the world; MRSA accounts for 30% of osteomyelitis with a positive microbiological diagnosis; and the severity of disease requires extended antibiotic therapy. Despite this, 15% of the cohort relapsed within 12 months and required readmission. Further strategies to reduce the severity and morbidity are needed.

ESPID-0758
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

SEROTYPE DISTRIBUTION AND ANTIMICROBIAL RESISTANCE OF INVASIVE PNEUMOCOCCAL ISOLATES IN CHILDREN

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Background and aims: Pneumococcal infections in children remain a major medical problem associated with high morbidity and mortality. The aim of this study was to evaluate serotypes and antibiotic resistance in invasive pneumococcal strains in children <5 years in Croatia from 2005 to 2014.

Methods: Invasive pneumococcal strains were collected through the Croatian microbiological laboratory network with country coverage >95%. Serotyping was performed by the Quellung reaction (Statens Serum Institute, Copenhagen). The antimicrobial susceptibility testing was performed by disc diffusion method according to EUCAST guidelines. MICs for penicillin and erythromycin were determined (E-test, Biomerieux, France). Macrolide resistant isolates were tested for *mefA* and *ermB* genes by PCR.

Results: Three hundred and five invasive pneumococcal isolates were isolated in a 10-year period. The most prevalent serotypes were 14 (84 isolates), 19A (44 isolates), 6B (40 isolates) and 23F (30 isolates), comprising 65% of all invasive pneumococcal isolates. Non-susceptibility to penicillin was 30,5%, mostly detected in serotypes 14 and 19A (Fig.1.). Macrolide susceptibility was tested in 80% of isolates. Resistance was 48%, mostly due to serotypes 14, 19A and 6B (Fig 2.). In 84 out of 118 tested isolates, genes for macrolide resistance were detected: 58 isolates (69%) were e*rm*B positive and 26 isolates (31%) were *mef*A positive.

Conclusions: Non-susceptibility to penicillin and resistance to macrolides was mostly associated with serotypes 14 and 19A. Serotype 14 is covered by all available vaccines, whereas serotype 19A is covered by 13-valent vaccine only (Fig.3.). Resistance to macrolides was mostly mediated by *ermB* gene.

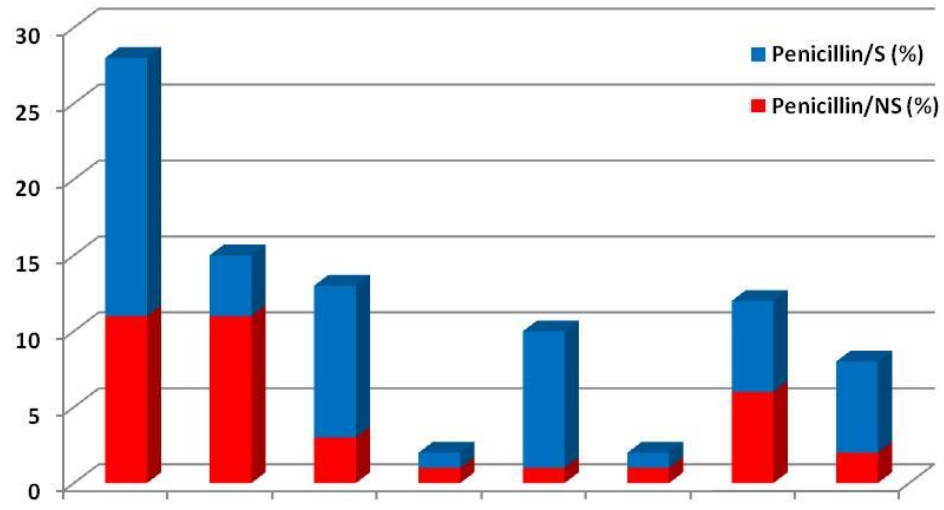


Fig.1. Serotype distribution and penicillin non-susceptibility, Croatia 2005-2014, 305 invasive isolates

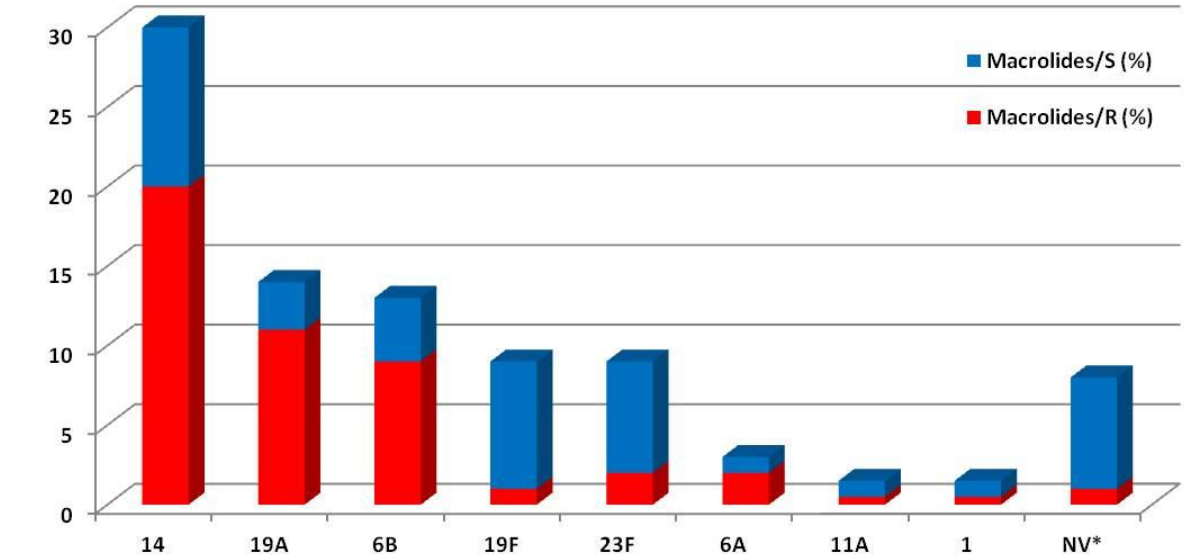
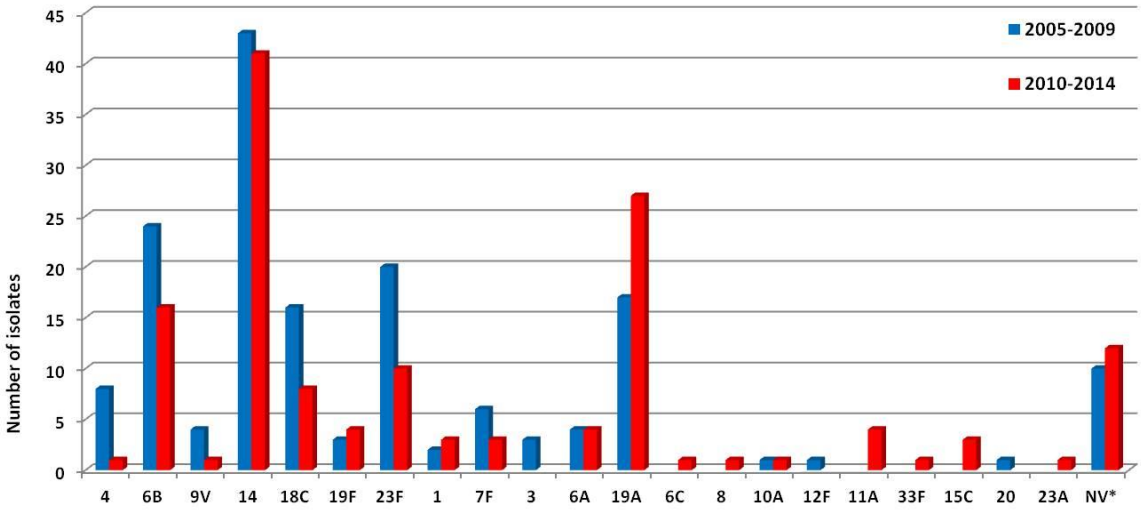


Fig.2. Serotype distribution and macrolide resistance, Croatia 2005-2014, 245 invasive isolates



*NV / non-vaccine type

Fig.3. Changes in serotype distribution, Croatia 2005-2009 # 2010-2014, 305 invasive isolates

ESPID-0822
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

NEONATAL INVASIVE HAEMOPHILUS INFLUENZAE DISEASE IN ENGLAND AND WALES: EPIDEMIOLOGY, CLINICAL CHARACTERISTICS AND OUTCOME

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Background

Non-typeable *Haemophilus influenzae* (NTHi) frequently causes non-invasive upper respiratory tract infections in children but can cause invasive disease, mainly in older adults. An increased burden of invasive NTHi disease in the perinatal period has been reported by a number of studies. Here we describe the epidemiology, clinical characteristics and outcome of neonatal invasive *H. influenzae* disease in England and Wales over a five-year period.

Methods

Public Health England conducts enhanced national surveillance of invasive *H. influenzae* disease in England and Wales. Detailed clinical information was obtained for all laboratory-confirmed cases in infants aged ≤31 days during 2009-2013.

Results

Overall, 118 live-born neonates had laboratory-confirmed invasive *H. influenzae* disease; 115 (97%) were NTHi, two serotype f (Hif) and one serotype b (Hib). NTHi was isolated within 48 hours of birth (early-onset) in 110/115 (96%) cases and 70/110 (64%) presented with septicaemia. Only 17 mothers (15%) had suspected bacterial infection requiring antibiotics during labour. Few (8/110, 7%) neonates had co-morbidities. The incidence of early-onset NTHi increased exponentially with prematurity from 0.9/100,000 (95% CI, 0.6-1.4) in term neonates to 342/100,000 (95% CI, 233.9-482.7) in neonates born at <28 weeks gestation (IRR, 365; 95% CI, 205-659; $P<0.001$). Case fatality for early-onset NTHi was 19% (21/110); each additional gestational week reduced the odds of dying by 21% (OR=0.79, 95% CI=0.69-0.9 0, $P<0.01$). A quarter of neonates who survived experienced long-term complications.

Conclusions

Early-onset neonatal NTHi disease is strongly associated with premature birth and causes significant morbidity and mortality.

ESPID-1072
SHORT ORAL PRESENTATION SESSION 1- EPIDEMIOLOGY AND PUBLIC HEALTH

Severity of pH1N1 infections in hospitalized children in the Netherlands - results of a nationwide retrospective study

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[5]Department of Medical Microbiology, Radboud university medical center, Nijmegen, The Netherlands

Background: During the H1N1 pandemic in 2009-2010 all children with flu like symptoms were extensively tested for influenza. In addition, the seasonal flu vaccine administered to risk groups was not protective. Therefore, this season is especially valuable to assess risk factors for severe disease in children caused by influenza in the Netherlands.

Methods: We performed a retrospective chart study on all infants (< 18 years) admitted to 77 out of the 91 Dutch hospitals with a RT-PCR confirmed H1N1 infection during the 2009-2010 pH1N1 season.

Results: 940 patients (56% male) were included, median age 3.0 year [IQR 0 - 9 years]. Median duration of hospitalization was 2.0 days [IQR 1-4 days] Twenty four percent needed supplemental oxygen, 63% were given antiviral treatment, 7% were admitted to the ICU and 4.6% needed mechanical ventilation. Fifteen patients died (1.6%) of which 4 were previously healthy. Thirty one percent of the patients above 6 months had an indication for flu vaccine according the Dutch guidelines. This group was more severely affected and overrepresented compared to the general population. In a multivariate model, neurologic condition, CF, heart conditions, tube feeding and atopic constitution were strongly correlated with length of stay. Neurologic, oncologic conditions and young age correlated with mortality.

Conclusions: This study gives a nationwide reflection of the flu pandemic in The Netherlands and recognizes most of the known risk groups for severe influenza infections. However, 70% of the admitted children had no indication for flu vaccination, highlighting the importance to reconsider current vaccination policy.

ESPID-0818
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

CHILDHOOD LIFE THREATENING INFECTIONS IN THE GAMBIA: EUCLIDS IN WEST AFRICA

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Background: Despite the importance of bacterial infections as a major cause of morbidity and mortality in African children, data on the causes and outcome of severe childhood sepsis and focal bacterial infection in West African children is limited**.**

Methods: Patients aged 1 month to 18 years presenting with sepsis or severe focal infection to two main refferal hospitals in The Gambia were studied. Basic demographic data, clinical features, outcome and pathogen identified using standard bacterial culture were documented. In addition samples were collected for further molecular diagnostics.

Results: Data collected from January 2013 to July 2014 is reported. Of the 267 patients recruited, 168 subjects (62.9%) were less than five years old and 113 (42.3%) were female. 208 (77.9%) had completed all EPI vaccinations. Half of all subjects had a history of pre-hospital antibiotics. Despite this, an organism was identified in 72 (27%) of cases with the most common isolates *S. aureus* (26, 35.1%), *S. pneumoniae* (13, 17.6%) and *N. meningitidis* (10, 13.5%). Patients with osteomyelitis and meningitis were most likely to have a positive culture (80% and 46.4% respectively). Overall mortality was 30 (11.2%) with 11 (33.3%) dying from meningitis/encephalitis.

Conclusion: Severe bacterial sepsis is a common cause of hospital admission in The Gambia with *S. aureus* being the most common pathogen. However, high rates of pre-hospital antibiotic use make conventional microbiology a poor diagnostic tool and there is an urgent need for access to simple, sensitive molecular diagnostics and improved clinical algorithms for case management.

ESPID-0994
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

COMPARISON OF BLOOD CULTURE AND TARGETED PCR FOR IDENTIFICATION OF BACTERIAL PATHOGENS IN CHILDREN WITH LIFE-THREATENING INFECTION

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[11], http://www.euclids-project.eu,, United Kingdom

Introduction

Blood cultures are slow and insensitive, particularly after pre-admission antibiotics. We investigated the diagnostic yield of targeted PCR in children with severe febrile illness.

Methods

Febrile children with severe focal or lifte-threatening infection were recruited at presentation by the EUCLIDS consortium between January 2012 and October 2014, alongside healthy controls. EDTA blood samples from 4 nodes (UK, Netherlands, Austria, Spain) were pretreated by lysozyme/lysostaphin digestion and matrix B bead lysis (MPBio), before nucleic acid extraction using Qiagen MDx Biorobots. We applied nested PCR for ten bacterial targets: *Acinetobacter baumanii, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae, Group A Streptococcus,* and *Group B Streptococcus*.

Results

We compared PCR and hospital blood culture results for these 10 pathogens for 608 febrile children, median age 46 months. 438 patients tested negative by both PCR and blood culture. In the remaining 170 patients, there were 183 pathogen detections - 112 by PCR and 110 by culture (Table). 39 detections were common to PCR and culture. There were 73 and 71 unique identifications by PCR and culture, in 66 and 70 patients, respectively. No *K.pneumoniae* tests were positive. No bacteria were identified in 34 healthy controls.

Conclusion

PCR increased the number of patients with detectable pathogen from 104 to 170 (163%). PCR and culture preferentially detected Gram-negative and Gram-positive organisms respectively. The findings are supported by negative results in controls. PCR holds promise for rapid detection of bacterial pathogens, and its clinical relevance should be studied further.

Pathogen detections by PCR and culture on blood

	A.baumanii	*E.coli*	Group A strep	Group B strep	*H.influenzae*	*N.meningitidis*	*P.aeruginosa*	*S.aureus*	*S.pneumoniae*
PCR detection total	5	5	6	1	13	34	14	9	25
Culture detection total	1	4	16	2	1	24	0	36	26
Detected by both (% total)	0 (0)	1 (13)	5 (30)	1 (50)	1 (7)	16 (38)	0 (0)	4 (10)	11 (28)
Found only by PCR	5	4	1	0	12	18	14	5	14
Found only by culture	1	3	11	1	0	8	0	32	15
Total patients	6	8	17	2	13	42	14	41	40

ESPID-1000
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

CLINICAL CHARACTERISTICS OF OSTEOMYELITIS AND SEPTIC ARTHRITIS IN CHILDREN: FIRST DATA FROM THE EUCLIDS NETWORK

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Background and aims

Bone and joint infections like osteomyelitis and septic arthritis occur in ~3-12/100.000 children per year in high-income countries with predominance in males. The most common causative pathogen is *Staphylococcus aureus*, however, only in 50% pathogen detection succeeds. The aim of this study is to describe clinical characteristics of osteomyelitis and septic arthritis in children recruited within the EUCLIDS network (www.euclids-project.eu).

Methods

Data was collected within the European Childhood Life-threatening Infectious Disease Study, an international and interdisciplinary network with the aim to study life-

threatening bacterial infections. 195 participating hospitals from 9 countries collected data from children aged between 1 month and 18 years.

Results

296 pro- and retrospective cases of bone and joint infections were recruited within the network between July 2012 and December 2014 (131 in UK, 46 in Austria, 39 in Switzerland, 38 in the Netherlands, 23 in Spain, and 19 in Gambia). 163 children had osteomyelitis, 104 had septicarthritis and 29 had both osteomyelitis and septic arthritis. Median age was 6 years (IQR 8.5 years), 57% children were male. In osteomyelitis most commonly the femur (30%) and tibia (27%) were affected whereas in septic arthritis it was the hip (35%) and knee (33%). The most common pathogen detected was *Staphylococcus aureus* (38%), however, in 39% of all cases no organism was identified.

Conclusion

The clinical characteristics of osteomyelitis and septic arthritis are still unchanged whereby in more than one third of our sample no causative organism was identified.

ESPID-1003

SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

EUCLIDS PROJECT: MENINGOCOCCAL DISEASE IN CHILDREN IN EUROPE 2012-2014

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BACKGROUND AND AIMS: Meningococcal disease is a life-threathening childhood infection. We describe the current characteristics of paediatric invasive meningococcal disease in Europe. Prospectively included in a clinical

network designed for the study of life-threatening bacterial infections (EUCLIDS project).

METHODS: From july 2012 to december 2014, 195 Participating hospitals from 9 countries (Austria, Germany, Italy, Lithuania, UK, Serbia & Montenegro, Spain, Swiss, The Netherlands) collected data from children aged 1 month to 18 years presenting with sepsis or severe focal infections including meningococcal disease. *Neisseria meningitidis* was isolated by routine cultures or molecular techniques

RESULTS: Among 1513 prospective inclusions a total of 127 meningococcal disease cases were identified. Median age was 24 M; P25=7M; P75= 4,5YR. 55.1% male. The majority of cases were due to serogrouped B (100, 78.7%). The remaining cases were due to serogroup C (n=8, 6.3%), Y (n=3, 2.4%), W (n=2, 1.6%), Z (n=2, 1.6%), unknown (n=12, 9.4%). Mortality was 3.2% (n=4) and major sequelae occurred in 6.3% (n=5) of survivors.

CONCLUSIONS: In Europe, invasive meningococcal disease is mainly caused by serogroup B meningococci. In children meningococcal disease especially affects Young infants. The disease continues to cause childhood deaths and disability in Europe. The recent availability of a vaccine against meningococcus B serogroup may change this scenario, and its inclusion in the national immunization program should be considered.

EUCLIDS (grant number FP7 GA no. 279185)

ESPID-1029

SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

CHARACTERISTICS OF INVASIVE COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS MUSCULOSKELETAL (CA-SA-M) INFECTIONS IN CHILDREN: A EUROPEAN MULTI-CENTRE STUDY (PISA STUDY)

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BACKGROUND AND AIMS

In the past few years there have been an increased number of publications describing invasive community-acquired *S. aureus* infections in children. The aim of the study was to describe the characteristics of CA-SA-M infections in Europe.

METHODS

A prospective, multi-centre European study was performed, analyzing data from children under 16 with an invasive CA-SA-M infection, from 1-10-2012 to 30-12-2014.

RESULTS

A total of 85 children (51 boys, 60%) with an invasive CA-SA musculoskeletal infection at twelve European centers were recruited. Median age was 9 years (IQR 5.5-12), 31 (36%) had suffered a recent trauma and 16.5% of them had an underlying disease. Attending to discharge diagnosis, 73% had osteomyelitis, 24% had arthritis and 3% had pyomiositis. Ten patients presented a multifocal infection (11%). The median hospital stay was 16 days (IQR 10-24). Sixty patients (70%) needed surgery at some point of the course; and twenty of them needed 2 or more surgeries. Ten patients (12%) needed PICU admission. At admission, median axilar temperature was 39ºC (IQR 38-39.7). Median CRP and white cell-count were 7.1 mg/dl (IQR 2.5-14) and 10000 cells/m3 (IQR 8200-14400), respectively. Prevalence of methicillin and clindamycin resistance was 6% and 8%. PVL data were collected in 70 cases, and it was present in 12 of them (17%).

CONCLUSIONS

Pediatric invasive CA-SA infections affect mostly musculoskeletal locations, and they need surgery in a large number of cases. PVL presence is high in CA-SA musculoskeletal infections in Europe but methicillin resistance is still uncommon.

ESPID-1036
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

EUCLIDS PROJECT: CHARACTERISTICS OF THE FIRST 2000 EUROPEAN PATIENTS WITH LIFE-THREATENING OR SEVERE FOCAL INFECTION

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Background and aim: Life threatening bacterial infections (LTBI) or severe focal infection (SFI) constitutes the main cause of hospitalization in children. The first 2000 patients recruited through EUCLIDS consortium clinical network (www.euclids-project.eu) are described.

Methods: Eligible patients were children from 1 month-to-18 years with LTBI or SFI admitted to any of the 195 hospitals of the 9 countries constituting the EUCLIDS consortium clinical network. From December-2012 to December-2014 a total of 3990 patients were included: 995 controls, 358 African-node patients(excluded from this analysis), 616 ineligible/incomplete. The remaining 2021 subjects were analysed.

Results: Median age was 58.30 months. 53.4% were male. 54.5% (n=1101) had a septic illness and 45.5% (n=920) a focal infection. 26 (1.6%) of children died. Patients were mainly diagnosed with pneumonia (n=312, 15.4%), meningitis or encephalitis (n=238, 11.8%) and septic shock (n=131, 6.5%). A causal microorganism was identified in 66.3% (n=1339) of the cases. The most prevalent was *S.aureus* (n=239, 11.8%) followed by *S.pneumoniae* (n=191, 9.5%). 12.3% of the patients were finally diagnosed with viral infection. 42.7% (n=756) patients needed to be admitted to PICU and during hospitalization, 37.0% (n=556) of the children required oxygen and 22.7% (n=366) invasive ventilation. Inotropes were necessary in 17.5% (n=265) of the cases.

Conclusions: The average mortality rate in children hospitalized due to LTBI or SFI in Europe is relatively low. Despite the application of the best standard of diagnosis work-up, a causative microorganism was identified in only two thirds of the cases.

EUCLIDS (grant number FP7 GA no. 279185)

ESPID-1052
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

HIGH INCIDENCE OF ENTEROVIRAL AND PARECHOVIRAL INFECTION IN CHILDREN WITH SEVERE INFECTIONS

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INTRODUCTION: The relationship between respiratory viral and bacterial infection is well described, but it is unclear if this extends to other viruses. We investigated the association between Human enterovirus (EV) and parechovirus (PeV) and bacterial infection in children.

METHODS: Blood was collected from children admitted with suspected sepsis or severe focal bacterial infection, recruited through the EUCLIDS consortium in UK, Netherlands, Spain and Austria, between July 2012 and December 2014. Ethics approval and informed consent was obtained for all sampling. A centralized viral and bacterial molecular protocol using nested PCR was used to detect 10 bacteria, EV and PeV in blood samples.

RESULTS: Combining data from hospital diagnostic tests and from our systematic PCR, we identified bacterial pathogens in 195 of 608 (32%) patients. In addition, case ascertainment rose from 7 and 3 cases for EV and PeV respectively, to 41 EV and 17 PeV cases. Bacterial coinfection was present in 6 (14%) and 10 (59%) EV and PeV cases respectively. Based on the overall rate of 32% bacterial identification, EV and PeV were significantly associated with decreased and increased bacterial infection respectively (P=0.02 and 0.03 - Fisher exact).

CONCLUSIONS: Molecular techniques significantly increase the microbiological diagnostic yield, improving the identification of viral and bacterial etiological agents in children admitted to hospital with life threatening bacterial infections. EV and PeV were unexpected findings in many cases. Co-infective patterns and clinical significance of this finding remains unclear and should be further investigated.

ESPID-0812
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

PRE-VACCINE MENINGITIS CAUSING STREPTOCOCCUS PNEUMONIAE SEROTYPES IN PAEDIATRIC PATIENTS IN ZAMBIA,

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Background

Zambia has been collecting data on laboratory confirmed meningitis cases in children below the age of 5 years, at the University Teaching Hospital (UTH) sentinel site. The country introduced the *Haemophilus influenzae* type b (Hib) vaccine in 2004 and PCV10 Pneumococcal vaccine in July 2013.

Methods

Results of 558 CSF for 2010 to 2013 from under 5 year olds were analysed. Blood and Chocolate agar were used for isolation of the pathogens and identified using conventional methods. Molecular analysis of CSF specimens was done using the Polymerase Chain Reaction (PCR) method. A total of 102 *Streptococcus pneumoniae* isolated were serotyped using the Quellung test. Antibiotic susceptibility testing was done on 65 strains of *S.pneumoniae* against Penicillin and Ceftriaxone using the E-Test according to CLSI guidelines.

Results

The most common pathogen was *Streptococcus pnemoniae (*84%). *Neisseria meiningitidis* and *Haemophilus influenzae* type b accounted for 10% and 6% respectively. A total of 22 different serotypes were identified. The vaccine serotypes included 1, 3, 4, 6A, 6B, 7F, 14,18C, 19A, 19F, and 23F, though vaccine serotypes 5 and 9V were not detected. The non-vaccine serotypes included 46, 10A/B, 10F, 15B, 15C, 18A, 18A/B/C/F, 18F, 19B/F, 25A/38, 6A/B. The most common pneumococcal serotypes were 1 (21%) and 46 (13%). The *S.pneumoniae* strains were 75% susceptible to penicillin, while 99% were susceptible and 1% intermediate for ceftriaxone.

Conclusion

Streptococcus pneumoniae is a major cause of meningitis in these children. Non-vaccine meningitis causing *S.pneumoniae* serotypes, and resistance to the first line drug penicillin have been detected.

ESPID-0902
SHORT ORAL PRESENTATION SESSION 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

ENTEROVIRUS RNA AND IGM KINETICS IN CEREBROSPINAL FLUID IN CHILDREN WITH MENINGITIS

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Aim was to evaluate timing of detection of enteroviral RNA and IgM in cerebrospinal fluid (CSF) in children with meningitis.

Methods: 109 children (63 females, 46 males, from 1.5 to 16 years) with acute meningitis, caused by enteroviruses ECHO6, ECHO30 and Coxsackie B5, were observed in Minsk children's hospital, during 2009.

Lumbar puncture was performed at admission, pleocytosis was 41 (16-123) /mm^3. CSF samples were tested for enterovirus RNA by PCR (RotorGene 3000, AmplisensEV tests), CSF and plasma samples – for IgM to enterovirus by ELISA.

Results: Enterovirus RNA in CSF was detected in all children tested at the day of clinical manifestation (n=9), in 94.6% tested at day 2 after onset (n=37), 96.7% at day 3 (n=30), 60% at day 4 (n=5), 42.9% at day 5 (n=7), 36.4% at day 6 (n=11), and 30.0% at day 7 or later (n=10).

IgM antibodies to enterovirus begin to appear in CSF at 5 (4-7) day after the onset of disease, in plasma – at 7 (6-9) day (Kaplan-Meier analysis). Earlier appearance of IgM in CSF comparing to blood (Cox-Mantel test, $p<0.05$) reflects intrathecal ahead of systemic antibodies synthesis.

Conclusions: Enterovirus RNA can almost always be detected in CSF during the first 3 days of disease (in 96.1%, n=76). Then from day 4 and later the rate of positive samples is progressively decreasing, so negative test at this period cannot exclude the enteroviral meningitis – here IgM testing should also be performed with CSF (from day 5) or blood (from day 7).

ESPID-0929
Short Oral Presentation Session 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGY AND MICROBIOLOGY OF BACTERIAL MENINGITIS IN COSTA RICAN CHILDREN PRIOR TO INTRODUCTION OF UNIVERSAL PNEUMOCOCCAL CONJUGATE VACCINATION, PERIOD 2004-2008

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BACKGROUND AND AIMS: Knowing the local epidemiology and microbiology of bacterial meningitis (BM) helps countries to provide evidence-based treatment decisions and vaccine introduction priorities. Our objective was to analyze the epidemiology and microbiology of children with BM hospitalized at the only pediatric tertiary referral hospital in Costa Rica prior to universal PCV7/PCV13 introduction in 2009 and 2011, respectively.

METHODS: Retrospective descriptive chart review study of children

RESULTS: We analyzed 117 patients. Average age at admission was 1.5 years; newborns and infants *S.pneumoniae* 30 (25.6%), *S.agalactiae* 20 (17.1%), *H. influenzae* sp. 9 (7.8%, only 1 Hib), *E.coli* 8 (6.8%), and *N.meningitidis* 7 (6%). Sequelae were reported in 51 (43.5%) patients, being the most common: hypoacusia/deafness, developmental delay and epilepsy. The lethality was 10.2% (12 patients).

Conclusions: BM is associated with significant morbidity and mortality rates in CR children. Most of these cases and their associated complications and sequelae, are now vaccine-preventable. Given the introduction of PCV in the national immunization program, this collected data will serve as the basis for analyzing its impact on BM.

ESPID-0223
Short Oral Presentation Session 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

INTERMITTENT, HIGH-DOSE NITRIC OXIDE INHALATION THERAPY FOR HOSPITALIZED 2-12 MONTH OLD INFANTS WITH BRONCHIOLITIS: A DOUBLE BLINDED, RANDOMIZED CONTROLLED TRIAL

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Background: Nitric oxide (NO) has been previously shown to possess *in vitro* and *ex vivo* broad spectrum antimicrobial activity. When administered via inhalation, it is safe in animal models as well as in healthy adults. The aims of this study were to determine safety, tolerability and efficacy of intermittent high-dose inhaled NO (HD-Inh-NO) for the treatment of hospitalized infants with bronchiolitis.

Methods: This was a double-blind, randomized controlled (HD-Inh-NO *vs.* oxygen only) study. HD-Inh-NO (160ppm) was given 5 times/day, for 30 min each time, to hospitalized 2-12m old infants with bronchiolitis. Inhaled FiO_2, NO, Met-Hemoglobin (MetHb), NO_2, Oxygen saturation (SaO_2) heart and respiratory rates, and blood pressure were continuously monitored. Efficacy was measured by length of hospitalization (LOS) and time to achieve $SaO_2 \geq 92\%$ in room air (if treated for >24h).

Results: 43 infants were enrolled; 25 were hospitalized for >24h and thus were evaluable for efficacy (HD-Inh-NO – 14; oxygen only -11). Among all 43 patients no differences in adverse and serious adverse events (AE/SAE) were found between the HD-Inh-NO (n =22/5) and the oxygen only group (n = 22/6). No HD-Inh-NO related AE/SAEs were documented. Mean LOS and time to achieve $SaO_2 \geq 92\%$ (n=25) were shortened by 28.3±29.4 and 34.8±34.6 hours respectively (p=0.032 for both) (**FIGURE**)

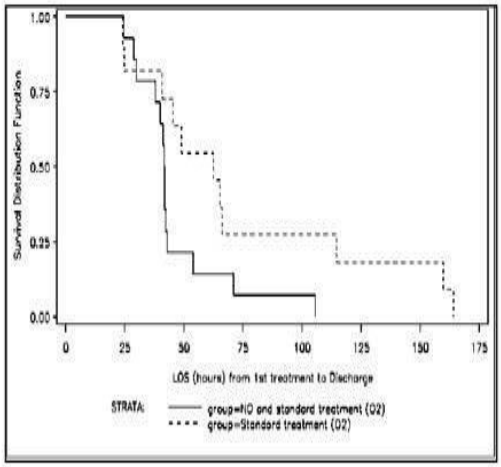
Conclusion: Intermittent high-dose (160ppm) nitric-oxide inhalation is safe and tolerated. HD-Inh-NO reduced hospitalization time and the duration of oxygen

requirement in young infants with bronchiolitis.

Figure: Comparison of length of stay in hospital and time to achieve ≥92% O_2 saturation in room air between HD-Inh-NO and oxygen only groups, among 2-12 month old infants with bronchiolitis hospitalized for >24 hours

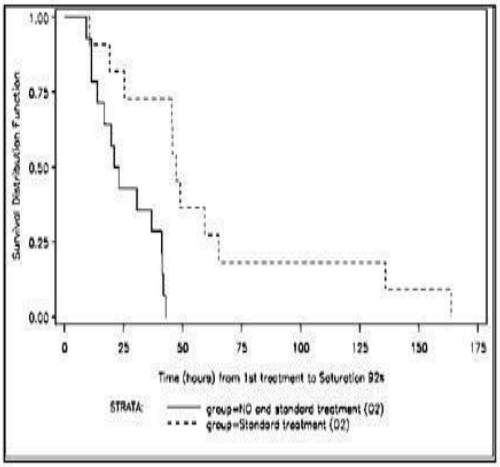
Length of stay (in hours)

	N	Mean	P-value
NO	14	46.03	0.032
Control	11	74.31	



Time to 92% in room air (in hours)

	N	Mean	P-value
NO	14	25.85	0.032
Control	11	60.64	



ESPID-0214
Short Oral Presentation Session 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

COMPARISON OF EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF EMERGENT HUMAN PARECHOVIRUS VS ENTERIOVIRUS INFECTIONS IN THE FIRST MONTH OF LIFE

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Background. Human parechoviruses (HPeVs) are emergent viral agents. Our aim was to investigate the prevalence of HPeV infections in infants up to 1 month of age in Spain and to analyse the clinical and epidemiological characteristics of the infected patients. To compare HPeV and enterovirus (EV) infections.

Methods. Descriptive prospective study currently on-going performed in different Spanish hospitals. Infants $\leq$ 1 month with neurological or systemic symptoms admitted to the participant centres were included. EV and HPeV detection by RT-PCR and further genotyping were determined in clinical samples. Primary outcomes were the rate of positive patients for EV and HPeV and the comparison of clinical data between them.

Results. Of the total of 84 infants included in the study during 2013, 32 were EV positive (38%) and 9 were HPeV positive (11%). HPeV type 3 was identified in 8 cases and HPeV-5 in one. Mean age of HPeV-positive patients was 18 days. In these

cases, diagnoses were fever without source (FWS) (67%), clinical sepsis (22%) and encephalitis (11%). Leukocytes in blood and cerbroespinal fluid (CSF) were normal. Pleocytosis ($p=0.03$) and meningitis ($p=0.001$) were significantly more frequent in patients with EV infections than with HPeVs.

Conclusions HPeV-3 infections are frequent in infants younger than 1 month mainly associated with FWS and without leukocytosis and pleocytosis in CSF, especially during spring and summer. In these cases, HPeV screening in CSF or blood is desirable to identify the etiologic agent and prevent unnecessary treatment and prolonged hospitalization.

ESPID-0299
Short Oral Presentation Session 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

THERAPEUTIC RESPONSES TO NON-CARBAPENEM ANTIBIOTICS IN FEBRILE URINARY TRACT INFECTION CAUSED BY EXTENDED-SPECTRUM B-LACTAMASE-PRODUCING ESCHERICHIA COLI AND KLEBSIELLA PNEUMONIAE

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Background and aims:Non-carbapenem antibiotics seem to be useful for treating urinary tractinfection (UTI) caused by extended-spectrum β-lactamase (ESBL)-producingmicroorganisms. This study was performed to evaluate therapeutic responses ofUTI caused by ESBL-producing microorganisms to non-carbapenem antibiotics.

Methods:Medical records of children who experienced febrile UTI caused by *Escherichia coli* and *Klebsiella pneumoniae* were retrospectivelyreviewed. The enrolled children were divided into the ESBL and non-ESBL groupsaccording to the positivity of ESBL of the causative microorganisms. Clinical, microbiological, andradiological findings were compared between the two groups.

Results:A total of 151 episodes (*E. coli* in 141episodes, *K. pneumoniae* in 10episodes) of febrile UTI were enrolled, and 14 (9.3%) of them were included inthe ESBL group (*E. coli* in 13episodes, *K. pneumoniae* in one episode).Third generation cephalosporin or aminopenicillin/β-lactamase inhibitor incombination with aminoglycosides was empirically administered in 77.5% ofchildren, and none received carbapenems empirically. During empirical therapy,fever disappeared in 88.5% of episodes and urine cultures became sterile in 96.5%of episodes. The type of empirical antibiotics and the frequencies of defervescenceand sterilization of urine during empirical antibiotic therapy were notsignificantly different between the two groups. The duration of fever and antibiotictherapy and the frequency of acute pyelonephritis on imaging studies were alsonot significantly different between the two groups.

Conclusions:β-lactam antibiotics in combination with aminoglycosides can be an alternativeto carbapenems in UTI caused by ESBL-producing microorganisms.

ESPID-1026
Short Oral Presentation Session 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

EVALUATION OF INVASIVE GROUP A STREPTOCOCCUS DISEASE IN CHILDREN FROM 2005-2013: INCIDENCE AND RISK FACTORS FOR DISEASE SEVERITY

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Background and aims: In the past years several studies have shown an increased incidence of invasive group A *Streptococcus* disease (IGASD); however, data in Spain is scarce. Aim: to evaluate the incidence and clinical syndromes of IGASD in children, and to determine risk factors associated to disease severity.

Methods: Retrospective, descriptive study in children ≤16 years with IGASD evaluated in a tertiary pediatric hospital in Madrid, Spain (2005-2013). Demographics, symptomatology, laboratory and outcome were reviewed. The first period of the study (P1=2005-2009) was compared with the second period (P2=2010-2013).

Results: Forty-six children with IGASD were evaluated (39% males; median age 52.8 months [IQR: 25.6–105.4]). An increased incidence was observed within the study period: 0.9(±0.4) cases/10^5inhabitants/year in P1 vs 2.8(±0.8) in P2 (p=0.008). Most common clinical presentations were pharyngeal/parapharyngeal abscess (24%), osteoarticular infection (17%) and pneumonia (15%). Antibiotic resistance was low (4% erythromycin; 2% clindamycin). The only difference between study periods was the rate of surgical procedures (39% P1 vs 74% P2;p<0.05). Disease severity was associated with pneumonia (56% PICU admissions; p<0.05), higher CRP, and neutrophil percentage at presentation (10 vs 20 mg/dl and 74% vs 86%, respectively;p<0.05). Younger children were more frequently admitted to PICU (27 vs 62 months;p=0.16).

Conclusions: In this cohort of children there was a significantly increased incidence of IGASD during an 8-year period, with no changes in epidemiology, clinical presentation or outcome, except for surgical procedures that were more common in P2. Disease severity was associated with younger age, pulmonary disease and higher inflammatory parameters.

ESPID-1047
Short Oral Presentation Session 2- SEVERE BACTERIAL AND VIRAL INFECTIONS

CIRCADIAN VARIATION IN CHILDREN WITH MENINGOCOCCAL DISEASE

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BACKGROUND: Meningococcal disease (MD) cause high mortality and morbidity due to impaired fibrinolysis and subsequent organ failure. Fibrinolysis is inhibited by plasminogen-activator-inhibitor-1 (PAI-1) and the 4G/5G polymorphism of the PAI-1 gene is involved as risk factor for poor outcome, with the highest risk in 4G/4G homozygotes producing highest concentrations of PAI-1. Beside genotype, the internal circadian system causes a peak - in the morning - in PAI-1 concentration. However, the circadian variation in MD has not been fully studied yet.

AIM: To study the circadian variation in children with MD.

METHODS: This study is a retrospective analysis of patients aged 3 weeks to 18 years with MD, who were previously enrolled in Rotterdam based meningococcal trials from 1988 to 2005. MD was diagnosed clinically or by positive culture.

RESULTS: For 184 patients with MD we analyzed time admitted to PICU in relation to PAI-1 genotype and PAI-1 concentration. 31 patients (17%) were admitted during the morning and 84 patients (46%) during the night. 4G/4G homozygotes had higher PAI-1 concentrations at all times during the day.

DISCUSSION: Regardless of the time of day, 4G/4G homozygotes are at risk for poor outcome in case of MD. Almost half of all MD patients were admitted to PICU at night. This study suggests parents of febrile children to be extra cautious just before their children go to sleep.

ESPID-0164
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

SEVERE ACUTE MASTOIDITIS ADMISSION IS NOT RELATED TO DELAYED ANTIBIOTIC TREATMENT FOR AN ANTECEDENT ACUTE OTITIS MEDIA

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Background and aims Acute mastoiditis (AM) is considered a complication of acute otitis media (AOM).Delayed antibiotic treatment (DAT) for AOM is recommended for children older than 6 months with non-severe illness, no risk factors for complications and no history of recurrent AOM. The aim of this study was to evaluate the relation between DAT for AOM and the severity of a following AM. Methods A prospective observational study of all children 0-14 years admitted with AM to eight hospitals between January 2007 and December 2012. Rates of severe AM (defined by one or more of the following: complication [mastoid sub periosteal abscess, brain abscess, sagital vein thrombosis], need for surgical procedure, duration of admission > 6 days) were calculated. Rates of severe AM in children with antecedent AOM treated with immediate antibiotics were compared to those with DAT. Results Antecedent AOM was diagnosed in 216 of 512 AM admissions (42.1%), of whom 159 (73%) were immediately treated with antibiotics, and 57 (27%) had DAT. For the immediate antibiotic therapy and DAT groups respectively, rates of complication were 19.5% vs. 10.5% (p=0.12), rates of need for surgical procedure were 30% vs. 10% (p=0.0033), and rates of more than six days admission were 37% vs. 29% (p=0.28). Results may reflect the significantly higher percentage of children with recurrent AOM in the immediate therapy, compared to the DAT groups respectively (29% vs. 8.7% (p=0.0021). Conclusions DAT for antecedent AOM is not associated with increasing the severity parameters in the following AM admission.

ESPID-0290
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF HUMAN PARAINFLUENZA VIRUS INFECTION OF CHILDREN IN SOUTHERN TAIWAN

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Background and aims: Human parainfluenza viruses (HPIVs) are important causes of respiratory tract infection. This study was designed to evaluate the epidemiology and clinical characteristics of the three types of HPIVs in a medical center of southern Taiwan.

Methods: All children

Results: Totally 144 patients with HPIV infection were identified, including 12 HPIV type 1 (8.3%), 58 HPIV type 2 (40.3%), and 74 HPIV type 3 (51.4%). 90.3% patients visited ER initially. The mean duration of fever before visiting hospital was 2.1 days. HPIV1 did not occur in January and summer season. HPIV2 occurred after June and peak in October. HPIV3 occurred throughout the year with a peak in July. The mean age of HPIV1 infected patients was 3.1 years; HPIV2 was 5.2 years; HPIV3 was 2.4 years (P

Conclusions: This study showed HPIVs clinical and epidemiologic features in children. HPIV2 was the most common type resulted in croup. HPIV3 was detected year round in younger age, associated with bronchiolitis, and might have fatal outcome.

ESPID-0333
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

IL-10 PROMOTER POLYMORPHISMS AND LUNG FUNCTION BY IMPULSE OSCILLOMETRY AT AGE 5-7-YEARS AFTER VIRAL BRONCHIOLITIS IN INFANCY

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Background Interleukin-10 (IL-10) seems to be associated with post-bronchiolitis wheezing and asthma in children. Therefore the genetic variation of IL-10 may be linked to post-bronchiolitis lung function disorders. The aim of this study was to evaluate the association of proximal promoter region polymorphisms of *IL10* rs1800896 (-1082 G/A), rs1800871 (-819 G/A), rs1800872 (-592 G/T) and distal promoter region *IL10* rs1800890 (-3575 T/A) polymorphism with impulse oscillometry (IOS) results at preschool age in children hospitalized for viral bronchiolitis at <6-months-of-age.

Methods Hundred-and-three former bronchiolitis patients performed baseline, post-exercise and post-bronchodilator IOS at 6.3-years-of-age (median). The measured parameters were airway resistance (Rrs5Hz), airway reactance (Xrs5Hz) at 5Hz and resistance at 20 Hz (Rrs20Hz), resonant frequency (Fres) and the frequency dependency of resistance (dRs/df). Data on single nucleotide polymorphisms (SNPs) of *IL10* rs1800896, rs1800871 and rs1800872 were available for 99 children and of *IL10* rs1800890 for 98 children.

Results *IL10* rs1800896, rs1800871 and rs1800872 genotype AGG/AAT and haplotype AAT, respectively were associated with higher Rrs5Hz (p=0.03 and p=0.09, respectively) and lower Xrs5Hz (p=0.06 and p=0.08) with baseline-IOS in adjusted analysis. At rs1800890, the genotype A/A and carriers of A-allele were associated with lower Xrs5Hz in baseline (p=0.04 and p=0.08, respectively) and post-exercise measurements (p=0.03 and p=0.03) in adjusted analysis.

Conclusion High IL-10-producing genotypes of rs1800896, rs1800871 and rs1800872 were associated with normal IOS results. Low-producing genotype AGG/AAT and

haplotype AAT, and likewise in rs1800890 presence of allele A may be associated with IOS abnormalities in former bronchiolitis patients at preschool age.

ESPID-0396
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MOLECULAR AND CLINICAL CHARACTERISTICS OF NEWLY EMERGING RSV-A ON1 GENOTYPE IN CENTRAL VIETNAM

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Abstract

Background: Respiratory Syncytial Virus (RSV) is a major viral etiology for Lower Respiratory Tract Infection among children. They can be categorized into subgroup-A/B and several genotypes based on genetic variation in G-glycoprotein. Since emergence of ON1 genotype from Canada in 2012, many nations have reported its emergence. By utilizing our acute respiratory infection (ARI) surveillance in Central Vietnam, we investigated the circulating RSV subgroups, genotype pattern, their clinical impact and molecular evolution of Vietnamese ON1.

Methods: A population-based ARI surveillance was established since 2007 in Nha-Trang, central Vietnam. Thirteen respiratory viruses were screened and RSV positive samples during Jan2010-Dec2012 were further investigated for subgroup and genotype. For clinical manifestation comparison, multivariate analysis was performed. Regarding to molecular evolution analysis, Bayesian MCMC was utilized. Also, N-glycosylation site analysis, selection pressure analysis were performed.

Results: During Jan2010-Dec2012, 1854 cases were enrolled, 426 (22.98%) of which were RSV positive. RSV-A showed slightly higher proportion compared to RSV-B during 2010-2011, and in 2012 RSV-A proportion increased up to 70% due to emergence of ON1. Regarding the clinical manifestation, ON1 increased risk of clinical pneumonia 2.26 (95%CI:1.37-3.72) times and chest X-ray abnormality 2.18 (95%CI:1.20-3.97) times higher than NA1. Majority of Vietnamese ON1 clustered in Lineage1 and have unique Lysine (K) at codon site 262, which was under selection pressure. Molecular evolutional rate of Vietnamese ON1 was faster than other world ON1 strains (2.61×10^-2 vs 6.03×10^-3)(substitution/site/year).

Conclusions: RSV-A ON1 emerged and became predominant in 2012. It was associated with increased clinical severity and faster molecular evolution.

ESPID-0411
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

IPD EVOLUTION IN MADRID CHILDREN BY AGE GROUP BEFORE AND AFTER THE DROP OF PCV13 VACCINATION RATES: HERACLES STUDY (2007-14)

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Background and aims: Madrid regional immunization plan (RIP) included PCV7 in 2006 in children <24 months, and subsequently switched to PCV13 in May-2010 (95% vaccination rate (VR)), later on excluded from the RIP in May-2012 for children born after May'12, reducing the vaccination rates down to 67%. We evaluated the impact of this decrease on the disease evolution by age groups in children <15 years (1.009.659 inhabitants in 2013).

Methods: A prospective, laboratory-confirmed surveillance of all hospitalized IPDs in children was performed. All isolates (for serotyping) and culture-negative pleural/cerebrospinal fluids (for PCR detection) were sent to a central laboratory. Incidence rates (IR) per 100,000 inhabitants were calculated using data from the National Statistics Institute. PCV13 vaccination rates were estimated using data from Intercontinental Marketing Services (IMS). Three principal age groups were analysed based on the following vaccination rates in 2013/14: 0-24 months (PCV13 3+1, private vaccination, 67% VR), 2-5 years (PCV13 2+1, full RIP vaccination, 95% VR) and >5 years (PCV7/13 3+1 or 2+1, combined private/RIP vaccination).

Results: The evolution of all and PCV13-type IPD cases and IRs, as well as the vaccination rates is presented in Table1.

Conclusions: After the drop of PCV13 vaccination rates down to 67% in the target population in 2013-14, children 0-24 months were the population most severely affected, presenting an increase of IPD IR, as well as the children >5

years. The population of children 2-5 years, still well vaccinated, maintained the IR decrease.

TABLE 1

IPDs cases and incidence rates (per 100.000 population) by period, age group and PCV13 type

		PCV7 RIP (2007-'08)	PCV7 RIP ('08-'09)	PCV7 RIP ('09-'10)	PCV13 RIP ('10-'11)	PCV13 RIP ('11-'12)	PCV13 non-RIP ('12-'13)	PCV13 non-RIP ('13-'14)
Vaccination rates		95%	95%	95%	95%	95%	82%	67%
PCV13-type IPD cases, N (IR)	0-24 months	40 (27,24)	60 (40,69)	46 (30,35)	23 (15,08)	11 (7,40)	4 (2,83)	5 (3,37)
	2-5 years	51 (23,81)	45 (20,61)	55 (25,09)	44 (20,00)	19 (8,55)	10 (4,57)	7 (3,28)
	>5 years	34 (5,77)	29 (4,77)	34 (5,44)	22 (3,43)	15 (2,29)	8 (1,23)	10 (1,51)
	Total	125 (13,16)	134 (13,76)	135 (13,55)	89 (8,78)	45 (4,38)	22 (2,18)	22 (2,18)
All IPD cases , N (IR)	0-24 months	56 (38,13)	74 (50,19)	66 (43,55)	38 (24,92)	31 (20,84)	23 (16,24)	29 (21,65)
	2-5 years	69 (32,22)	56 (25,64)	64 (29,20)	50 (22,72)	28 (12,61)	19 (8,68)	13 (6,08)
	>5 years	38 (6,45)	37 (6,08)	39 (6,24)	27 (4,21)	20 (3,05)	12 (1,85)	16 (2,42)
	Total	163 (17,15)	167 (17,15)	169 (16,96)	115 (11,34)	79 (7,70)	54 (5,35)	58 (5,74)

ESPID-0674
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

EFFECT OF PCV10 ON THE NATURAL ANTIBODIES AND ANTIBODY RESPONSES AGAINST PROTEIN ANTIGENS FROM STREPTOCOCCUS PNEUMONIAE, HAEMOPHILUS INFLUENZAE AND MORAXELLA CATARRHALIS IN CHILDREN WITH COMMUNITY-ACQUIRED-PNEUMONIA

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Background and aims: *Streptococcus pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis* are common causative agents of respiratory infections. Pneumococcal conjugate vaccines (PCV) have been introduced recently, but their effect on the natural immunity against protein antigens from these pathogens has not been elucidated.

Methods: This was an age-matched case-control study that evaluated the influence of 10-valent PCV (PCV10) vaccination on the baseline levels of antibodies and on the frequencies of antibody increases against proteins from *S. pneumoniae, H. influenzae* and *M. catarrhalis* in serum samples of children with community-acquired-pneumonia(CAP). Eight pneumococcal proteins (Ply, CbpA, PspA1 and 2, PcpA, PhtD, StkP and PcsB), three proteins from *H. influenzae* (including Protein D) and five *M. catarrhalis* proteins were investigated.

Results: The study group comprised 38 vaccinated children and 114 age-matched controls (median age[25^{th}-75^{th} percentile]: 14.5[9.8-18.8] *vs.* 14.6[10-19] months, respectively; p=0.997), all with CAP. There was no difference on clinical baseline characteristics between vaccinated and unvaccinated children. Vaccinated children had significantly lower levels of antibodies against four pneumococcal antigens

(p=0.048 for Ply; p=0.018 for PspA; p=0.001 for StkP; and p=0.028 for PcsB) and higher levels of antibodies against *M. catarrhalis* (p=0.015). Nevertheless, the vaccination status did not significantly affect the rates of antibody increases against *S. pneumoniae, H. influenzae* and *M. catarrhalis.*

Conclusions: In spite of the differences that have been found on the baseline level of antibodies, no effect from pneumococcal vaccination was observed on the rate of antibody increases with CAP against protein antigens from *S. pneumoniae, H. influenzae* and *M.catarrhalis*

ESPID-0109
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

VITAMIN A AND ZINC AS ADJUNCTS IN TREATMENT OF CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT INFECTION - A RANDOMIZED CONTROLLED TRIAL

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Objectives: To study the effect of zinc and vitamin A individually or in combination on duration of resolution of symptoms of Acute lower respiratory tract infection (ALRI). **Methods:** This double blind Randomized Controlled Trial conducted in a tertiary care hospital in South India included 320 children (2months – 5years of age) with ALRI. They were randomized into 4 groups to receive adjuncts either zinc, vitamin A, a combination of both zinc and vitamin A, or no adjuncts along with standard ALRI treatment. Parameters including duration of normalization of temperature and respiratory rate, disappearance of chest indrawing , duration of oxygen requirement, IV fluid requirement, ICU stay and mechanical ventilation, hospital stay, need for change of antibiotics, development of complications, rate of readmission within 3 months and mortality were observed in all 4 groups and compared**. Results:** There was no gross difference in duration of resolution of ALRI, treatment failure rates and readmission rates among the four groups. However, subgroup analysis showed significant decrease in duration of mechanical ventilation and ICU stay among infants who received a combination of zinc and vitamin A. The incidence of change in antibiotics was also significantly reduced by 30% in infants who received combination of zinc and vitamin A. **Conclusion**: There was no added benefit for the use of zinc, vitamin A or their combination as adjuncts in children with ALRI. However, zinc and vitamin A combination may be useful for infants with severe ALRI.

ESPID-0168
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ACUTE MASTOIDITIS (AM) IN CHILDREN

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Objectives. To describe the epidemiologic, microbiologic, clinical and therapeutic aspects of AM in children <15 years of age during the 4-year period following the introduction of PCVs in Israel.

Patients and methods. The medical records of all children with a discharge diagnosis of AM were reviewed. PCV7 and PCV13 were introduced in the national immunization program in 7/2009 and 11/2010, respectively.

Results. A total of 66 AM episodes occurred in 61 patients. Forty-four (66.6%) cases occurred among patients <4 years, recent acute otitis media (AOM) history was reported in 27.1% and 28.8% patients received previous antibiotics for AOM. Postauricular swelling, postauricular sensitivity, protrusion of auricle and postauricular edema (93.8%, 90.6%, 85.9% and 95.7%, respectively) were the most common signs of AM. Leukocytosis >15,000 WBC/mm^3 was found in 39 (59.1%) cases. Cultures were performed in 52/66 episodes (positive in 27, 51.92%); 32 pathogens were recovered. The most frequent pathogens were *S. pneumoniae* (15/52, 28.85%), *S. pyogenes* (9, 17.3%) and nontypeable *H. influenzae* (5, 9.62%). Eight (53.3%) *S. pneumoniae* isolates were susceptible to penicillin. Mean incidence of overall and pneumococcal AM were 11.1 and 2.58 cases/100,000, with no changes during the study years. Surgical intervention was required in 19 (28.8%) patients.

Conclusions. 1) AM occurs frequently in patients without previous AOM history or previous antibiotic treatment; 2) *S. pneumoniae* and *S. pyogenes* continued to be the main etiologic agents of AM during the postvaccination period; 3) No changes were recorded in overall AM and in pneumococcal AM incidence during the postvaccination period.

ESPID-0367
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RISK FACTORS FOR BACTEREMIA IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA: A CASE-CONTROL STUDY.

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Background: Few researches have analyzed risk factors associated with development of bacteremia in hospitalized patients with bacterial community-acquired pneumonia (CAP).

Aim: To identify risk factors associated with bacteremia in hospitalized children with typical bacterial CAP.

Methods: Eleven center, retrospective, case-control study, from 2009 onwards. Cases: hospitalized children with bacteremic CAP. Controls: children admitted with typical bacterial pneumonia (RCP >80 and >15 000 WBC/mm3) and negative blood cultures. Immunodeficient children were excluded.

Results: We recruited 88 cases and 88 controls. Up to 18% had received 1 or 2 doses of PCV13, and 62% some dose of PCV7. *S. pneumoniae* caused most bacteremia

(N=69; 78.4%). Serotypes were obtained in 62 patients (70%), 79% were serotypes included in PCV13. The most frequent were 1 (n=31; 50%), 19A (n=9; 14%) and 7F (n=6; 9%). *H. influenzae* was isolated in 5 patients, and *S. aureus* in 5 patients (5,7%). Bacteremia was associated with the following risk factors: male sex [p=0.004, RR: 1.5 (95%CI: 1.1-2.1)], empyema [p=0.004, RR: 1.5 (95%CI: 1.1-2.1)] (but not simple parapneumonic effusion), and age <2 years [p=0.03, RR: 1.3 (95%CI: 1.0-1.8)]. Any dose of PCV13 protected against bacteremia [p=0.047, RR: 0.69 (95%CI: 0.5-0.96)]. Patients with ≥3 doses of PCV13 had half the risk of bacteremia [p=0.006, RR: 0.5 (95%CI: 0.3-0.9)] than children with <3 doses.

Conclusions: In this sample of children with typical CAP, PCV13 protected against bacteremia. Male sex, age <2 years, and empyema (but not simple effusion) were risk factors for bacteremia.

ESPID-0397
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF INFANTS AND CHILDREN WITH LABORATORY-CONFIRMED PERTUSSIS IN A SECOND LEVEL HOSPITAL IN COSTA RICA

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***Background and aims**:* To describe the epidemiological and clinical characteristics of children with pertussis at a second level hospital in Costa Rica.

Methods: Retrospective descriptive study, from Jan-1-2006 to Dec-31-2010, of ambulatory and hospitalized patients aged <12 years with PCR-confirmed pertussis, obtained from nasopharyngeal aspirates, and performed at the National Reference Laboratory (INCIENSA).

Results: 97 patients were included in this analysis, of which 71 (73.2%) required hospitalization; the prevalence was 13.8/1000 hospital discharges. Infants (<12 months) represented 46.6% of the cases, with a median age of 3.6 months; 20 (20.6%) patients were ≤60 days old. 54% were ≥1 year, with a median age of 3.9 years. Symptoms onset date to diagnosis were 8.6 days in infants and 10 days in older children. The main risk factors detected were asthma (26.8%) and prematurity (12.4%) and one child had an incomplete vaccine schedule for age. Only 27.8% children were clinically suspected to have pertussis prior to PCR confirmation. Predominant clinical findings in infants were paroxysmal cough (35.6%) and cyanosis (35.5%), and non-specific cough (82.7%) and rales (96.1%) in older children, with significant statistical difference (p <0.001). Main documented complications were respiratory type: pneumonia (28.5%), atelectasis (5.4%) and pleural effusion (1.0%). No deaths occurred.

Conclusion: Despite primary schedule national vaccination coverage rates >90%, pertussis occurred at a significant rate in children older than 1 year of age. Of concern,

a low index of clinical suspicion was seen in this population. New pertussis vaccination strategies should be considered in Costa Rica.

ESPID-0520
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RISK-FACTOR ANALYSIS AND MOLECULAR EPIDEMIOLOGY OF RESPIRATORY ADENOVIRUS INFECTION IN CHILDREN IN TAIWAN, 2009-2013

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Objectives:Respiratory infections caused by human adenoviruses (HAdV) of species B, C, and E (HAdV-B, -C, -E) are worldwide. A significant increase of adenoviral infections is observed in Taiwan. We conducted this study to understand molecular epidemiology of respiratory HAdV and the risk factors of severe HAdV infections in Taiwanese children.

Materials and Methods:We collected pediatric cases of adenovirus infection hospitalized in a medical center in northern Taiwan between 2009 and 2013 to analyze their clinical characteristics and risk factors of severe adenovirus infection. The genotype of HAdV isolates were determined by sequencing the partial hexon and fiber genes. The nucleotide sequences were then compared by phylogenetic analysis.
Results:The 129 patients had a median age of 40.1months (interquartile range 21.9-57.5 months) and included 74 boys and 55 girls. The 30 severe HAdV infections need ICU care. Of the viral isolates, 68 (52.7%) were HAdV-B,35.7% as HAdV-C, and 10.1% as HAdV-E, including 59 (45.7%) with HAdV-3, 26 (20.2%) with HAdV-2, 13 (10.1%) with HAdV-4, 9 (7.0%) with HAdV-7, 6 (4.7%) with HAdV-5, 2 (1.6%) with HAdV-6, 12 (9.3%) with mixed and 2 (1.6%) untyped HAdV. Three major clades were identified with high bootstrap values including HAdV types B, E and C. In multivariate analysis, the risk factors for severe HAdV infection were serotype 7 (odds ratio (OR) 6.6, p=0.029), cerebral palsy (OR 35.4, $p < 0.001$) and prematurity (OR 9.4, p=0.006).
Conclusion:HAdV-3 is the most common serotype. Infected with HAdV-7, cerebral palsy and prematurity are risk factors of severe HAdV infections.

ESPID-0830
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CHANGES IN RESPIRATORY VIRUSES' EPIDEMIOLOGICAL TRENDS ACROSS AGE GROUPS IN FRANCE – A 3 YEARS RETROSPECTIVE STUDY

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Background and aims.

Respiratory viruses' prevalence records in children are mainly restricted to specific populations or viruses. We described respiratory virus's identifications across age groups in a French hospital over 3 years.

Methods.

All nasopharyngeal Multiplex-PCR and RSV-immunochromatography (RSV-IC) diagnostic tests requested by clinicians between 2011 and 2014 were retrospectively included.

Results.

Of the 380 Multiplex-PCR tests performed (345 children), viruses' prevalence varied across age groups (Figure 1). Viral infections and co-infections were significantly higher in children aged 6 to 36 months (81% and 25% respectively) than in other groups ($p \leq 0.04$). Rhinoviruses were most prevalent in the <6 months age group than in other groups (70%; $p \leq 0.002$), while Adenovirus were most prevalent in the 6 to 36 months age group (20%; $p=0.16$ when compared to children aged 3 to 15 years and $p \leq 0.02$ for other age groups). Influenza prevalence was lower in children than in adults (3 vs 22%, $p<0.001$). Seasonality of non-Influenza viruses is depicted in Figure 2.

Of the 1529 RSV-IC tests performed (1508 children, all < 36 months), 31% were positive. Among negative RSV-IC tests also tested by Multiplex-PCR, 28/62 (45%) were positives for respiratory viruses, including 1 RSV positive test.

Conclusion.

This study underlines respiratory viruses' variations across ages. RSV-IC tests underestimated respiratory viruses' prevalence and Multiplex-PCR seems recommended for children with serious symptomatic respiratory diseases. New prospective clinical studies are needed to assess the impact of these respiratory conditions.

Figure 1. Respiratory viruses prevalence across ages

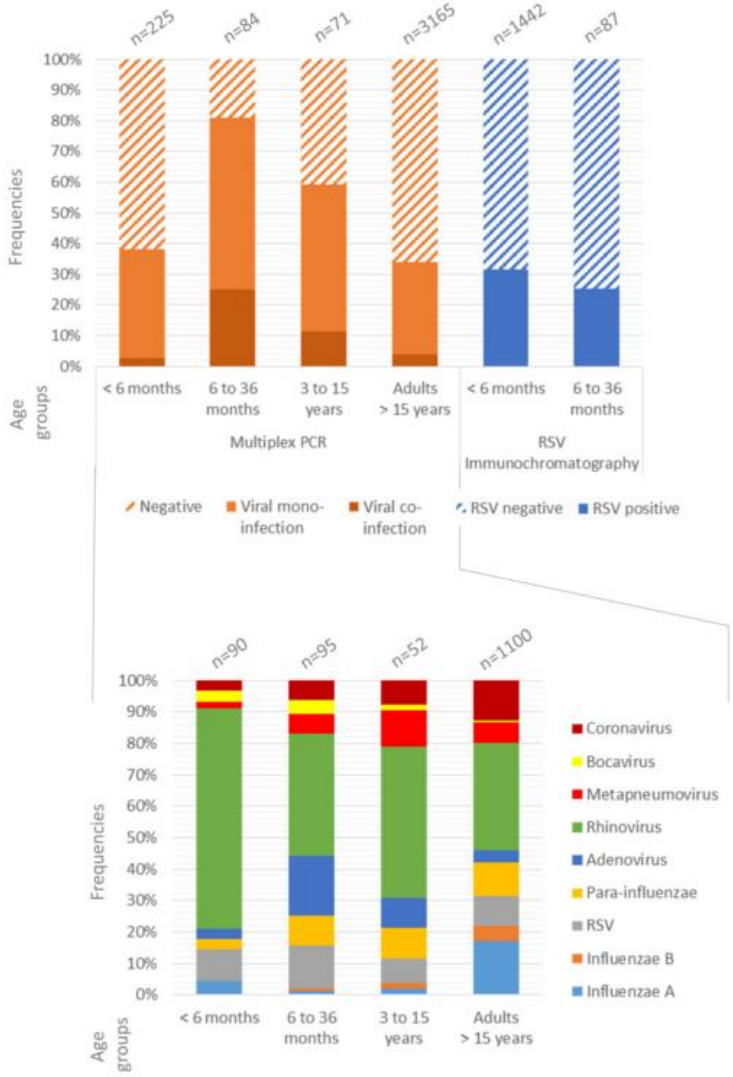
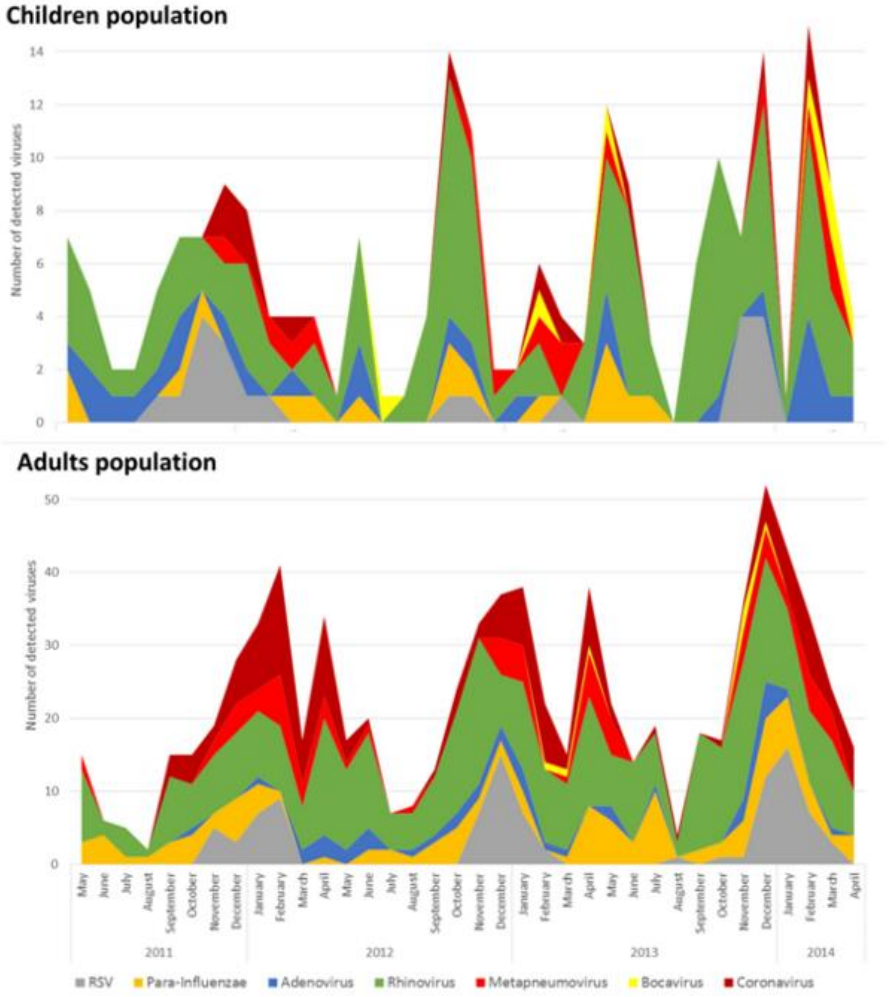


Figure 2. Seasonality of respiratory viruses identified by Multiplex-PCR



ESPID-0950
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DIFFERENCES IN PATHOGEN DISTRIBUTION AND S. PNEUMONIAE (SP) SEROTYPES IN FIRST AND SUBSEQUENT EPISODES OF AOM WITH EXUDATE (HERMES STUDY)

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Background and aims: This study aimed to assess the collected otopathogens and Sp serotype distribution in children (2m-≤8y) with episodes of acute otitis media with effusion (AOMe) in a well defined county in Barcelona. Pneumococcal conjugate vaccines were not included in the general pediatric immunization program in this population, where the estimated PCV13 uptake was 56%.

Methods: This was a prospective, epidemiologic study conducted between June 2011-June 2013. Middle ear swabs from all identified children with AOMe were analysed in a central laboratory. In culture negative ear samples, PCR detection of Sp and *H. influenzae* (Hi) was performed. First AOMe episodes were compared to those with previous history of acute otitis media (AOM).

Results: 397 cases of AOMe were identified. Table 1 and Graph 1 show the distribution of pathogens and Sp serotypes depending on the AOM episode (first or subsequent). 14% of all AOMe cases were fully vaccinated with PCV13 (3+1 schedule). PCV13 serotype coverage was higher in the first vs. subsequent episodes (58% vs. 32%).

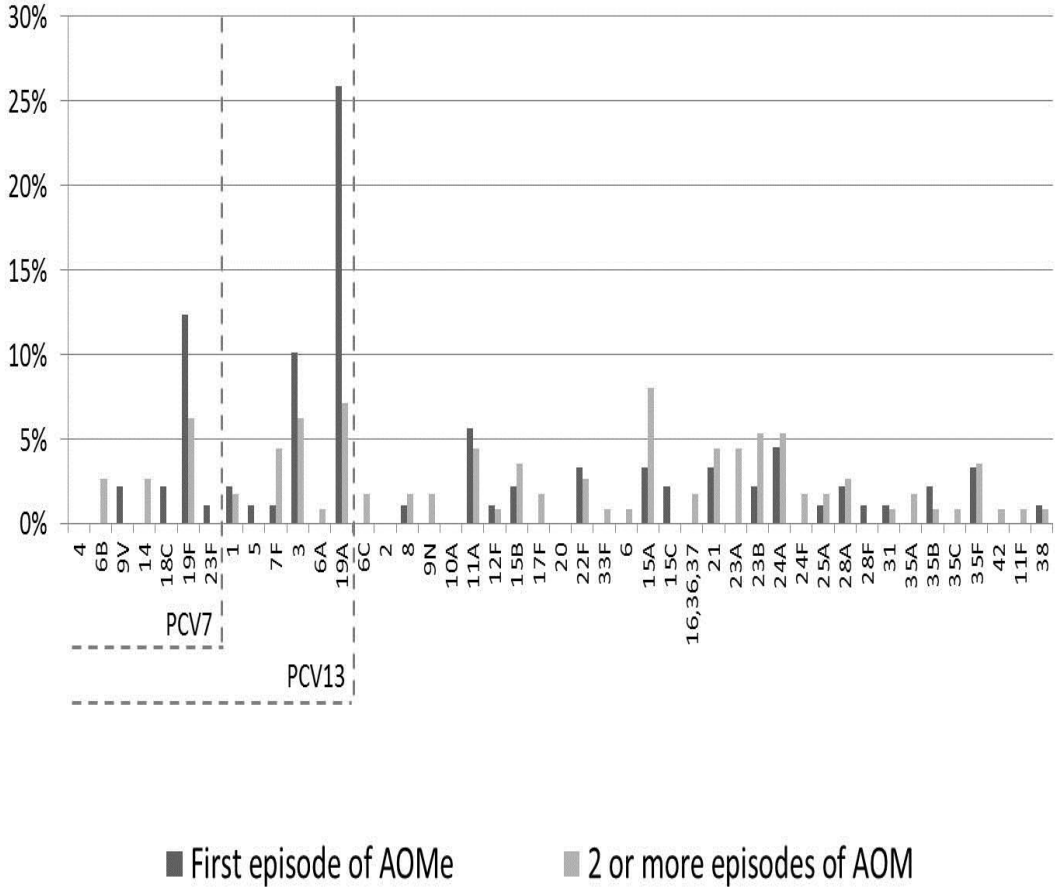
Conclusions: Sp maintained the role of the most frequently identified pathogen in the first cases of AOMe, substituted in subsequent cases by Hi as the predominant pathogen. First cases also presented a higher percentage of PCV13-preventable serotypes compared to subsequent episodes. Furthermore, in accordance with the estimated vaccination rates, first episodes also presented a high percentage of serotypes 19A, 3 and even 19F.

Table 1. Distribution of pathogens at middle ear depending on the number of episodes of AOMe

AOM by pathogen		Sp N (%)	Hi N (%)	Sp +Hi N (%)	S. pyogenes N (%)	S. aureus N (%)	Others N (%)	No pathogen confirmed N (%)	Total N (%)
Number of previous episodes of AOM	Total n(%)*	68 (17)	107 (27)	83 (21)	54 (14)	21 (5)	30 (7)	34 (9)	397 (100)
	First episode of AOMe	37 (27)	19 (14)	23 (17)	25 (18)	8 (6)	13 (9)	13 (9)	138 (100)
	2 or more AOM episodes	25 (11)	82 (37)	48 (21)	26 (12)	11 (5)	15 (7)	17 (8)	224 (100)
PCV13 vaccination history. Full vaccination (3+1) (%)		6 (9)	17 (16)	18(22)	5 (9)	1 (5)	2 (7)	6 (18)	55 (14)

** Including cases with unknown history of AOM (n=35).*

Graph 1. Distribution of *S. pneumoniae* serotypes isolated from the middle ear smear, depending on the episode of AOMe



ESPID-0935
Short Oral Presentation Session 3- UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ROLE OF VIRAL CO-DETECTION IN THE SEVERITY OF HOSPITALIZED INFANTS WITH BORDETELLA PERTUSSIS INFECTION

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Backgound and aims: The role of respiratory viruses (RV) in pertussis disease severity is not well understood. We aimed to characterize factors associated with pertussis severity defined as need for PICU admission, with special focus on RV co-detection.

Methods: A prospective multicentric study was performed at 5 pediatric hospitals in Spain (2013-2014). Infants hospitalized with laboratory confirmed pertussis were enrolled and nasal wash samples collected within 72h of admission for RV detection by multiplex real-time PCR. Vaccine status, clinical parameters and viral co-detection were assessed.

Results: A total of 79 infants with *B. pertussis* infection were enrolled. Median age was 61 days [IQR: 37-93.8], 56.4% were males and 63.6% non-vaccinated. Multiplex-RV-PCR was available in 30 infants, and a RV was detected in 15 (50%): 11 Rhinovirus, 1 Parainfluenza- type 3, 1 RSV-A, 1 Coronavirus-NL63 and 1 Metapneumovirus. 24% (19/79) of infants in the overall cohort required PICU admission (27% (4/15) of those with viral co-detection), 5 mechanical ventilation and 3 exchange transfusion therapy. All children survived. Risk factors for PICU admission are listed in Figure 1. In the subset of infants tested for RV, viral co-detection was not associated with higher PICU admission rates.

Conclusions: Although RVs were identified at a high rate, vaccination status, O_2 saturation, heart rate at admission and demographic factors but not viral co-detections were associated with enhanced disease severity in infants hospitalized with *B. pertussis*.

Figure 1 Risk factors for PICU admission	All Children (n=79) OR (95% CI)	p-value	Tested for RV (n=30) OR (95% CI)	p-value
Weight (kg)	0.47(0.26-0.83)	0.01	0.34(0.11-0.98)	0.047
Height (cm)	0.97(0.9-1.03)	0.31	0.77 (0.6-0.98)	0.041
Heart rate (bpm)	1.05(1.01-1.08)	0.009	1.03(0.98-1.08)	0.23
Respiratory rate (rpm)	1.03(0.99-1.07)	0.1	1.01(0.94-1.08)	0.85
Oxygen saturation (%)	0.83 (0.7-0.99)	0.038	0.67(0.43-1.1)	0.12
Leucocytes > 20000 /mm³	2,05(0,7-6,1)	0.2	0.81(0.06-6.44)	0.88
Lymphocytes > 15000/mm³	0.97(0.27-3.56)	0.969	0.95(0.24-3.7)	0.98
Neutrophils > 5000/mm³	2.93(0.95-9.1)	0.06	2.75(0.2-38)	0.45
Platelets > 500000/mm³	0.97(0.33-2.8)	0.95	0.56(0.07-4.01)	0.57
Age (days)	0.99(0.98-1.01)	0.43	1.79(0.7-4.8)	0.25
CRP (mg/dL)	1.28(0.99-1.78)	0.13	1.0(0.99-1.01)	0.52
Viral co-detection	---	---	2.36(0.36-15.5)	0.37
No pertussis vaccination	7.13(1.51-33.8)	0.013	4.2(0.43-41.9)	0.22

ESPID-1077
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

MARKED REDUCTION OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN AFTER PCV-10 IMMUNISATION

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Background and aims. Iceland introduced pneumococcal conjugate vaccine (PCV-10, Synflorix®) in the childhood vaccination program in 2011, without catch up. Our aim was to monitor changes in the incidence of invasive pneumococcal disease (IPD) and serotypes in children (

Material. All IPD in Iceland are recorded at the Department of Microbiology, Landspitali University Hospital. Information on age, mortality and serotypes was gathered for pre- and post vaccine periods, i.e. 2009-2011 and 2012-2014. Information on the population and mortality was obtained from national registries.

Results. A total of 19 and 1 IPD were diagnosed in children (2

Conclusions. A marked decline in IPD in children was observed following the vaccine implementation.

ESPID-0665
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

VACCINE FAILURES IN PATIENTS PROPERLY VACCINATED WITH 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims:

13-valent pneumococcal conjugate vaccine (PCV13) was marketed in Spain in 2010 but it is not financed by the Spanish health system. Vaccination coverage is around 50%. Although initial data in our country indicate a decrease in invasive pneumococcal disease (IPD), some vaccine failures have been observed. The aim of this study is to analyze vaccine failures following PCV13.

Methods:

During 2012 and 2013, all IPD cases in children younger than 5 years in three pediatric hospitals in Barcelona area were prospectively recruited. IPD was defined based on culture isolation of *Streptococcus pneumoniae* or DNA detection by real-time PCR. Two types of vaccine failures were contemplated: post-primary vaccine failure (IPD due to a serotype included in PCV13 after receiving all 3 doses of the primary series, with age < 16 months) and complete vaccine failure (IPD due to a PCV13 serotype after receiving a complete vaccination course of PCV13 as stated in the package insert)

Results:

81 patients were included. 3 were < 7 months, 32 between 7 and 23 months, and 46 between 24 and 59 months. The most common causative serotypes were serotype 3 (17 cases), serotype1 (13 cases) and serotype 19A (8 cases). Seven complete vaccine failures and 3 post-primary vaccine failures were observed. Serotype 3 was isolated in 7 patients and serotype 19A in the remaining 3.

Conclusions:

Serotype 3, followed by serotype 19A, were the most frequent serotypes involved in PCV13 failures in a geographic area with 50% coverage.

ESPID-0335
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

HOSPITALIZATION DUE TO PNEUMONIA BEFORE AND AFTER INTRODUCTION OF INFANT PNEUMOCOCCAL CONJUGATE VACCINATION

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Background and aims: Introduction of seven-valent pneumococcal conjugate vaccine (PCV7) for infants in 2006 resulted in reduction of invasive pneumococcal disease in children and elderly. This study aims to estimate the impact of infant PCV on community-acquired pneumonia (CAP) hospitalizations by age-group.

Methods: Inpatient discharge codes according to International Classification of Diseases-9 were collected from the National Medical Registration for the years 1999-2005 (pre–PCV7) and 2008-2012 (post-PCV7). CAP was defined as a main discharge diagnosis for all-cause pneumonia, or meningitis, septicemia or empyema with all-cause pneumonia as secondary discharge diagnosis. Age-group specific interrupted time-series analysis was performed using multivariable Poisson regression including month and comparing slopes of hospitalization rates pre- and post-PCV7.

Results: For all age-groups pneumonia hospitalization rates from 2008 onwards showed limited changes as compared to rates from 1999-2005 (Table), but proved not significant for 2-4-year-olds.

Conclusions: A reduction in CAP hospitalization rates following introduction of PCV7 was seen in all age groups, except for 2-4-year-olds. The strongest reduction was seen in children up to 1-year-old and elderly aged 65 years or over.

Age-group	Hospitalization rate ratio per year for 1999-2005 (95%CI)	Hospitalization rate ratio per year for 2008-2012 (95%CI)	p-value
0-6 months	0.98 (0.96-1.00)	0.89 (0.86-0.92)	<0.001
6 months-1 year	1.03 (1.01-1.04)	0.97 (0.95-0.99)	<0.001
2-4 years	1.05 (1.03-1.07)	1.03 (1.00-1.05)	0.118

5-17 years	1.04 (1.03-1.06)	1.00 (0.98-1.03)	0.009
18-49 years	1.01 (1.00-1.02)	0.97 (0.96-0.98)	<0.001
50-64 years	1.00 (1.00-1.01)	0.98 (0.97-0.99)	<0.001
65+ years	1.01 (1.00-1.01)	0.96 (0.96-0.97)	<0.001

ESPID-0378
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

REDUCED DOSE SCHEDULES OF PNEUMOCOCCAL CONJUGATE VACCINE IN PREMATURE INFANTS PRIME FOR IMPROVED RESPONSE IN INFANCY

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BACKGROUND & AIMS

Studies in term infants suggest that immunisation schedules containing more priming doses of PCV13 result in higher antibody concentrations after the primary course but not after the booster dose. We aimed to assess the immunogenicity of a 12 month booster dose of PCV13 in premature infants following 3 different primary PCV13 schedules.

METHODS

210 infants (

RESULTS

The median gestational age was 29^{+6} weeks (range 23^{+2}-34^{+6}). Prior to booster vaccination, higher IgG GMCs were seen in group 3 for 12/13 serotypes. IgG GMCs following the booster dose are shown in figure 1 and demonstrate significantly higher GMCs for group 1 compared to group 3 (9 serotypes) and group 2 (1 serotype). Group 3 had lower fold increases in antibody following vaccination.

CONCLUSION

The 2-4-6 month schedule was associated with increased post-primary and pre-booster antibody concentrations but a decreased response to booster vaccination compared with 2/4 and 2/3/4 month schedules. This may reflect differences in memory formation during primary vaccination as well as suppression by high antibody concentrations at the time of booster vaccination. Further work to explore this and subsequent persistence of antibody is required.

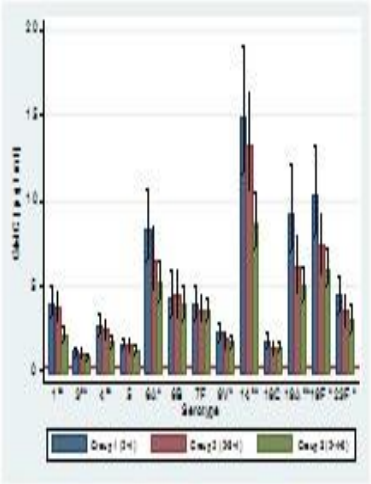

Figure 1: IgG GMCs for the PCV13 pneumococcal serotypes at 13 months of age by priming schedule received. a: significant difference between group 1 & 3, b: significant difference between groups 2 & 3, c: significant difference between groups 1 & 3 ($p<0.05$). Red horizontal line indicates 0.35µg/mL (correlate of protection).

ESPID-0654
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

EFFECT OF PROPHYLACTIC PARACETAMOL ADMINISTRATION ON IMMUNOGENICITY/FEVER FOLLOWING 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D-CONJUGATE VACCINE (PHID-CV) IMMUNIZATION IN INFANTS

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Background and aims: We assessed whether delayed prophylactic paracetamol administration at primary vaccination or immediate prophylactic paracetamol administration at booster vaccination only, impacts post-PHiD-CV immunogenicity and fever.

Methods: Participants of this phase IV, open-label, randomized study (NCT01235949) received PHiD-CV at ages 3,4,5 and 12-15 months. A subset of 217 infants were 1:1:1-randomized to receive, after each vaccination, 3 doses (6-8 hours apart, total daily dose given orally ≤60 mg/kg) of immediate-paracetamol (starting at vaccination, N=71), delayed-paracetamol (starting 4-6 hours post-vaccination, N=72) or no-paracetamol (N=74). Children with immediate-paracetamol at priming received no-antipyretics at boosting (N=67) and children with delayed-paracetamol or no-

paracetamol at priming received immediate-paracetamol at boosting (N=68 and N=67, respectively). An additional group receiving no-antipyretics at primary (N=199) and booster vaccination (N=62) was used as control. Objectives presented: PHiD-CV immunogenicity 1 month post-primary/post-booster vaccination, and fever within 4 days post-vaccination.

Results: Immune responses are presented in the table. Trends for lower post-vaccination fever rates (rectal temperature ≥38.0°C) in infants receiving prophylactic paracetamol at primary (32.9%-38.0% with paracetamol versus 54.1% for no-paracetamol) and booster vaccination (20.9%-28.1% with immediate-paracetamol versus 31.8% for no-paracetamol) were observed.

Conclusions: Trends for lower post-priming antibody GMCs were seen with delayed or immediate prophylactic paracetamol administration at primary vaccination. This trend was observed post-booster in infants receiving immediate-paracetamol at priming only, but not in infants receiving immediate-paracetamol at boosting only. Post-vaccination fever tended to be lower following immediate or delayed prophylactic paracetamol administration.

Funding: GlaxoSmithKline Biologicals SA

Table. Serotype-specific pneumococcal (GSK 22F-ELISA) and protein D (GSK ELISA) antibody responses post-primary and post-booster vaccination (according-to-protocol cohorts for immunogenicity)

At priming:	Immediate-paracetamol		Delayed-paracetamol		No-paracetamol*		No-antipyretics	
At boosting:	No-paracetamol*		Immediate-paracetamol		Immediate-paracetamol		No-antipyretics	
Antibody	Post-pri N=55	Post-bst N=50	Post-pri N=55	Post-bst N=47	Post-pri N=56	Post-bst N=48	Post-pri N=164	Post-bst N=43
	% of subjects with antibody concentration ≥ 0.2 µg/mL							
1	96.3	95.7	98.0	100	100	97.9	99.4	97.6
4	96.4	100	100	100	100	100	99.4	100
5	100	100	100	100	100	97.9	99.4	100
6B	79.2	91.7	72.5	97.8	87.3	100	84.7	100
7F	100	100	100	100	100	97.9	100	100
9V	100	100	100	100	98.1	97.9	98.7	100
14	100	100	100	100	100	100	99.4	100
18C	98.1	100	100	100	100	100	98.7	100
19F	100	100	100	97.7	100	97.9	99.4	100
23F	87.0	95.7	81.1	93.2	90.9	97.9	92.0	95.1
6A$	35.8	83.7	30.0	87.2	49.1	83.0	43.3	92.7
19A$	41.5	83.0	50.0	77.3	56.6	87.2	40.1	78.0
	Antibody GMC							
1	1.32	1.76	1.38	2.14	1.95	2.84	1.90	2.84
4	1.57	3.27	1.95	3.31	2.59	4.28	2.21	4.07
5	1.95	2.62	2.36	3.58	3.05	4.33	2.77	4.48
6B	0.49	1.74	0.42	1.84	0.72	2.29	0.60	2.51
7F	2.18	3.89	2.45	4.63	2.95	4.52	2.77	4.93
9V	1.67	3.11	1.82	3.49	2.40	3.90	2.18	4.05
14	3.44	4.72	4.12	5.52	5.17	5.62	4.77	6.30
18C	3.08	6.18	4.08	8.66	4.96	8.17	4.34	8.68
19F	4.95	5.94	5.20	5.54	6.98	6.66	4.96	7.34
23F	0.77	2.50	0.74	2.53	1.00	3.15	1.07	3.33
6A$	0.11	0.81	0.12	0.87	0.19	0.98	0.15	1.40
19A$	0.15	0.74	0.17	0.63	0.25	1.11	0.16	0.97
PD	1109.6	1482.7	1348.6	1517.3	1667.9	2082.5	1557.7	2285.5

*no prophylactic antipyretics were administered in this group at the respective time points; $cross-reactive serotypes; 22F-ELISA, enzyme-linked immunosorbent assay with serotype 22F polysaccharide adsorption; post-pri, 1 month after 3-dose primary vaccination; post-bst, 1 month after booster vaccination; N, maximum number of infants with available results following primary/booster vaccination with PHiD-CV co-administered with diphtheria-tetanus-acellular pertussis (DTPa)-combined vaccine; GMC, geometric mean concentration; PD, protein D.

ESPID-0704
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

INDIRECT IMPACT OF PNEUMOCOCCAL HAEMOPHILUS INFLUENZAE PROTEIN-D CONJUGATE VACCINE (PHID-CV10) ON HOSPITAL-DIAGNOSED PNEUMONIA IN CLUSTER-RANDOMIZED TRIAL

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Background. In the nation-wide double-blind cluster-randomized Finnish Invasive Pneumococcal disease (FinIP) trial we assessed the indirect impact of PHiD-CV10 (GSK Vaccines) on clinical pneumonia using hospital diagnoses. We have earlier shown indirect impact against laboratory-confirmed invasive pneumococcal disease (IPD) and non-confirmed suspected IPD in unvaccinated population >=5 years of age.
Methods. Children <19 months received PHiD-CV10 in 48 clusters or hepatitis B/A vaccine as control in 24 clusters according to infant 3+1/2+1 schedules or catch-up schedules. Hospitals' in/outpatient discharge reports with ICD-10 diagnoses compatible with pneumonia (ICD-10 code: J10.0/J11.0/J12-J18/J85.1/J86) were collected from national Care Register for the whole population. Annual incidences in the unvaccinated population aged >=5 years were compared between the PHiD-CV10 and control clusters. National vaccination program with PHiD-CV10 using 3, 5 and 12 months schedule without a catch-up started in Sep-2010.
Results. Altogether, >41,000 children were enrolled from May-2009 to Oct-2010. Trial vaccination coverage varied from 29 to 61% in the PHiD-CV10 clusters. Clinical pneumonia incidences were similar in the unvaccinated population >=5 years of age between the PHiD-CV10 and control clusters from 2009 through end 2013. However, there were less empyema cases in the PHiD-CV10 clusters in 2011, but not after that.
Conclusions. We did not detect indirect impact of the PHiD-CV10 vaccine against clinical pneumonia in the unvaccinated population in this clinical trial setting with low vaccination coverage. The only suggestion towards indirect effect was lower incidence

of empyema in the PHiD-CV10 clusters in 2011.

Table. Hospital-diagnosed pneumonia in unvaccinated population ≥5 years in 2011 to 2013

	Endpoint	Rate* in PHiD-CV10 clusters	Rate* in Control clusters	Indirect VE (%)	95% CI
2011	Hospital-diagnosed pneumonia, any	9.7	9.6	0	-9 to 8
	Hospital-treated primary pneumonia	5.8	5.9	3	-8 to 13
	Empyema	0.07	0.08	24	4 to 40
2012	Hospital-diagnosed pneumonia, any	9.4	9.1	-3	-12 to 6
	Hospital-treated primary pneumonia	5.5	5.4	-1	-13 to 10
	Empyema	0.08	0.07	-3	-38 to 23
2013	Hospital-diagnosed pneumonia, any	8.9	8.6	-3	-12 to 6
	Hospital-treated primary pneumonia	5.1	5.0	-2	-14 to 9
	Empyema	0.08	0.09	7	-19 to 27
	*rate= episodes/1000 person-years, cluster-specific averages				

ESPID-0735
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

IMPACT OF 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) ON INVASIVE PNEUMOCOCCAL DISEASE (IPD) CAUSED BY PCV10-RELATED SEROTYPES AMONG VACCINE-ELIGIBLE CHILDREN

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Background: PCV10 was introduced into the Finnish National Vaccination Programme (NVP) in September 2010 with a 2+1 schedule (3,5,12 months) without catch-up. We evaluated the impact of PCV10 on PCV10-related (serotypes belonging to the same serogroup as vaccine types, e.g. 19A and 6A) IPD among vaccine-eligible children during the first four years after the NVP introduction.

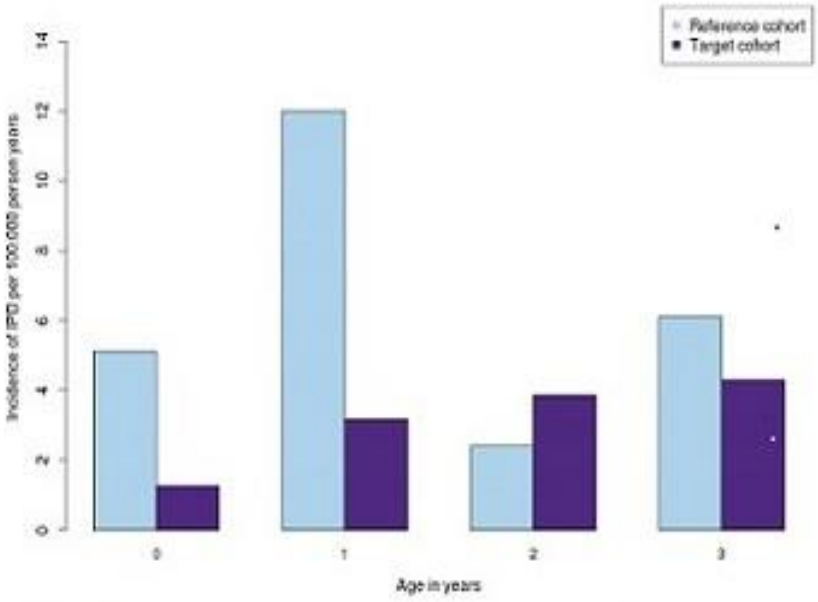
Methods: The target cohort eligible for NVP (children born 06/2010-09/2014) was compared with a season and age-matched (3-54 months) reference cohort before NVP-introduction (children born 06/2004-09/2008). The cohorts were stratified into two age-groups, <24 months and >=24 months. National Infectious Disease Register data were used to calculate culture-confirmed serotype-specific IPD-rates.

Results. By the end of 2014, 16 PCV10-related IPD cases were observed in the target cohort. Figure shows PCV10-related IPD incidence by age in the cohorts. Different rate reductions were observed for children <24 months and >=24 months (table). In the target cohort, 6/8 IPD cases were age-appropriately vaccinated in the younger age group and 5/8 in the older age group.

Conclusion: PCV10 offers cross-protection against PCV10-related serotypes up to 24 months of age. In children >=24 months of age we observed no significant protection. This may be related to antibody waning, increased infection pressure due to replacement, or both.

Table. Incidence rates of IPD due to PCV-related serotypes in reference and target cohorts with corresponding rate reductions during the Finnish NVP

Age-group	Incidence of IPD due to PCV-related serotypes, per 100 000 person-years (N)		Relative rate reduction, % (95% CI)	Absolute rate reduction, per 100 000 person-years (95% CI)
	Reference cohort	Target cohort		
	Follow-up per age-group: 355445 and 195582 years	Follow-up per age-group: 361437 and 204481 years	Target cohort vs. reference cohort	Target cohort vs. reference cohort
<24 months, a	8.4 (30)	2.2 (8)	73.8 (45.5, 88.8)	6.2 (2.8, 9.6)
-6A	3.1 (11)	0.0 (0)	100 (60.8, 100)	3.1 (1.3, 4.9)
-19A	4.5 (16)	1.4 (5)	69.3 (21.6, 89.9)	3.1 (0.6, 5.6)
>=24 months,	3.6 (7)	3.9 (8)	-9.3 (-211.8, 60.8)	-0.3 (-4.1, 3.5)
-6A	2.6 (5)	0.5 (1)	80.9 (-18.6, 99.0)	2.1 (-0.4, 4.5)
-19A	1.0 (2)	2.9 (6)	-186.9 (-1858.5, 33.9)	-1.9 (-4.7, 0.8)



[Incidence of PCV10-related IPD in reference and target cohorts by age-group.]

ESPID-0829
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

INDIRECT IMPACT OF TEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) ON HOSPITAL-DIAGNOSED PNEUMONIA AMONG UNVACCINATED CHILDREN IN FINLAND

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Background. PCV10 was introduced into Finnish National Vaccination Programme (NVP) for children born Jun'2010 and later with no catch-up. We investigated the indirect impact of PCV10 on hospital-diagnosed pneumonia in unvaccinated children during the first three years after NVP-introduction.

Methods. We conducted pneumonia surveillance during 2011-2013 in the target cohort (N=116,672) of unvaccinated children not eligible for NVP (Birthdates Jan'2008-May'2010). Children who received PCV10 in a clinical trial during 2009-2010 (N=30,972) were excluded. Comparative data were collected for years 2004-2006 and 2006-2008 with two age- and season-matched reference cohorts: Birthdates Jan'2001-May'2003 (A, N=134,822) and Jan´2003-May´2005 (B, N=138,050) (Figure). Hospital inpatient and outpatient discharge reports with ICD-10-coded diagnoses were collected from National Care Register and used for calculation of pneumonia rates before and after NVP-implementation. Hospital-diagnosed pneumonia was defined as ICD-10 codes compatible with pneumonia (J10.0/J11.0/J12-J18/J85.1/J86). Hospital-treated primary pneumonia was defined as hospitalisation at least overnight and final primary diagnosis compatible with pneumonia.

Results. Table reports the pneumonia rates by cohort and calendar-time, and rate reductions in 2011 and 2012-2013 compared with season and age-matched periods before NVP.

Conclusions. In unvaccinated children, reductions in clinical pneumonia were observed two years after NVP implementation. This is consistent with our earlier findings in the same study cohort, which suggested that PCV10 elicits herd protection against IPD.

Figure: Cohorts for comparing indirect impact of PCV10

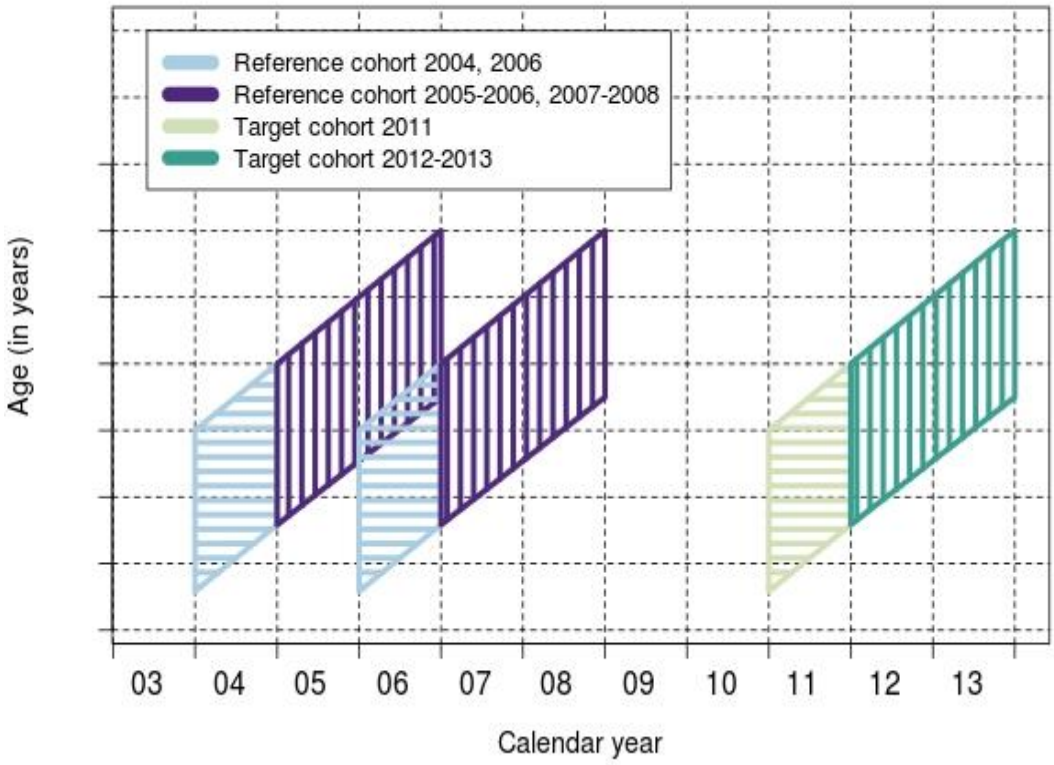

Table: Pneumonia rates per 1,000 person-years (N episodes)

Cohort	Reference cohort A Born Jan´01-May´03		Reference cohort B Born Jan´04-May´06		Target cohort Born Jan´08-May´10		Relative rate reduction, % (95% CI)	
Year of observation	2004	2005-06	2006	2007-08	2011	2012-13	2011 vs 2004&2006	2012-13 vs 2005-06&2007-08
Hospital-diagnosed pneumonia	7.4 (1007)	5.9 (1600)	8.9 (1242)	6.7 (1878)	10.1 (1232)	5.5 (1363)	-24 (-32, -15)	**12 (6, 17)**
Hospital-treated primary pneumonia	3.9 (536)	3.0 (811)	4.8 (669)	3.5 (972)	4.7 (576)	2.3 (570)	-8 (-19, 2)	**28 (21, 35)**

ESPID-0046
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASE ASSOCIATED WITH PNEUMOCOCCAL CONJUGATE VACCINE FAILURES IN SINGAPORE: A CASE SERIES.

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Introduction

The 7-valent (PCV-7) and 13-valent (PCV-13) pneumococcal conjugate vaccine were included in the National Childhood Immunisation Programme (NCIP) in Singapore since October 2009 for the prevention of invasive pneumococcal disease (IPD).

Methods

We retrospectively identified and reviewed the clinical information of vaccine failures associated with IPD in children at the KK Women's and Children's Hospital, Singapore from 2008 to 2014.

Results

4 children with a median age of 4 years old (range 2.08 – 5.83) presented with IPD caused by vaccine serotypes despite being vaccinated with the recommended immunisation schedule. 3 received PCV-13 and 1 received PCV-7. Of the 3 PCV-13 failure cases, isolates identified from 2 cases (one with left-sided pneumonia complicated by empyema and the other with bilateral otitis media with bacteremia) were of *Streptococcus pneumoniae* serotype 19a while the remaining case (left-sided pneumonia complicated by empyema and haemolytic uremic syndrome) was of serotype 3. The isolate recovered from the PCV-7 failure case, who presented with right-sided pneumonia complicated by empyema was of serotype 14. All 3 cases of pneumonia required video-assisted thoracic surgery and chest tube placement. Two required intensive care unit admission. Median length of hospitalization was 10.5 days (range: 7 – 43). Median duration of culture-appropriate antibiotic therapy was 31.5 days (range: 14 – 42). Median time interval between the pneumococcal vaccination and onset of IPD was 23.5 months (range: 7 – 36). All 4 cases recovered without sequelae.

Conclusion:

Our findings warrant further investigation to evaluate the protection afforded against various pneumococcal serotypes.

ESPID-0225
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

NEAR DISAPPEARANCE OF ANTIBIOTIC-RESISTANT PNEUMOCOCCAL OTITIS MEDIA, ASSOCIATED WITH HIGH PCV7/PCV13 UPTAKE AND SUBSTANTIAL DECREASE OF PCV13-SEROTYPES NASOPHARYNGEAL CARRIAGE

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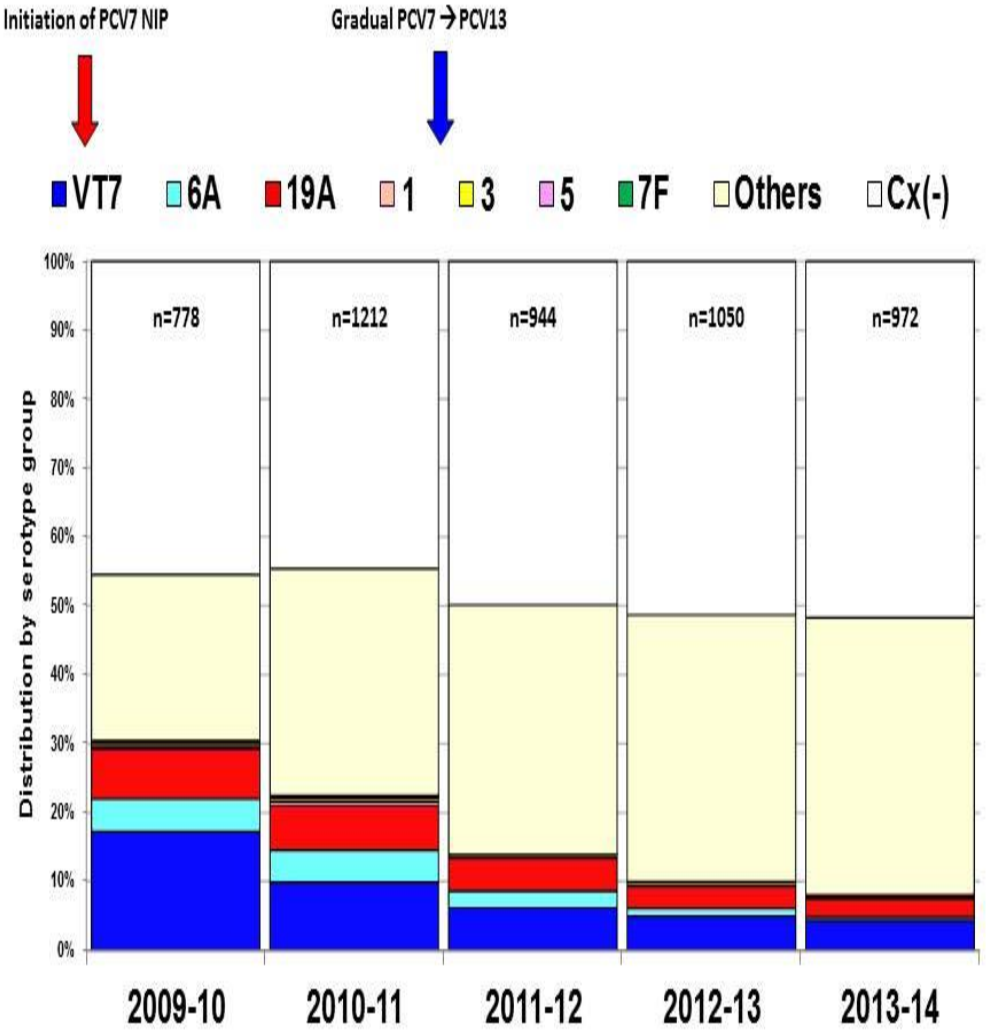
Background: PCV13 serotypes constitute ~80% of pneumococcal otitis media (Pn-OM), and most antibiotic-resistant Pn-OM (AR-Pn-OM). In southern Israel, sequential PCV7/PCV13 introduction resulted in 77% and ~90% reduction of Pn-OM and vaccine-serotype Pn-OM, respectively (*Ben-Shimol, CID 2014*). We assessed dynamics of AR-Pn-OM necessitating middle ear fluid culture (enriched with complex OM) in children

Methods: Vaccine uptake, population at risk, patient population, culture and antibiogram evaluation of Pn-OM were previously described (*Ben-Shimol, CID 2014*; *Dagan, JID 2014*). Nasopharyngeal swabs were collected daily (November 2009 through June 2014) at the pediatric emergency department; pneumococcal isolates were serotyped (*Dagan, CID 2013*).

Results: By June 2011 and December 2012, ~80% and ~90% of children 7-11m received ≥2 PCV7 and PCV13 doses, respectively. Pneumococcal carriage decreased by 11.5% comparing pre-PCV7 period (2009-2010) to 2013-2014. Respective decreases in PCV7 and additional PCV13-serotypes were 74.9% and 72.0% (**Figure 1)**. Penicillin-resistance, macrolide-resistance and dual penicillin-macrolide non-susceptibility were reduced from mean annual rates (per 1,000 children) of 2.5, 2.8 and 2.3 in the pre-PCV7 period to 1.3, 1.4 and 1.6 after PCV7 implementation; and 0.3, 0.2 and 0.2 after PCV13 (2013-2014), respectively (reductions of 88%, 93% and 91%, respectively, p**Figure 2)**

Conclusions: PCV7/PCV13 sequential introduction resulted in rapid and substantial reduction of AR-Pn-OM, in parallel with rapid and high vaccine uptake and near disappearance of PCV13-serotypes nasopharyngeal carriage.

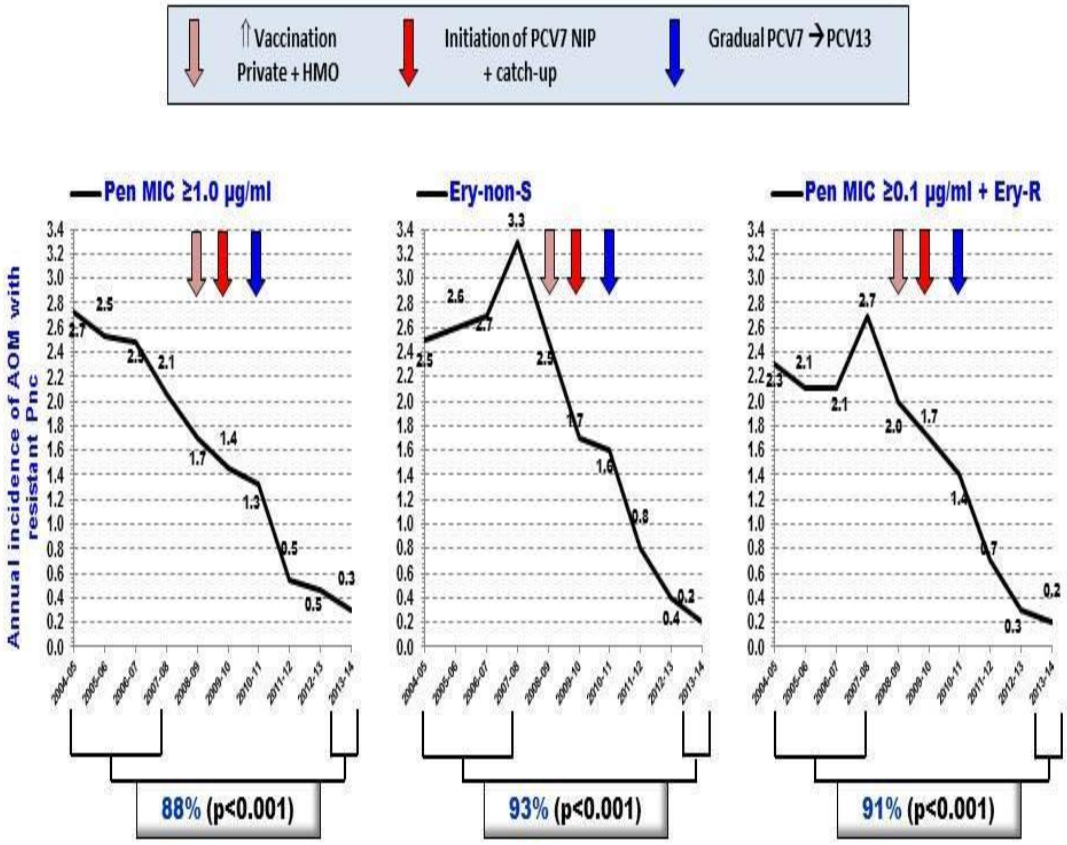
Figure 1. Pneumococcal Carriage in Children <2 Year Attending Pediatric Emergency Room, Southern Israel



* Each year represents the period between July and June

** VT7 – PCV7 serotypes, others – non-PCV13 serotypes, Cx(-) – culture negative

Figure 2. Non-susceptible Pneumococcal OM Rates (per 1,000 children) in Children <2 Years in Southern Israel



* Each year represents the period between July and June

ESPID-0362
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

LONG-TERM ANTIBODY PERSISTENCE AFTER 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN PRETERM (PT) INFANTS COMPARED WITH FULL-TERM (FT) INFANTS

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BACKGROUND: PT infants may be at increased risk of pneumococcal disease. PT immune responses are lower than FT when measured shortly after vaccination. Antibody persistence over longer periods has not been evaluated.

METHODS: 200 infants were vaccinated with PCV13 at 2, 3, 4, and 12 months of age. Serotype-specific anticapsular IgG antibodies and opsonophagocytic activity (OPA) were measured at 5, 12, 13, 24, and 36 months of age.

RESULTS: At 1 and 2 years after last vaccination, IgG GMCs for all serotypes in both groups remained above pre-toddler dose levels. IgG GMCs were significantly lower in PT than FT for a majority of serotypes at both 1 year (n=160 [80 PT, 80 FT]) and 2 years (n=142 [71 PT, 71 FT]) after last vaccination (**Table**). OPA results (subset of subjects) support these findings.

TABLE. PT:FT IgG GMC Ratios, by serotype and time after last vaccination.

	1	3	4	5	6A	6B	7F
Year 1	0.76*	0.59*	0.81	0.67*	0.68*	0.63*	0.82
Year 2	0.82	0.66	0.80	0.68*	0.67*	0.53*	0.89
	9V	**14**	**18C**	**19A**	**19F**	**23F**	
Year 1	0.62*	0.83	0.50*	0.51*	0.54*	0.47*	
Year 2	0.74	0.77	0.56*	0.53*	0.45*	0.56*	

*Upper limit of 95% confidence interval <1.

Conclusions: Measured 1 and 2 years after vaccination, IgG antibody and functionality induced by PCV13 remain preserved above pre-toddler dose responses,

although at lower levels for PT than FT for most serotypes. The routine vaccination schedule is likely to afford protection against IPD in both preterm and term infants.

ESPID-0607
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

EFFECTIVENESS OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE AGAINST ALVEOLAR PNEUMONIA: A MATCHED CASE-CONTROL STUDY

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Background. The mostcommon invasive pneumococcal disease was pneumonia in children in Taiwan. Our aim was to assess the effectiveness of 13-valent pneumococcalconjugate vaccine (PCV13) against community-acquired alveolar pneumonia inTaiwan.

Methods. All childrenaged 3-71 months who were diagnosed with community-acquired pneumonia withalveolar consolidation were included at 5 medical institutions during theperiod 2012-2014. One controlwithout any respiratory symptom, matched for age and admission hospital wasselected for each case. Conditional logistic regression was used to estimatethe matched odds ratio.

Results. Of 186 caseswith alveolar pneumonia, 26 children (14%) received one dose, 5 (2.7%) twodoses, 7 (3.8%) three doses, and 10 (5.4%) four doses, compared with 186controls of whom 64 (34.4%) received four doses, 4 (2.2%) three doses, 3 (1.6%)two doses, and 16 (8.6%) one dose. Effectivenessagainst alveolar pneumonia was 76% (95% CI 58-87) for at least one dose, 77%(95% CI 56–88) for one dose, and 85% (95% CI 32–96) for four doses.

Conclusions. *Streptococcus pneumoniae* accounted forthe majority cause of alveolar pneumonia. PCV13 significantly protected againstradiologically-confirmed alveolar pneumonia in children.

ESPID-0641
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

NASOPHARYNGEAL CARRIAGE FOLLOWING DIFFERENT INFANT VACCINATION SCHEDULES WITH THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D-CONJUGATE VACCINE IN SOUTH AFRICA

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Background and Aims: The 10-valent pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine (PHiD-CV) administered according to different vaccination schedules (**2+1**, **3+0**, **3+1**) in HIV unexposed-uninfected infants in South Africa was shown to be immunogenic.[1] Here, we present bacterial nasopharyngeal carriage (NPC) results in the same children up to 2 years of age.

Methods: In this phase III, open, controlled, single center study (NCT00829010), 300 healthy South African infants (subset born to HIV-negative mothers) were randomized 1:1:1 to receive PHiD-CV according to a **2+1** schedule (primary: 6 and 14 weeks of age; booster: 9–10 months of age), a **3+0** schedule (primary: 6, 10 and 14 weeks of age; no booster), or a **3+1** schedule (primary: 6, 10 and 14 weeks of age; booster: 9–10 months of age). Between 6 weeks of age and 24–27 months of age, 8 nasopharyngeal swabs were collected and cultured using routine microbiological methods to identify bacterial pathogens.

Results: Vaccine-type *Streptococcus pneumoniae* NPC rates ranged between 7.0% (pre-vaccination) and 31.9%, with no major differences between the 3 groups (Table). NPC rates of *S. pneumoniae* (any serotype), *H. influenzae* (non-typeable), and *Staphylococcus aureus* did not differ significantly between groups vaccinated with various schedules.

Conclusions: Infant vaccination schedule did not significantly change the impact of PHiD-CV on bacterial NPC in healthy children.

Funding: GlaxoSmithKline Biologicals SA

[1]Madhi, ESPID 2012

TABLE

Occurrence of *Streptococcus pneumoniae* in nasopharyngeal swabs (total vaccinated cohort)

Age	PHiD-CV vaccination schedule					
	2+1		3+0		3+1	
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
Any vaccine serotype*						
6–12 weeks (pre-vaccination)	100	**7.0** (2.9; 13.9)	100	**14.0** (7.9; 22.4)	100	**14.0** (7.9; 22.4)
18 weeks (1 month post-primary vaccination)	98	**31.6** (22.6; 41.8)	95	**22.1** (14.2; 31.8)	98	**26.5** (18.1; 36.4)
9–10 months (at booster visit)	98	**20.4** (12.9; 29.7)	94	**18.1** (10.9; 27.4)	98	**26.5** (18.1; 36.4)
10–11 months	98	**23.5** (15.5; 33.1)	94	**22.3** (14.4; 32.1)	98	**23.5** (15.5; 33.1)
12–13 months	97	**28.9** (20.1; 39.0)	94	**27.7** (18.9; 37.8)	98	**28.6** (19.9; 38.6)
15–18 months	98	**23.5** (15.5; 33.1)	94	**28.7** (19.9; 39.0)	98	**27.6** (19.0; 37.5)
16–19 months	98	**24.5** (16.4; 34.2)	94	**31.9** (22.7; 42.3)	98	**20.4** (12.9; 29.7)
24–27 months	98	**20.4** (12.9; 29.7)	92	**26.1** (17.5; 36.3)	97	**19.6** (12.2; 28.9)
Any serotype						
6–12 weeks (pre-vaccination)	100	**17.0** (10.2; 25.8)	100	**30.0** (21.2; 40.0)	100	**25.0** (16.9; 34.7)
18 weeks (1 month post-primary vaccination)	98	**65.3** (55.0; 74.6)	95	**57.9** (47.3; 68.0)	98	**59.2** (48.8; 69.0)
9–10 months (at booster visit)	98	**68.4** (58.2; 77.4)	94	**71.3** (61.0; 80.1)	98	**66.3** (56.1; 75.6)
10–11 months	98	**71.4** (61.4; 80.1)	94	**70.2** (59.9; 79.2)	98	**63.3** (52.9; 72.8)
12–13 months	97	**72.2** (62.1; 80.8)	94	**66.0** (55.5; 75.4)	98	**68.4** (58.2; 77.4)
15–18 months	98	**71.4** (61.4; 80.1)	94	**74.5** (64.4; 82.9)	98	**70.4** (60.3; 79.2)
16–19 months	98	**69.4** (59.3; 78.3)	94	**74.5** (64.4; 82.9)	98	**63.3** (52.9; 72.8)
24–27 months	98	**67.3** (57.1; 76.5)	92	**65.2** (54.6; 74.9)	97	**64.9** (54.6; 74.4)

**Pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.*

N, number of swabs cultured at the considered visit; %, percentage of positive swabs at the considered visit; 95% CI, 95% confidence interval.

ESPID-0652
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

EFFECT OF PROPHYLACTIC IBUPROFEN ADMINISTRATION ON IMMUNOGENICITY/FEVER FOLLOWING 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D-CONJUGATE VACCINE (PHID-CV) IMMUNIZATION IN INFANTS

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Background and aims: We assessed whether immediate or delayed prophylactic ibuprofen administration impacts post-PHiD-CV immunogenicity and fever.

Methods: In this phase IV, open-label study (NCT01235949), 595 infants vaccinated with PHiD-CV (ages 3,4,5 and 12-15 months) were 1:1:1-randomized to receive, after each vaccination, 3 doses (6-8 hours apart, total daily dose given orally ≤30 mg/kg) of immediate-ibuprofen (starting at vaccination), delayed-ibuprofen (starting 4-6 hours post-vaccination) or no-ibuprofen at priming. At boosting, each group was 1:1:1-randomized to receive either 3 doses of immediate-ibuprofen or delayed-ibuprofen, or no-ibuprofen. Results presented: non-inferiority of the immune response to PHiD-CV primary vaccination with immediate- or delayed-ibuprofen versus no-ibuprofen, post-

priming fever (both confirmatory objectives) and post-booster immunogenicity and fever.

Results: Non-inferiority of PHiD-CV post-priming immunogenicity with immediate-ibuprofen or delayed-ibuprofen versus no-ibuprofen was demonstrated. No statistically significant decreases in anti-pneumococcal/protein D antibody GMCs were observed with immediate- or delayed-ibuprofen versus no-ibuprofen (Table). No significant reductions in post-priming fever (rectal temperature ≥38.0°C within 4 days post-vaccination) were observed with immediate- (61.4%) or delayed-ibuprofen (51.3%) versus no-ibuprofen (61.3%). Post-booster immune responses were in similar ranges in all groups; percentages of infants with antibody concentrations ≥0.2 mg/mL were 91.5%-100%; antibody GMCs increased from post-priming for most vaccine serotypes. Post-booster fever rates, regardless of prophylactic antipyretic administration at priming, were 31.7%-34.9% (immediate-ibuprofen), 31.1%-36.5% (delayed-ibuprofen) and 25.4%-45.9% (no-ibuprofen).

Conclusions: Immediate or delayed prophylactic ibuprofen administration did not significantly impact post-primary PHiD-CV immunogenicity or fever. Similar trends were observed post-boosting.

Funding: GlaxoSmithKline Biologicals SA

Table. Serotype-specific pneumococcal (GSK 22F-ELISA) and protein D (GSK ELISA) antibody responses, and each pair-wise group comparison at 1 month post-primary vaccination (ATP for immunogenicity)

Antibody	% of subjects with ab conc ≥ 0.2 µg/mL			Difference in % of subjects with ab conc ≥ 0.2 µg/mL	
	imm-IBU N=154	del-IBU N=158	no-IBU* N=164	no-IBU* minus imm-IBU 98.25% CI (LL; UL)	no-IBU* minus del-IBU 98.25% CI (LL; UL)
1	100	100	99.4	-0.62 (-4.52; **3.17**)	-0.62 (-4.52; **2.91**)
4	99.3	100	99.4	0.06 (-3.94; **4.38**)	-0.63 (-4.57; **2.91**)
5	100	100	99.4	-0.64 (-4.63; **3.19**)	-0.64 (-4.63; **2.92**)
6B	84.0	87.1	84.7	0.69 (-9.40; 10.99)	-2.38 (-12.02; **7.22**)
7F	99.4	100	100	0.65 (-2.70; **4.71**)	0.00 (-3.34; **3.48**)
9V	99.3	100	98.7	-0.58 (-5.05; **3.82**)	-1.27 (-5.66; **2.32**)
14	100	99.4	99.4	-0.65 (-4.68; **3.15**)	0.00 (-4.08; **4.12**)
18C	99.3	99.4	98.7	-0.58 (-5.04; **3.85**)	-0.62 (-5.08; **3.54**)
19F	100	98.7	99.4	-0.63 (-4.60; **3.14**)	0.67 (-3.40; **5.20**)
23F	91.9	89.2	92.0	0.08 (-7.66; **8.10**)	2.73 (-5.30; 11.04)
Antibody	**GMC**			**GMC ratio**	
	imm-IBU N=154	**del-IBU N=158**	**no-IBU* N=164**	**imm-IBU / no-IBU* 99.8% CI (LL; UL)**	**del-IBU / no-IBU* 99.8% CI (LL; UL)**
1	1.82	1.71	1.90	0.96 (0.71; **1.29**)	0.90 (0.67; **1.21**)
4	2.25	2.21	2.21	1.02 (0.77; **1.35**)	1.00 (0.76; **1.32**)
5	2.93	2.39	2.77	1.06 (0.80; **1.41**)	0.86 (0.66; **1.14**)
6B	0.67	0.76	0.60	1.12 (0.72; **1.74**)	1.28 (0.83; **1.97**)
7F	2.87	2.83	2.77	1.04 (0.79; **1.35**)	1.02 (0.80; **1.31**)
9V	2.10	2.01	2.18	0.96 (0.70; **1.31**)	0.92 (0.69; **1.22**)
14	4.76	4.52	4.77	1.00 (0.71; **1.40**)	0.95 (0.68; **1.32**)
18C	3.85	3.80	4.34	0.89 (0.60; **1.31**)	0.88 (0.60; **1.27**)
19F	6.11	5.04	4.96	1.23 (0.87; **1.75**)	1.02 (0.72; **1.44**)
23F	1.04	0.92	1.07	0.97 (0.66; **1.44**)	0.86 (0.58; **1.27**)
Protein D	1461.28	1353.13	1557.75	0.94 (0.69; **1.28**)	0.87 (0.64; **1.17**)

*no prophylactic antipyretics were administered in this group. Criteria for demonstration of non-inferiority: UL of the 2-sided 98.25% CI of the difference (no-IBU minus imm-IBU or del-IBU) in post-primary % of subjects with ab conc ≥0.2 µg/mL was <10% for ≥7 out of 10 PHiD-CV serotypes (even in case of a statistically significant decrease in GMCs, defined as UL of the 2-sided 99.8% CI of the post-primary GMC ratio [imm-IBU or del-IBU over no-IBU] <1 for ≥1 vaccine serotype or protein D). 22F-ELISA, enzyme-linked immunosorbent assay with serotype 22F polysaccharide adsorption; ATP, according-to-protocol cohort; N, maximum number of infants with available results following primary vaccination with PHiD-CV co-administered with diphtheria-tetanus-acellular pertussis (DTPa)-combined vaccine; ab conc, antibody concentration; imm, immediate; del, delayed; IBU, ibuprofen; GMC, geometric mean antibody concentration; CI, confidence interval; LL, lower limit; UL, upper limit.

ESPID-0676
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

EFFECTS OF 6 YEARS OF IMMUNIZATION WITH HIGHER-VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN GERMAN CHILDREN

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Background and aims: A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) was issued for German children ≤2 years in 2006. In 2009, two higher-valent PCVs (PCV10, PCV13) were licenced in Germany. Here, we present data on invasive pneumococcal disease (IPD) -cases sent in for serotyping in the nine years following the start of PCV-vaccination.

Methods: Pneumococcal isolates recovered from children with IPD were sent to the GNRCS. Serotyping was performed using the Neufeld-Quellung-reaction.

Results: From July 2012-June 2013, an increase in IPD cases among children <2 years was observed for the first time since the introduction of childhood vaccination (98 vs. 75 cases in 2011-2012). In 2013-2014, this trend was again reversed (81 cases). Cases with PCV7 serotypes have almost disappeared (2 of 81 cases in 2013-2014). Among the PCV13-non-PCV7 serotypes, reductions were observed for serotypes 1 (-91%), 6A (-100%), 7F (-94%) and 19A (-71%) after the introduction of higher-valent vaccination in 2009. Serotype 3 showed a reduction from eight cases in 2009-2010 to four cases in 2011-2012, but did not reduce further. Among the remaining twelve PCV13 cases in children <2 years reported in 2013-2014, nine children were not vaccinated and three were incompletely vaccinated. Among the nonvaccine serotypes, 10A, 12F, 15B/C, 24F and 38 were most prominent.

Conclusions: Almost nine years after the general vaccination recommendation PCV7 and PCV13-non-PCV7 serotypes have almost disappeared among children <2y. A temporary increase in non-vaccine serotypes has become apparent in 2012-2013, however, a net reduction of cases was still observed.

ESPID-0702
Short Oral Presentation Session 4- PNEUMOCOCCAL VACCINATION

VACCINE EFFECTIVENESS (VE) OF THE PNEUMOCOCCAL HAEMOPHILUS INFLUENZAE PROTEIN-D CONJUGATE VACCINE (PHID-CV10) AGAINST HOSPITAL-DIAGNOSED PNEUMONIA - FINIP TRIAL EXTENDED FOLLOW-UP

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Background. VE of pneumococcal conjugate vaccines (PCV) against clinical pneumonia in infants has varied in different trials from 0 to 7%. We recently reported high effectiveness of the PHiD-CV10 (GSK Vaccines) against hospital-diagnosed pneumonia (VE 27%, 95%CI 9-42%) using clinical hospital diagnoses during the blinded follow-up of the Finnish Invasive Pneumococcal disease (FinIP) vaccine trial. Now, we evaluated the longer-term impact against pneumonia.
Methods. FinIP vaccine trial was cluster-randomized, double-blind trial in children <19 months who received either PHiD-CV10 (52 clusters) or hepatitis B/A vaccine as control (26 clusters) according to 3+1 or 2+1 (infants <7 months) or catch-up schedules (children 7-18 months) in 2009-2011. We extended unblinded follow-up for 2012-13 and collected hospitals' in/outpatient discharge notifications with ICD-10 diagnoses compatible with hospital-diagnosed pneumonia (HDP, ICD-10/J10.0/J11.0/J12-J18/J85.1/J86) from national Care Register. PHiD-CV10 was included in National Vaccination Programme (NVP) in September 2010.
Results. Altogether >47,000 children were enrolled. Table shows results for pooled infant 3+1 and 2+1 schedules. The separate VE estimates for the schedules were similar. No VE could be shown for catch-up schedules, either.
Conclusions. The incidence of hospital-diagnosed pneumonia was low in children 2 to 4 years of age followed up during PCV-NVP era. In contrast to the high VE during the blinded follow-up, no impact was detected against pneumonia in the long-term

follow-up. The findings are consistent with long-term observational data from the US.

Table. Vaccine effectiveness of the PHiD-CV10 against hospital-diagnosed pneumonia in infants vaccinated with either 3+1 or 2+1 schedule.

	Incidence in **2012**, per 1000 person-years		Vaccine effectiveness in **2012**	Incidence in **2013**, per 1000 person-years		Vaccine effectiveness in **2013**
Pneumonia endpoint	PHiD-CV10 clusters	Control clusters	% (95% CI)	PHiD-CV10 clusters	Control clusters	% (95% CI)
Any hospital-diagnosed pneumonia	8.2	9.0	6% (-24 to 28%)	5.7	5.1	-12% (-60 to 20%)
Hospital-treated primary pneumonia	3.8	4.3	0% (-46 to 31%)	2.5	1.9	-24% (-110 to 24%)

ESPID-1019
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

SIGLEC-1 ON MONOCYTES CONTRIBUTES TO T CELL IMPAIRMENT AFTER RESPIRATORY SYNCYTIAL VIRUS INFECTION

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Background: Respiratory syncytial virus (RSV) infections are a major burden on our health care system. An impaired T cell response is thought to be responsible for recurrent infections in children, adults and elderly. Several factors, including soluble factors and viral proteins, have been shown to contribute to RSV-mediated impairment of T cells. Monocytes are attracted to the site of infection and could play an important role in disease development. The effect of monocytes and its receptors on T cell regulation after RSV infection are yet to be elucidated.

Methods: Peripheral blood mononuclear cells (PBMCs) or monocytes from healthy adults were stimulated with RSV A2. The induction of SIGLEC-1 on monocytes was determined by micro-array and flow cytometry. The effects of RSV and Poly(I:C), as TLR3 agonist, on T cell responsiveness was determined by measuring mitogen-induced T cell proliferation by CFSE and interferon gamma release (IFN-γ) by ELISA. Finally, blocking of SIGLEC-1 was performed to evaluate the role of SIGLEC-1 on the observed RSV- and TLR3-induced T cell impairment.

Results: SIGLEC-1 was induced on monocytes after stimulation with RSV or Poly(I:C). After stimulation with RSV or Poly(I:C), mitogen-induced T cell proliferation and IFN-γ release was significantly impaired. Most importantly, blocking SIGLEC-1 partially restored the RSV- and TLR3-induced impairment of T proliferation and IFN-γ release.

Conclusion: Our data provide evidence of receptor-mediated T cell suppression by monocytes via SIGLEC-1 during RSV infection. Insights into the inhibitory mechanisms of RSV on T cell immunity will proof useful in the understanding of disease pathogenesis.

ESPID-0240
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

POLYMORPHISMS OF IL10 SNPS -592T/G AND -819A/G ARE ASSOCIATED WITH ATOPY AFTER INFANTILE BRONCHIOLITIS LEADING TO HOSPITALIZATION

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Bronchiolitis is a well-known risk factor for asthma and allergy development. Alterations in host immune responses are potential drivers for increased asthma and allergy risk. IL-10 is a pleiotropic anti-inflammatory cytokine that controls both Th-1 and Th2-type immune responses. We demonstrated earlier that IL10-1082 SNP associates with rhinovirus etiology of bronchiolitis, and that allele G carriage is protective for preschool asthma. Hypothesis for our present study was that IL10 SNPs are associated with Th2-skewed immune responses, which may lead to increased preschool age asthma and atopy prevalence after bronchiolitis.
187 infants were hospitalized for bronchiolitis at <6 months of age. Asthma and allergies were studied from a total of 166(89%) children at 6.5 years(mean). 139(84%) DNA samples were available for IL10-592 and -819 and 141(85%) for IL10-3572 genotyping. SNPs IL10-592 and -819 are in full linkage. Atopy was defined as having doctor-diagnosed atopic dermatitis and/or food-allergy.

Preschool age asthma was present in 19(11.5%) and asthma between 1-6 years in 37(22.3%) children. No associations between investigated SNPs and asthma or wheezing symptoms during childhood could be shown. Current atopy was present in 55(40%) children. Carriers of minor alleles at -592 and -819 were more often atopics, as 25/49(51%) of allele T (-592) and G (-819) carriers had preschool atopy (vs. 30/90(33%) atopy prevalence among homozygotes for major alleles, p=0.04).

These preliminary results suggest that IL10-592 and -819 are associated with atopy in preschool age after infantile bronchiolitis hospitalization. IL10-3572 did not associate with atopy or asthma.

ESPID-0496
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

GENETIC SUSCEPTIBILITY TO NOROVIRUS GII.4 SYDNEY STRAIN INFECTIONS IN TAIWANESE CHILDREN

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Background: A comprehensive evaluation of associations between the susceptibility to norovirus infections and potential host determinants including secretor status (determined by *FUT2*), Lewis enzyme function (determined by *FUT3*) and ABO types were not available in the recent norovirus epidemic caused by GII.4 Sydney strain.

Methods: A 1:1 matched case-control study was conducted in northern Taiwan from February 2013 to December 2014. The cases were children under 18 years old, hospitalized due to gastroenteritis and found to have laboratory-confirmed norovirus infection. The controls were healthy children matched to cases by age and gender. Norovirus genotype was determined by PCR sequencing of VP1 gene. The distributions of *FUT2*, *FUT3* and ABO genotypes were determined by molecular methods and compared between cases with distinct severities and controls.

Results: A total of 136 case-control pairs were included and 77.4% of the cases were caused by GII.4 Sydney strain. The secretor and non-functional mutations of *FUT3* were more commonly identified in cases than in controls (94.1% versus 77.9%, P <0.001, and 21.3% versus 11.0%, P =0.022, respectively). The distributions of ABO type did not differ significantly between the two groups (P =0.137). In case patients, a higher mean Vesikari score was identified in secretors (12.07±2.55 versus 10.63±2.13) and in those with non-functional mutations of *FUT3* (12.09±2.59 versus 11.59±2.38) compared to their counterparts respectively, but without statistic significance (P >0.1 for both comparisons).

Conclusion: Children of secretor and with non-functional mutations of *FUT3* had increased susceptibility to the epidemic Sydney strain infections in Taiwan.

ESPID-0515
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

ANTIGENIC MAP OF INFLUENZA A/H3N2 VIRUS PRODUCED WITH HUMAN PRIMARY INFECTION ANTISERA

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Introduction

Antigenic characterization of influenza viruses for surveillance and vaccine strain recommendation is typically based on hemagglutination inhibition (HI) assays using virus isolates and a panel of singly-infected ferret antisera, that can subsequently be visualized in antigenic maps. This study aimed to perform similar studies, using first-infection human serology data rather than ferret serology data.

Methods

Sera collected between 1995 and 2011 from children between 9 and 24 months old were tested against a panel of 23 influenza viruses by means of HI tests. For comparison, 24 ferret sera were tested against the same panel of viruses.

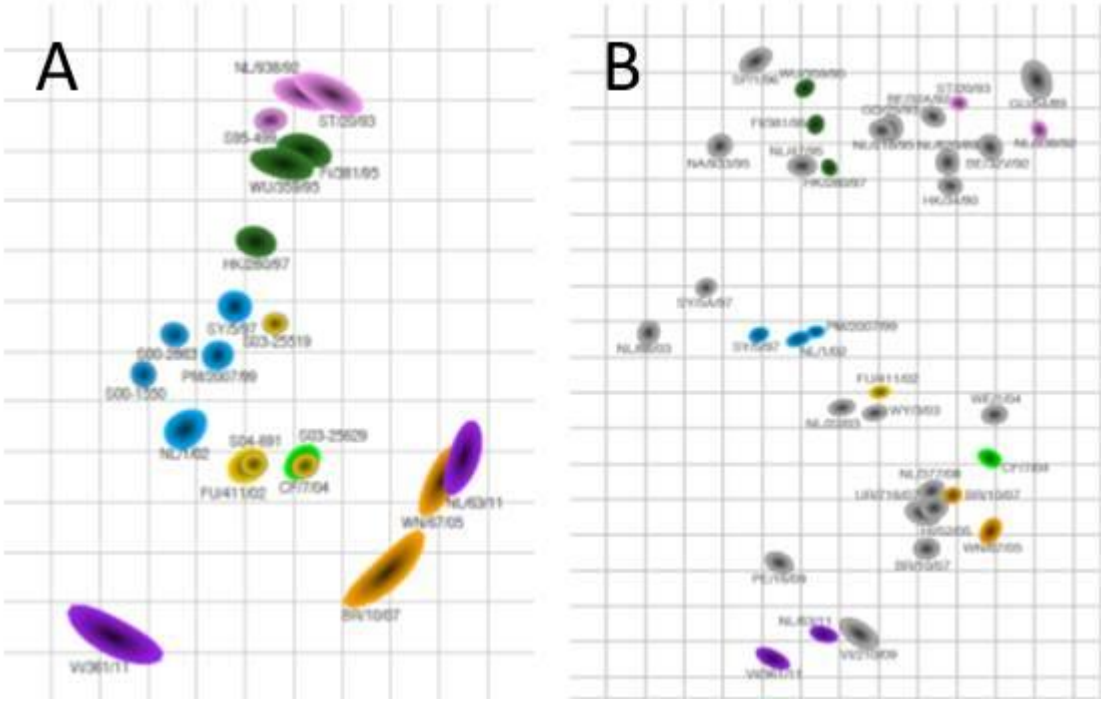
Result

Of the positive human sera, 6 were high-responders, showing HI patterns that would be expected from primary infection antisera. An antigenic map based on the HI data for these sera (figure 1 A) was globally similar to the results using the ferret data (figure 1B), but not identical, with differences often exceeding two antigenic units. The remaining 11 sera were low-responders, some of which had widely dispersed titer patterns with reactivity to strains that circulated decades before the child was born, or after the serum was drawn.

Conclusion

Globally, similar antigenic clusters of viruses are observed in the human map as in the ferret map, but the local differences indicate that the human and ferret immune system may see antigenic properties of viruses differently.

Figure 1. An antigenic map of the HI data for A) Human and B) Ferret sera



ESPID-0690
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

SEVERE CHILDHOOD GUILLAIN-BARRÉ SYNDROME ASSOCIATED WITH MYCOPLASMA PNEUMONIAE INFECTION: A CASE SERIES

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Objective: To describe children with severe Guillain-Barré syndrome (GBS) following a recent infection with *Mycoplasma pneumoniae*.

Methods: Seven children were identified with recent *M. pneumoniae* infection and severe GBS that presented to 2 hospitals between 1992 and 2012. The case definition for severe GBS included respiratory failure, CNS involvement, or death. The cases were described in view of clinical features and investigations of antibody responses to *M. pneumoniae* in blood and CSF.

Results: Five patients presented with GBS, 1 patient with Bickerstaff brain stem encephalitis (BBE), and 1 patient with acute-onset chronic inflammatory demyelinating polyneuropathy (A-CIDP). Five patients were mechanically ventilated, 3 patients had CNS involvement, and 1 patient died (GBS). Most patients had nonspecific clinical symptoms at onset (headache, unsteady gait, and pain) and at admission (nuchal rigidity and ataxia). Patients showed a rapidly progressive disease course (71%). Antibodies against *M. pneumoniae* were detected in all patients and were found to be intrathecally synthesized in 2 cases (GBS and BBE), which proves CNS infection. One patient died, one patient was still unable to walk unaided at 6 months, and long-term residuals were seen in 4 patients.

Conclusions: In pediatric patients with a spectrum of severe subtypes of GBS,

including respiratory failure, BBE, and A-CIDP, a recent infection with *M. pneumoniae* was demonstrated. These patients may present with nonspecific clinical features of GBS, that predispose a potentially life-threatening delay in diagnosis.

ESPID-0762
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

INDUCTION OF BACTERIAL AND FUNGAL-SPECIFIC T-CELL RESPONSES IN HUMAN ADENOIDS AS POTENTIAL FIRST-LINE ORGANS OF PATHOGEN-DEFENSE

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Background: Infants are in particular susceptible to infections. Adenoids are strategically located representing the first contact point of inhaled bacteria and fungi with the immune system.

Aims: In this study, we investigate cellular mechanisms of $CD4^+$ T cells from adenoids of infants to study the antigen specific response to *Staphylococcus aureus*, *Staphylococcus epidermis,* and *Candida albicans* in infants.

Methods: T cells from surgically excised adenoids, cord blood and peripheral blood from healthy donors were characterized by flow cytometry and functional assays. Intracellular stainings and CFSE-dilution experiments were performed. $CD14^+$ monocytes were incubated with extracts of *Staphylococcus aureus*, *Staphylococcus epidermis,* and *Candida albicans* to stimulate adenoid T cells. In addition, cryo tissue sections of the adenoids were analyzed by Imaging Cycler Microscopy (ICM).

Results: Adenoid $CD4^+$ CD45RA and $CD4^+$ CD45R0 T cells proliferate and up regulate the activation-associated molecule CD25 in response to *Staphylococcus aureus*, *Staphylococcus epidermis,* and *Candida albicans*. The T-cell proliferation can be reduced by blockade of HLA-DR using specific antibodies demonstrating antigen-specificity. High numbers of responsive T cells are identified in human adenoids compared to peripheral blood. An inverse correlation between the percentages of proliferating T cells and age of infants is observed in adenoids. For therapeutic interventions, an adenoid-specific hierarchical pattern of cell-cell interactions was identified in adenoids.

Conclusions: Functional bacterial and fungal-specific T cells are identified in adenoids of infants and adults with age-dependent characteristics. Findings will help

to understand the relationship between pathogens and T cells and to optimize intervention strategies.

ESPID-0900
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

INTERLEUKIN-15 EXPRESSION INFLUENCES DISEASE SEVERITY IN VIRAL BRONCHIOLITIS THROUGH ALTERED SIGNALLING IN NATURAL KILLER CELLS.

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Background. Disease severity in viral bronchiolitis is influenced by host innate immunity. Disease progression is difficult to predict, with no reliable laboratory markers.

Objectives. To assess the role of interleukin-15 (IL-15) in disease pathogenesis, and it's potential as a marker of disease severity.

Methods. A prospective observational study was conducted in children hospitalized for viral bronchiolitis and healthy age-matched controls. Quantitative PCR, ELISA, and flow cytometry were performed to compare IL-15 related immunological parameters between groups. miRNA-seq and PCR were performed subsequently on natural killer (NK) cells from study participants.

Results. Ninety-nine cases and 43 controls were recruited. Peripheral blood mononuclear cell (PBMC) IL-15 mRNA expression was significantly higher in those with moderate severity bronchiolitis as compared to controls ($P<0.0001$) and those with severe disease ($P=0.01$). Serum IL-15 levels were significantly elevated in children with bronchiolitis ($P<0.0001$), and elevated further in those with severe disease ($P=0.005$). The relative frequency of NK cells in peripheral blood was significantly reduced ($P=0.008$) in participants with bronchiolitis. IL-15 was expressed intracellularly in a sub-population of dendritic cells that was significantly expanded in children with bronchiolitis. The NK cell microRNA (miR) transcriptome of children with bronchiolitis differed from controls, with 21 miR significantly up-regulated. Seven of 19 mRNA targets of de-regulated microRNA were differentially

expressed in bronchiolitis including *JAK3* (*P*=0.002), *STAT5A* (*P*=0.029), and *NFKB1* (*P*=0.02) that are components of the IL-15 signalling pathway.

Conclusions. IL-15 expression and changes in IL-15 related signalling in NK cells may influence disease severity in viral bronchiolitis.

ESPID-0948
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

SEQUENTIAL TRANSMIGRATION OF T-CELLS AND PMNS ACROSS THE BLOOD- CSF BARRIER IN VITRO

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Background: Aseptic meningitis caused by viruses exhibits a high morbidity rate in young children and is nearly three times as common as acute bacterial meningitis. In particular Echovirus 30 (EV30) from the genus of enteroviruses has been proven to be the most dominant meningitis-causing pathogen in Europe, Asia and America. Previously, it has been shown that enterovirus interacts with choroid plexus epithelial cells and can bind to transmigrating myeloid cells to gain access to the CNS. Methods: We used an inverted inverted cell culture system with human chouroid plexus papilloma cells (HIBCPP) acting as a human in vitro model of the blood cerebrospinal fluid barrier (BCSFB) to analyze leukcocyte transmigration. Results: We could show that 24 hours after an infection with EV30 the transepithelial electrical resistance (TEER) significantly decreases and dextran flux significantly increases, whereas without the virus the TEER value and dextran efflux remain unaffected, which indicates an influence of the infection on barrier function. Transmigration of T-lymphocytes (T-cells) and polymorphonuclear leukocytes (PMNs) also significantly increases following viral infection. Moreover, transmigration is augmented through the addition of the chemokines CXCL-12 for T-cells and IL-8 for PMNs. Furthermore, co-incubation of PMNs with T-cells increases the sequential transmigration through the BCSFB of both cell types. Conclusions: In conclusion, this study will further broaden the knowledge about the pathogenesis of viral meningitis and may help with the development of new diagnostic and therapeutic aspects. Further investigation of potential involved chemokines and integrins in the transmigration process are needed.

ESPID-0960
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

EFFECT OF MYCOPHENOLATE MOFETIL ON CELLULAR AND INFLAMMATORY RESPONSES IN A MODEL OF STAPHYLOCOCCUS AUREUS SEPSIS

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Background and aims

Host infection triggers simultaneously an innate immune response and regulatory mechanisms in order to eradicate the invasive pathogens without damaging the host tissues. We recently discovered the modulatory role of IMPDHII enzyme on Toll like receptor 2 (TLR2) signaling. Besides, mycophenolate mofetil (MMF), a specific inhibitor of IMPDHII and an immunosuppressive therapy used in transplantation, enhances NF-κB activity in vitro. We aimed to determine the effect of MMF on survival and innate immune response in a murine model of sepsis.

Methods

C57BL/6J mice infected intraperitoneally (i.p.) with *Staphylococcus aureus* (10^8 CFU) were treated i.p. with low dose of MMF (20mg/kg QD) the day before until day 3 after the infection. Bacterial dissemination and clearance were evaluated by blood, liver and peritoneum cultures. Immune response was evaluated by flow cytometry, oxidative burst and phagocytosis activity, and cytokine production.

Results

Mice infected by *S. aureus* (mainly recognized by TLR2) and treated with MMF survived better than non-treated ones (48% vs 10%, $p<0.001$). MMF improved bacterial clearance and prevents from hematogenous dissemination. Cytokines (IL-1, IL-6, KC, TNFa and IL-10) decreased in treated mice. Monocytes Ly6C+, polymorphonuclear and dendritc cell rate was enhanced by MMF treatment, and MMF tended to increase oxydative burst of PMNs and phagocytosis of macrophages.

Conclusion

Low dose of MMF modulates host response during *S. aureus* sepsis and protected infected mice from fatal outcome. This work brings new perspectives in pathogenesis of severe infections.

ESPID-0988
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

IN-VITRO DISEASE MODEL FOR NEMO DEFICIENCY

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Background and aims

Patients with defects in *nemo*, which encodes for the NFκB essential modulator, suffer from life threatening bacterial infections. On the cellular level, several immune cell types including macrophages are severely impaired in the response to bacterial effectors and homeostasis. Analysing functional consequences of human NEMO-deficiency in macrophage activation and development is hampered by limited patient material.

Methods

We derived an induced pluripotent stem cell (iPSC) line from a patient with a point mutation resulting in a premature stop-codon in *nemo*, who had a history of live threatening invasive infections with *S. aureus* and other bacteria.

iPSC were differentiated into macrophages with M-CSF and IL-3 and characterized for surface markers associated with macrophage development and polarization.

Results

iPSC-derived macrophages closely resembled alternatively-activated monocyte-derived human macrophages. Single cell development did not differ between NEMO-deficient and normal iPSC-derived macrophages.

Conclusions

Macrophage differentiation from iPSC is not affected by NEMO-deficiency. The established macrophage model offers the perspective to unravel the impaired antibacterial response in NEMO- deficiency.

ESPID-0889
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

OSPONOPHAGOCYTIC KILLING ASSAY OF SPECIFIC ANTIBODIES AGAINST B CELL EPITOPES WITHIN VIRULENT SURFACE OF S. PNEUMONIAE PROTEINS

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Background

We have previously identified the 10 most immunodominant B-cell epitopes within S. Pneumoniae proteins (PnPs) targeted by paediatric immune response during invasive pneumococcal disease(IPD). Further characterization of antibodies against 4 selected epitopes (CbpD-peptide4, PhtD-peptide19, PhtE-peptide40 and ZmpB-pep125) revealed that they were specifically detected in IPD patients' sera and exhibited consistent surface binding to different pneumococcal serotypes. Two epitopes (PhtD-pep19 and PhtE-pep40) were found to reside within zinc-binding domains of PhtD and PhtE proteins. In this study we aim to investigate their functional potentional in vitro using Osponophagocytic Killing Assay (OPKA)

Methods

Specific antibodies against the four synthetic peptides (CbpD-peptide4, PhtD-peptide19, PhtE-peptide40 and ZmpB-pep125) isolated from sera taken from 28 children convalescing from IPD and were evaluated for their specificity by relevant ELISA where the selected peptides were used as capture antigens. Opsonophagocytic activity of purified antipeptide antibodies against PS 1, 3 and 19A was evaluated by OPKA using human polymorphonuclear leukocytes isolated from a healthy adult. Control sera taken by individuals with history of no pneumococcal infection and no vaccination. OPKA titer ≥ 8 reflected the threshold effectiveness.

RESULTS

The OPKA titer of purified antibodies for peptides CbpD-peptide4, PhtD-peptide19, PhtE-peptide40 and ZmpB-pep125 against serotype1 were 24,24,32,24 respectively, against serotype3 were 24,24,32,24 respectively and for serotype19A were 24,24,32,24 respectively. All OPKA titers of control sera were 4.

Conclusion

Our findings indicate that the selected epitopes were recognized by antipeptide antibodies with promising in vitro functional characteristics that require further evaluation in vivo.

ESPID-0680
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

CELL MEDIATED IMMUNITY AGAINST VARICELLA-ZOSTER VIRUS WITH AND WITHOUT UNIVERSAL VARICELLA IMMUNIZATION. A COMPARISON BETWEEN GREECE AND BELGIUM

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Background: Varicella-zoster virus (VZV) infection and vaccination induce VZV-specific antibody and T cell-mediated immunity (CMI), which both may be boosted endogenously and/or by exogenous VZV re-exposure. When CMI declines, VZV reactivation can cause herpes zoster (HZ). Whether HZ incidence may rise following exogenous boosting opportunity reduction through universal VZV vaccination remains controversial. Universal childhood VZV vaccination is implemented in Greece (2005) but not in Belgium. We aimed to examine how differences in boosting opportunities impacts VZV immune responses by comparing Belgian and Greek residents.

Methods: A total of 340 age-matched subjects were recruited, including children (108), adolescents (78), parents (85) and elderly population (69). Belgian population and Greek adults had history of medically diagnosed chickenpox while susceptible Greek children had received two VZV-vaccine doses. Peripheral blood mononuclear cells (PBMCs) and serum were isolated and cryopreserved in liquid nitrogen and -80°C, respectively. All samples were analyzed in Belgium. After thawing, PBMCs were stimulated with VZV antigens. CMI was assessed using Human interferon-γ/Interleukin-2 Dual-Color Fluorospot (Mabtech AB, Sweden). Statistical analysis was performed with SPSS v.20.

Results: No consistent statistical significant differences in either immune response between the Greek and Belgian subgroups were noted.

Conclusions: Preliminary results suggest that individuals residing in an area where universal VZV vaccination has been implemented do not present with a reduced CMI compared to age matched controls from a country where wild virus prevails. Further analyses will focus on VZV-CMI as a function of time since last VZV exposure. These observations support universal children vaccination implementation.

ESPID-0745
Short Oral Presentation Session 5- HOST-PATHOGEN INTERACTIONS

COMBINING VIRAL- AND BACTERIAL-INDUCED HOST PROTEINS FOR DIAGNOSING SERIOUS BACTERIAL INFECTIONS IN FEBRILE CHILDREN

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Background and aims

Febrile children with serious bacterial infections (SBI) are at high risk for adverse outcomes. We previously developed a computational signature for accurately distinguishing between acute bacterial and viral infections that integrates measurements of novel viral- and traditional bacterial-induced proteins: TNF-related apoptosis-inducing ligand, Interferon gamma-induced protein-10 and C-reactive protein (CRP). Here, we evaluate the signature performance on SBI patients and compare it to routine laboratory parameters.

Methods

We prospectively recruited 356 children (≤18 years) with a suspected acute infection. Diagnosis was determined by three independent experts on the basis of clinical and microbiological data. SBI was defined using predetermined criteria. Using the signature, a bacterial likelihood score was computed for each patient.

Results

Unanimous diagnosis of the experts was attained in 211 viral and 86 bacterial patients, of whom 37 had SBI (12 urinary tract infection; 23 pneumonia; 1 bacteremia; 1 meningitis). In the remaining 59 patients, unanimous diagnosis was not attained. The signature had a specificity of 0.93±0.04 and sensitivity of 0.92±0.06 for differentiating between bacterial and viral infections (34 patients had equivocal test results). Sensitivity of SBI detection was slightly higher than bacterial infections in general (0.94±0.07; 4 SBI patients had equivocal test results), and outperformed traditional clinical parameters such as WBC (0.73±0.15), ANC (0.73±0.15) and CRP (0.79±0.14), when applying routinely used cutoffs.

Conclusions

The present host-signature provides valuable information over routine laboratory parameters. It can aid in the timely identification of children with SBI and in distinguishing them from children with viral infections.

ESPID-0431
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

LONG TERM RESULTS OF A ONCE-DAILY LOPINAVIR/RITONAVIR REGIMEN IN THE TREATMENT OF HIV-1 INFECTED PEDIATRIC PATIENTS.

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Introduction: Lopinavir/ritonavir (LPV/r) is the first choice protease inhibitor in the treatment of HIV-1 infected pediatric patients. Current guidelines advise a twice daily regimen. Once daily dosing shows mean pharmacokinetic parameters comparable to LPV/r once daily in adults, with higher variability in children. Long-term clinical follow-up has not been reported.

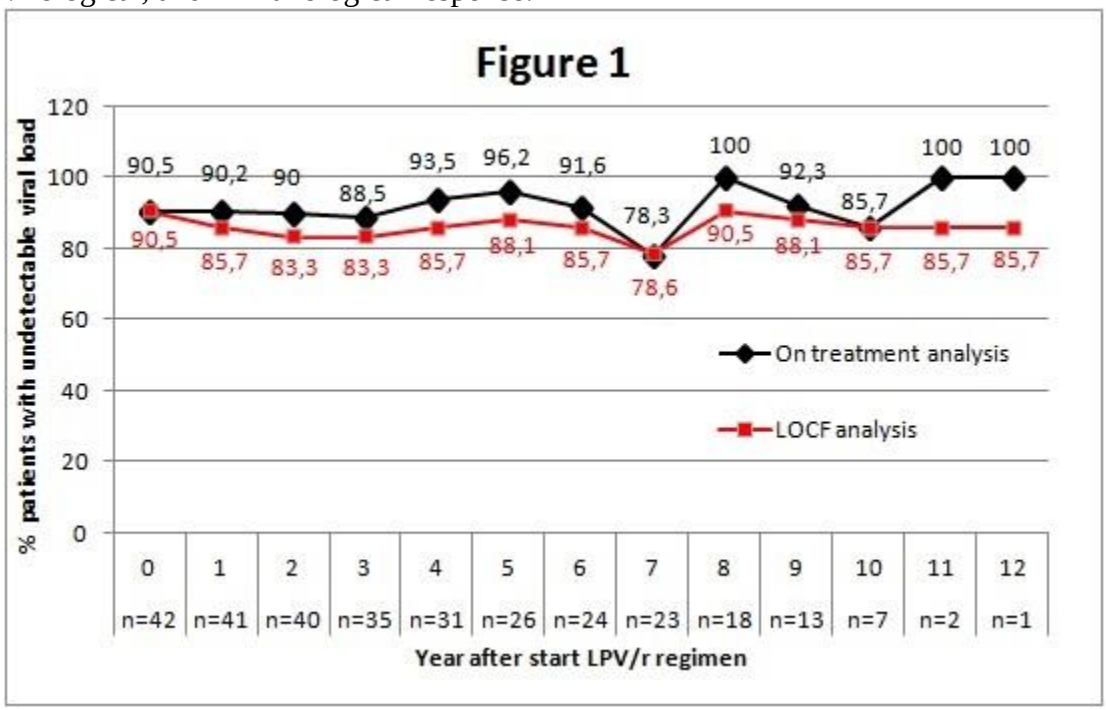
Aim: To evaluate the long term effectiveness of a once-daily regimen of LPV/r in HIV-1 infected children.

Methods: Children (aged 0-18), who started a once-daily LPV/r regimen in our center were included. At start, intensive pharmacokinetic analysis was performed. Every 3 months LPV levels, HIV-RNA copies, CD4- and CD8 numbers and blood chemistry were determined. The percentage of patients with undetectable viral loads (<50 copies/ml) was determined with an on treatment- and last observation carried forward (LOCF) analysis. Adverse events were reported at each visit.

Results: Forty-two patients (median age 6,4 years) were included. Median follow-up was 74 months (range 3-137). The percentage of patients with an undetectable viral load varied between 78-100% (on treatment) and 79-91% (LOCF) (figure 1). CD4 and CD8 counts remained stable at normal values. Geometric mean AUC_{last} was 168.4 h*mg/L and C_{last} 1.27 mg/L. In 19 (45,2%) patients LPV dose was adjusted during follow-up at least once because of an inadequate trough level. Adverse events were mainly gastro-intestinal, and no reason to stop treatment.

Conclusion: A once-daily LPV/r containing regimen in HIV-1 infected children with intensive clinical and therapeutic drug monitoring can lead to a good clinical,

virological, and immunological response.



ESPID-0781
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

RILPIVIRINE/EMTRICITABINE/TENOFOVIR THERAPY IN A HIV-INFECTED ADOLESCENT COHORT: OUR EXPERIENCE

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Background and aims: combined antiretroviral therapy (cART) reduces HIV morbidity and mortality but is associated with toxicities. Rilpivirine is a new non-nucleoside reverse transcriptase inhibitor (NNRTI), that has been co-formulated with emtricitabine and tenofovir RPV/FTC/TDF into a single-tablet regimen (STR). No data exist on the safety and efficacy of this STR in children under the age of 18 years. The aim is to describe our experience in HIV-infected adolescent treated with RPV/FTC/TDF.
Methods: clinical records from HIV-infected teenager treated with RPV/FTC/TDF in our tertiary-care pediatric hospital in Spain were retrospectively analyzed in an observational ongoing study.
Results: a total of 7 virologically suppressed (HIV-1 RNA<20 cop/mL for > 6 months) ART-experienced adolescent were switched to RPV/FTC/TDF. Median age at initiation was 15,3 years (SD 11,5-20,5); 5/7 were males and median body mass index was 22,6 Kg/m^2 (19,2-26,3). Five patients were on a protease inhibitor and two on a NNRTI regimen. Median time on RPV/FTC/TDF treatment was 16 months (2-22). Median total-cholesterol and triglycerides decreased from 170 mg/dL to 135 mg/dL (p-value=0.042) and 112 mg/dL to 87 mg/dL (p-value=0.225) respectively. Median CD4 (%) baseline and at time of last visit was 466 cells/uL and 696 cells/uL (p-value=0.893). All patients maintained HIV-1 RNA < 20 cop/mL whilst no adverse events were observed.
Conclusions: STR with RPV/FTC/TDF was well tolerated and associated with excellent adherence and favorable changes in lipid profile; efficacy was not found to be inferior compared to previous received cART.

ESPID-0114
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

REFERENCE CURVES FOR ALBERTA INFANT MOTOR SCALE FOR BRAZILIAN CHILDREN BORN TO HIV-SEROPOSITIVE MOTHERS: PERCENTILS FOR CLINICAL DESCRIPTION AND FOLLOW-UP

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Background: HIV has affinity for immune system and central nervous system. There are 2.5 million children living with HIV/AIDS in the world. In Brazil, there were 608.230 cases of AIDS between 1980 and June 2011. Of these, 2.32% (14,127 cases) in children under five years, which 32.61% reported in the state of São Paulo. Children exposed to HIV have increased risks to neurodevelopment delay.

Aim: To develop the reference curve for Alberta Infant Motor Scale for Brazilian children born to seropositive mothers.

Methods: Monthly evaluated 104 children from 0 to 18 months, who were under treatment in Santos, São Paulo. We used Alberta Infant Motor Scale, with 58 motors criteria, distributed in 4 subscales (prone, supine, sitting and standing). We obtained raw scores and percentiles. Percentiles are grouped by motor development categories: below 5%, is considered an abnormal motor performance; between 5% and 25%, suspect motor performance, and above 25%, normal motor performance.

Results: 415 assessments were made. We created a reference curve with the reference values for the children exposed to HIV, for every percentile, with the average raw score for each month, deviations, minimum and maximum values of score and percentile expected. from the 15th month onwards, the curve reaches a plateau, as well as reference curve of the Brazilian scale. The greater variability is observed between the 3rd and the 15th month.

Conclusions: values found in this study indicate that the HIV-exposed assessed children have similar patterns of motor development when compared to general brazilian pediatric population.

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Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

RESPONSE TO HVC TREATMENT IN A COHORT OF VERTICALLY HIV-HVC CO-INFECTED PATIENTS

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Background: To date, data are scarce regarding the natural history of vertically HIV/HVC co-infected children and the response to anti-HVC treatment.

Methods: Cross-sectional study within the Spanish National Cohort of Vertically HIV-HVC co-infected patients

Results: Fifty HIV-HVC co-infected patients were included, 68% had been transferred already to adult units at the moment of inclusion in the study. Mean age was 20 ±4.5 years, 56% were female. Median CD4 T-cell count was 788 cel/mm³ [516-980], 88% had HIV-RNA <50 cop/mL. Genotype 1 represented 66%; genotype 4, 21%; genotype 3, 11%; and genotype 2, 2%. Transient elastometry data were available for 40 patients; of them, 22 (55%) showed liver fibrosis stage F1, 9 (25%) F2, 3(7.5%) F3 y 5(12.5%) F4. Progression to F3 occurred at a median age of 18 years [14-19]. Fifteen patients had received treatment for HVC infection (9 corresponded to genotype 1, 3 to genotype 3 and 3 to genotype 4). Treatment reached sustained virological response only in 5 patients (33.3%), one of them after being retreated. Of treated patients, 4 had been diagnosed of liver fibrosis stage F1-F2 and one F3. Treatment combinations included interferon (1 pt), peg-interferon/interferon +ribavirine (12pt), +telaprevir (2pt).

Conclusions: Our results suggest that HVC co-infection in vertically HIV infected patients progress slowly during childhood. Only 20% of children progress to liver fibrosis, most of them at the end of adolescence. Rates of sustained viral response were very low in this unique cohort, arousing the need of new therapeutic approaches for this population.

ESPID-0944
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

VERTICALLY VS HORIZONTALLY HIV INFECTED YOUTHS AFTER TRANSITION TO ADULT UNITS IN SPAIN

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Background:

Due to the success of ART, many vertically HIV-infected children (VHI) are being transferred to adult units in Spain. Our aim was to evaluate the transition process and

to address the clinical situation of the cohort in comparison to their horizontally HIV-infected peers (HHI).

Methods

Cross-sectional analysis including patients transferred to adult units (1997-2012). Variables were analyzed before and one year after transition, and during follow-up. The cohort was compared to a cohort of HHI, on ART for at least one year.

Results

182 VHY were transferred during the study period, 58.2% female (longitudinal data available in 147). Median age at transition: 17.9y [17-19]. From 81 virologically suppressed patients, 86.4% maintained suppression after transition. A 69.9% of patients transferred with CV>50cop/mL, achieved viral suppression after transition. No association was found between evolution and gender or age at transition. Compared to a cohort of 46 HHI (61% heterosexual), VHY were younger (24±3.7 *vs* 26.5±3.1, p<0.01). Despite 27% *vs* 6.5% were on CDC stage C (p<0.01) and had lower CD4 nadir (202[78-364] *vs* 286[170-370], p=0.17), their CD4 T-cell count was higher (744[IQR 505-990] *vs* 542[391-662], p<0.01). CV<50 cop/mL: 80% *vs* 73%, p=0.41. On NNRTI: 27% vs 50% (p=0.04) and 74% vs 83% on a QD regimen (p=0.41).

Conclusions

Despite years of infection, the immunological situation of VHI is comparable to that of their HII peers, and remains stable or improves after transition in 75% of subjects. However, strategies are needed in order to increase engagement in care during transition

ESPID-0365
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SERVICE EVALUATION OF THE CLINICAL VALUE OF STOOL MICROSCOPY AND CULTURE IN PAEDIATRIC ONCOLOGY UNIT

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Aims

Diarrhoea is a common symptom in paediatric oncology patients. Although, stool samples are still commonly sent for microscopy and culture, the value of these tests in paediatric oncology patients with diarrhoea is not clear. A number of studies suggested the limited role of attempting to isolate routine enteric pathogens as a cause of diarrhoea in hospitalized patients, however the diagnostic value of testing in children with oncological conditions has not been reported. Therefore, we conducted a service evaluation to estimate diagnostic yield of stool cultures in oncology patients.

Methods

Records from the Microbiology Laboratory from September 2009 to October 2014 were reviewed to collect data on the number of stool cultures performed in patients treated at a Regional Paediatric Oncology Unit.

Results

A total of 842 stool cultures from 250 patients were performed over the 5-year period. A significant number of children had more than one culture done (average 3.4 per patient). Out of 842 samples tested over 5 years, only 1 was positive for *Campylobacter* (0.1 %). Medical records review showed that this patient presented from the community with a history of abdominal pain and weight loss.

Conclusions

A comprehensive service evaluation of all stool culture tests performed in paediatric oncology patients during a 5-year period have demonstrated very low utility of routine stool cultures for patients with diarrhoea. We suggest that the implementation of practice guidelines for ordering stool cultures could result in cost savings of approximately £2,200 per year and more efficient utilisation of resources.

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HIGH PREVALENCE OF BRONCHIECTASIS IN CARTILAGE-HAIR HYPOPLASIA: CLINICAL AND LABORATORY CORRELATIONS AND COMPARISON OF LUNG HRCT AND MRI IMAGING MODALITIES

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Background: Cartilage-hair hypoplasia (CHH) is a syndrome with severe short stature, immunodeficiency, and various comorbidities. Repeated sinopulmonary bacterial infections are common and increase the risk of bronchiectasis (BE). We aimed to investigate the prevalence of BE, associated clinical and laboratory abnormalities and diagnostic performance of lung MRI compared to HRCT.Methods: Eighteen patients with genetically confirmed CHH were randomly selected from the national CHH cohort. They underwent interviewing, blood sampling, and lung HRCT (18/18) and MR imaging (16/18). Results: Study included 3 males and 15 females (median age 35, range 2-68 years). HRCT showed BE in 5/18 patients (28%). There was a good correlation between HRCT and MRI scores (modified Helbich score), in assessing BE. Patients with BE more often had repeated sinus infections (4/5, 80%), pneumonias (3/5, 60%) and persistent cough for ≥ 1 year (2/5, 40%) than patients without BE (62%; 38%; and 23%, respectively). Lymphopenia was found in 11/18, B-cell deficiency in 11/18, T-cell deficiency in 10/18 and low switched memory B-cell count in 15/18 patients; none had hypogammaglobulinemia. Laboratory parameters did not differ between patients with and without BE. Conclusions: BE were present in 28% of CHH patients and were associated with a history of pneumonias, repeated sinus infections and chronic cough, but not with any specific laboratory immunological parameters. MRI showed a good correlation with HRCT for assessing BE and can be used in the follow-up of lung changes in order to reduce radiation exposure.

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VIRIDANS GROUP STREPTOCOCCAL INFECTIONS IN CHILDREN FOLLOWING CHEMOTHERAPY OR STEM CELL TRANSPLANTATION– A TEN YEAR RETROSPECTIVE REVIEW FROM A TERTIARY PAEDIATRIC HOSPITAL

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Background and Aims : Viridans group streptococci (VGS) are associated with high mortality rates in immunocompromised hosts due to the potential to cause viridans group streptococcal shock syndrome (VSSS). Rising levels of penicillin resistance have encouraged the use of empirical vancomycin, although this should probably only be targeted to those with known risk factors. There are no recent paediatric studies describing VGS in children with cancer in Europe to inform antimicrobial therapy. The aim of this study was to describe the characteristics, outcome and resistance patterns of children with VGS bacteraemia undergoing treatment of malignancy or haematopoietic stem cell transplant in a tertiary referral centre in the U.K.

Methods: Patients aged 0-18 years admitted to a tertiary paediatric haemato-oncology centre with VGS bacteraemia from 2003-2013 were included in the study. All data was collected retrospectively from electronic records and case notes.

Results: 54 episodes occurred in 46 patients. The most common underlying diagnoses were acute myeloid leukaemia and relapsed acute lymphoblastic leukaemia, *Streptococcus mitis* the most frequent organism. 30 % of isolates were resistant to penicillin and 100% sensitive to vancomycin. There were 8 episodes of VSSS (14.8%); 6 resulted in admission to intensive care and 3 of these patients died of multi organ failure

Conclusion: Patient characteristics were in keeping with known risk factors for VGS. The potentially fatal nature of VGS infection is confirmed. Research is needed to develop bedside risk stratification scores that identify children at risk of VSSS to guide empirical antimicrobial therapy in febrile neutropenia.

ESPID-0938
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

BROAD SPECTRUM OF INFECTIONS IN PATIENTS WITH STAT1 GAIN OF FUNCTION MUTATIONS

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Background:

The clinical phenotype of STAT1 gain-of-function (GOF) mutations was first described as autoimmunity and chronic mucocutaneous candidiasis (CMC) due to an impaired IL17 response.

Aim:

To further characterize the infection susceptibility of STAT1 GOF mutations.

Methods:

A retrospective case review was conducted of childhood presentations of STAT1 GOF patients at the NIH Clinical Center.

Results:

Fifteen patients (8 M, 7 F; 12 kindreds) were identified. Median presentation age was 2 years (1wk-18y). 13 patients presented with infection, one with early diabetes mellitus, and one with nonspecific gastrointestinal symptoms. Eleven patients had fungal infections (CMC=7, coccidioidomycosis=2, histoplasmosis=1, cryptococcosis=1, aspergillosis=1). Bacterial infections were predominantly sinopulmonary (7 had bronchiectasis), 3 had recurrent soft tissue infections and one had spinal osteomyelitis. Ten patients experienced recurrent HSV or VZV or persistent EBV viremia, 2 had confirmed viral CNS infections (VZV, JCV), and one had extensive molluscum contagiosum. Six patients had mycobacterial infection (*Mycobacterium fortuitum*=3, *M. avium* =1, TB=1, BCG=1). Nine developed autoimmune complications: hypothyroidism (n=8), diabetes mellitus (n=4), enteropathy (n=3) and hemolytic anemia (n=2). Two had cerebral aneurysms. 4

patients died at ages 4, 13, 17, 19 years (cerebral aneurysm, catheter-related candidemia, lung surgery complications, PML). One patient with IPEX-like syndrome had successful bone marrow transplantation; others received prophylactic antimicrobials and/or IVIG replacement.

Conclusions:

STAT1 GOF mutations cause diverse clinical presentations with a surprisingly high rate of mycobacterial and viral infections, suggesting a functional overlap between gain-and loss-of-function mutations. This broad infection susceptibility may warrant adaptation of diagnostic and therapeutic protocols for these patients.

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Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

CLINICAL EPIDEMIOLOGY OF INVASIVE FUNGAL INFECTIONS(IFI) IN CHILDREN AND NEONATES: RESULTS OF A MULTI-CENTER NATIONAL PROSPECTIVE STUDY.

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Introduction In 2009, the Dutch Pediatric Mycology Network was initiated to investigate the clinical epidemiology of paediatric IFI to gain up-to-date insights in the current management and outcome of paediatric IFI.

Methods Eight university hospitals participated by entering anonymously data in a secure web-based registry 'PedMyc'. Paediatric patients treated with a systemic antifungal agent for a suspected/proven IFI were included. Inclusion, underlying conditions, host-factors, diagnostic procedures, intervention and outcome were registered in the database.

Results From 2009 to 2013, 118 paediatric patients (27 neonates; 91 children) were included and started with antifungal treatment for suspected/proven IFI. Of the 27 neonates, 19 (70%) were born with a GA < 28 weeks and 14 (52%) had a BW < 1000g. Median age of the 91 children was 10.4 years and the majority (66%) had an underlying haematological disorder. Antifungal therapy was started for suspected or proven IFI in 68 (58%) and 50 (42%) patients respectively. Treatment was started in neonates for mainly proven IC (78%); in infants and children for suspected IA (60%). Of the 55 patients with suspected IA, only 28 (51%) could be classified as probable IA. Neonatal IC (78% caused by *C. albicans*) was treated with fluconazole in 87%, probable/proven IA with either voriconazole (67%) or liposomal amphotericin B (28%), although dosages prescribed varied substantially. Reported 3-months survival rate for neonatal IC was 80% and 65% for probable/proven IA.

Conclusion Generation of this specific paediatric epidemiology data shows new insights into the fungal epidemiology, antifungal prescription practices and outcomes.

ESPID-0061
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EARLY DETERMINANTS OF DENGUE HAEMORRHAGIC FEVER IN SRI LANKAN CHILDREN

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Background and aims

Dengue infection shows series of biochemical changes during the course of illness. Our aim was to describe the biochemical changes in dengue haemorrhagic fever (DHF) and to evaluate their usefulness as early determinants of critical stage.

Method

Children (5–12 years) admitted to Professorial Paediatric Ward, Lady Ridgeway Hospital, Colombo, Sri Lanka with a clinical diagnosis of dengue infection were recruited. Study was approved by institutional ethical review committee and informed written consent was obtained from parents. Blood was collected on admission for full blood count (FBC), ALT, AST, albumin and cholesterol and repeated at 12 hourly time intervals from onset of illness

Results

Among 130 (Dengue IgM positive) recruited subjects, 30 had DHF. Significant drops in the white cells, platelets, albumin and cholesterol were observed at the time of entering into the critical phase. According to ROC analysis, WBC less than 3,500/µL (sensitivity 76.9%, specificity 51.7%), platelets crossing 100,000/µL (sensitivity 78.9% , specificity 78.3%) between 60-72 hours from onset of illness and albumin level crossing 37.5g/L (sensitivity 86.7%, specificity 77.8%) and reduction in cholesterol level by 0.38 mmol/L (sensitivity 81.8%, specificity 75.4%) between 72-96 hours from onset of illness were best determinants of entering into critical phase in DHF.

Conclusions

FBC done between 2.5-3 days and albumin and cholesterol levels between 3-4 days were highly valid predictors of entering into critical phase. Therefore it is important to time these investigations correctly in the management of suspected cases of dengue fever in order to suspect DHF with greater accuracy.

ESPID-0642
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

PREVALENCE AND INTENSITY OF SOIL TRANSMITTED HELMINTHS INFECTION AMONG SCHOOL AGE CHILDREN IN SLUM AREA IN NORTH SUMATERA,INDONESIA

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Background Soil transmitted helminths (STH) are among the most prevalent and highly neglected tropical diseases, especially in developing countries. This infection occurs most commonly in school age children and becomes one of the major health in Indonesia.

Methods A cross sectional study was conducted in 5 elementery schools in fisherman village in North Sumatera province, Indonesia. A survey questionnaire was filled, anthropometric measurements and stool sample for STH were taken. A descriptive analysis was carried out to determine the characteristics of samples and chi-square was used for categorical comparison.

Results A total of 1711 school aged children were scereened of which 24.14% had one or more STH. Trichuriasis was the most prevalent (61%) followed by mixed infection of ascariasis and trichuriasis (22.5%) and ascariasis (16.5%). Most of the infection had light intensity regardless the type of STH (Ascariasis 70.6%, trichuriasis 82.1% and mixed 66.7%, p=0.005). Most of the samples found to be mild malnutrition (63%), and among malnutrition samples, light intensity was most common compare to moderate intensity (65.5% vs 54%, p=0.04).

Conclusion Moderate prevalence with light intensity of parasites of STH infection found in school aged children in slum area in North Sumatera, Indonesia. The high prevalence of malnutrition and its association with STH infection is of concern for determining the integrated interventions to reduce disease.

Acknowledgement Authors thank the teachers, participants and their parents for contributing in this study.

ESPID-0928
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

RAPID ANTIGEN TEST FOR DETECTION OF GIARDIA LAMBLIA VERSUS MICROSCOPY FOR DIAGNOSIS GIARDIASIS IN PAEDIATRIC CLINICAL PRACTICE

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Background and aims

Giardiasis is the most frequent pediatric parasitation overworld. Fecal sample´s microscopic examination(standard diagnosis) is cheaper, can quantify giardiasis and detect simultaneous parasitations.

Recently rapid tests of Giardia´s antigen(RT) are available, being faster and easier than microscopy, don't require microbiologist, and detect Cryptosporidium. Initially reported high sensibilities and specificities for RT, but didn´t correlationated with our experience. Until now, there aren´t studies in big series of pediatric patients.

Our aim is to check one RT in a representative sample of children comparing to microscopy, to establish the real RT usefulness in clinical practice.

Methods

2780 fecal samples among internationally-adopted-children and immigrants were analyzed along four years. A rapid-membrane-enzymeinmunoassay for qualitative detection of Giardia cyst antigen(QuickChek©–Alere) was applied to all samples compared with microscopy in the same samples preserved in sodium-acetate-formalin (gold standard).

Results

The RT was positive in 134/196 microscopy positives and in 26/2584 of microscopy negative samples. The RT was negative in 2558/2584 negative and 62/196 positive microscopy samples.

The RT had a sensitivity=68,37% and specificity=98,99%. In our sample (internationally-adopted-children and immigrants) with prevalence of giardiasis 7%, positive predictive value=83,75% and negative predictive value=97,63%, with good concordance (Kappa=0,736(standard error=0.019,Z=39.039,p<0.001)).

Conclusions

RT presents high negative predictive value in our sample(low prevalence of giardiasis).Therefore, we can use RT as screening in adopted/inmigrant children or in other poblations with low prevalence.

Nevertheless, if high suspect of giardiasis(sintomatics…), RT shouldn´t replace the microscopy as screening due to its low sensitivity, it can be considered only if a microbiologist isn´t available.

ESPID-0940
Short Oral Presentation Session 6- HIV, Infections in IMMUNOCOMPROMISED and Tropical Diseases

RISK FACTORS FOR GASTROINTESTINAL SYNDROME IN TRAVELLER CHILDREN: AN OBSERVATIONAL STUDY FROM SPANISH +REDIVI DATABASE

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Background and aims:

Gastrointestinal symptoms are a common cause of consultation on children travelling to or coming from developing countries. Aim of this study is to identify risk factors associated with gastrointestinal syndrome in traveller children.

Methods:

Prospective observational analytical and multicentric study on database "+ Redivi", Spanish Tropical Medicine network on imported diseases, from January 2009 to December 2013. Statistical analysis was performed with Stata 13.1 package.

Results:

Children with gastrointestinal symptoms represented 13.5% (82/606) of total paediatric consultations. Overall mean age was 8.5 years (IQR 4.4-12.4), 54.0% male, 59.8% were living in Spain, and travel duration mean was 148.7 days (SD 266.3

days). Most of them were immigrants (65.8%), followed by visiting friends and relatives (VFRs) 28.5%, and tourists 5.6%. 69.0% of children were not visited for pre-travel advice. All HIV-infected children were immigrants 4/606 (0.77%). A significant association was found between having a gastrointestinal disorder and age <2-y old ($p<0.005$) and travel duration ($p<0.05$). When adjusting the presence of a gastrointestinal symptom and travel duration by age, OR=0.73 (CI95% 0.54-0.97) ($p<0.05$). Immigrants had less gastrointestinal disorders compared with tourists ($p<0.05$). The most prevalent infection was protozoan 23.8% (144/606), and *Giardia intestinalis* was the most common infectious agent 10.1% (61/606).

Conclusions:

Traveller children with a gastrointestinal syndrome represent a 13.5% of the total paediatric consultations in the "+Redivi". Risk factors for it are age<2-y old, travel duration, and tourism as travel proposal. *Giardia intestinalis* is the most common infectious agent causing a gastrointestinal disorder in traveller children.

ESPID-0521
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

PANTON-VALENTINE LEUKOCIDIN (PVL) PRESENCE AND NOT METHICILLIN-RESISTANCE IS ASSOCIATED WITH SEVERE INVASIVE COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS INFECTIONS IN CHILDREN: AN EUROPEAN MULTI-CENTRE (PISA) STUDY

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BACKGROUND AND AIMS

Staphylococcus aureus including methicillin-resistant strains can cause severe community-acquired invasive infections (CA-SA-I). The aim of the study was to describe the characteristics of CA-SA-I and to analyze possible factors associated with disease severity in Europe.

METHODS

A prospective, multi-centre European study, analyzing epidemiologic, clinical, and microbiology data in children <16 years with CA-SA-I during 2012-2014. Severe infection was defined as invasive infection leading to death or admission to the

paediatric intensive care unit (PICU) because of hemodynamic instability or respiratory failure.

RESULTS

A total of 155 children (89 boys) with CA-SA-I from 12 centres in 7 European countries were recruited. Median age was 7.1±5.4 years; and 28% had an underlying disease. The most common primary diagnoses were musculoskeletal infections (bone, joint, muscle: 55%), bacteraemia (18%) and pneumonia (15%). PICU admission (26 patients, 17%) was mainly due to septic shock; 3 patients (2%) died. Prevalence rates of methicillin and clindamycin resistance were 8.5% and 7% respectively. PVL+ strains comprised 20% of isolates tested (23/121). Presence of PVL ($p=0.018$, OR 3.15 (1.18 to 8.43)) and higher initial CRP values (17.4 vs. 8.7 mg/dL, $p<0.01$) were associated with severe compared to CA-SA-I non-severe cases, also using multivariate analysis. No other differences, including methicillin-resistance prevalence, between the groups were observed.

CONCLUSIONS

CA-SA-I in children occurs across Europe and require PICU admission in a significant number of children. PVL, but not methicillin-resistance, is associated with increased disease severity, the later still being uncommon in CA-SA-I in Europe.

ESPID-0633
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

ASSOCIATION OF HIV-1 INFECTION IN PREGNANT WOMEN AND GROUP B STREPTOCOCCUS CAPSULAR AND SURFACE-PROTEIN ANTIBODY CONCENTRATIONS AND TRANSPLACENTAL TRANSFER

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Background: HIV-exposed infants are at increased risk of invasive Group B *Streptococcus* (GBS) disease. We aimed to establish whether maternal HIV-infection negatively influences antibody concentrations and transplacental antibody transfer.

Methods: Maternal antibody concentrations and cord-maternal ratios (CMR) were compared between HIV-infected and HIV-uninfected mother-newborn dyads against GBS capsular serotypes: Ia, Ib, III, V and GBS surface-proteins: pilus island (PI) PI-1,PI-2a, PI-2b, Fibrinogen-binding protein A (FbsA) and GBS Immunogenic Bacterial Adhesin (BibA).

Results: Median GBS capsular and surface-protein antibody concentrations (µg/ml) were lower in HIV-infected compared to HIV-uninfected women for serotypes Ib (0.06 vs. 0.09;p=0.033) and V (0.40 vs.0.59; p=0.040); and for PI-1 (549 vs. 1020; p=0.016), PI-2a (1130 vs. 1972; p=0.015), PI-2b (611vs. 1072; p=0.015) and FbsA (1444 vs.2169; p<0.001). The adjusted odds of an antibody concentration ≥2µg/ml was 0.33 (95%CI: 0.15-0.75; p=0.008) for serotype Ia and 0.34 (95%CI: 0.12-1.00; p=0.049) for serotype III when comparing HIV-infected to -uninfected women. The CMR's were 37.4% (p<0.001)and 32.5% (p=0.027) lower in HIV-infected compared to HIV-uninfected mother-newborn dyads for serotypes Ia and III. No correlation was found between GBS antibody concentrations and CD4+ lymphocyte count or HIV viral loads.

Conclusions: Infants born to HIV-infected women are at increased risk of invasive GBS disease due to lower maternal antibody concentrations and deficient transplacental antibody transfer. Maternal GBS vaccine formulations may require modified dosing schedules in HIV-infected women.

ESPID-0406
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASE (IPD) ASSESSMENT: RELEVANCE OF SERUM QMPCR IN A MULTICENTRIC SEROTYPE STUDY FROM INDIA

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Background & Aim: Pneumococcal infection remains the leading cause of death from vaccine preventable infectious diseases in India. However, establishing *Streptococcus pneumoniae* as an etiology of invasive pneumococcal infection is still challenging by conventional culture methods. The limitations of existing diagnostic tests impact the ability to detect IPD in patients, obtain accurate burden data and access effectiveness of control measures. This study was designed to compare multiplex real time PCR (qmPCR) method with the culture method in IPD infections and to evaluate the reliability of qmPCR method.

Method: Seven hundred and fifty children ≤5 years clinically diagnosed with IPD having abnormal chest-X-ray, raised CBC, positive CRP and PCT test results were included into the study. Automated blood culture and corresponding serum qmPCR were performed in all patients. Evaluation was done against culture isolates and control serum specimens.

Result: 38 (5%) strains of *S. pneumoniae* were isolated by culture. The positivity for pneumococcal infection escalated to 236 (31.5%) when serum specimens were subjected to qmPCR assay. The sensitivity and specificity of the assay was 100% with lower limit of detection of 4 genome copies/ul.

Conclusion: Conventional culture methods are not always adequate to detect IPD. Our study establishes that qmPCR is a reliable and superior assay for the rapid identification of *S. pneumoniae* from serum specimens. Widespread use of this accurate and affordable technique will contribute to the success of treatment and provide true estimate of disease burden.

ESPID-0691
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

BIOMARKER AND GENE EXPRESSION RESPONSE TO LOW DOSE CORTICOSTEROID THERAPY IN CHILDREN WITH SEVERE SEPTIC SHOCK – A RANDOMISED CONTROLLED TRIAL

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Aims: We explored the effects of replacement dose corticosteroids on immune, coagulation, endocrine parameters and whole-genome RNA expression levels in children with severe sepsis.

Methods: Children with severe sepsis were randomised 2:1 to standard care plus hydrocortisone (25 mg/m2/q 6 hourly for 48 hours) or to standard care. Endocrine, coagulation and cytokine pathways were analysed by Luminex and ELISA. Gene expression in peripheral blood was measured by Illumina BeadChip array in n=9 steroid and n=5 controls >5 years old at 10 time-points to t=144 hours, and at 6-8 weeks.

Results: Descriptive analysis showed no clinically significant differences in baseline clinical data. Other than cortisol, no differences were seen in all endocrine, immune

and coagulation parameters and clinical outcomes between the steroid (n=20) and control (n=9) groups. Similarly, there were no significant differences in gene expression levels at a false discovery rate of 5%.

Within gene subsets from studies of paediatric septic shock (retrospective), glucocorticoid receptor signalling and sepsis severity biomarkers, significant over-representation of significant genes were observed (most pronounced at 12 hours). T-cell receptor signalling (Reactome) pathway analysis showed significant association at 12 hours, $p=2.6x10^{-8}$. The significant genes within this pathway result in its relative down-regulation in the corticosteroid group between 6 and 24 hours.

Conclusions: We found no evidence that 48 hour replacement dose corticosteroids influence clinical, coagulation or immunological parameters in paediatric sepsis. T-cell receptor signalling is down-regulated between 6 and 24 hours.

ESPID-0555
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

DEVELOPING A SEPSIS SIX PATHWAY FOR PAEDIATRIC EMERGENCY DEPARTMENTS

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Background: The Surviving Sepsis campaign has brought focus to the early management of sepsis. We developed a modified Sepsis Six tool, appropriate to the assessment and treatment of paediatric patients in an emergency department (ED) setting, adapted from similar initiatives from PICU and paediatric oncology. Our paediatric-specific document replaces some of the investigations used in Sepsis Six with guidance on judicious use of fluid resuscitation and escalation to PICU assessment.

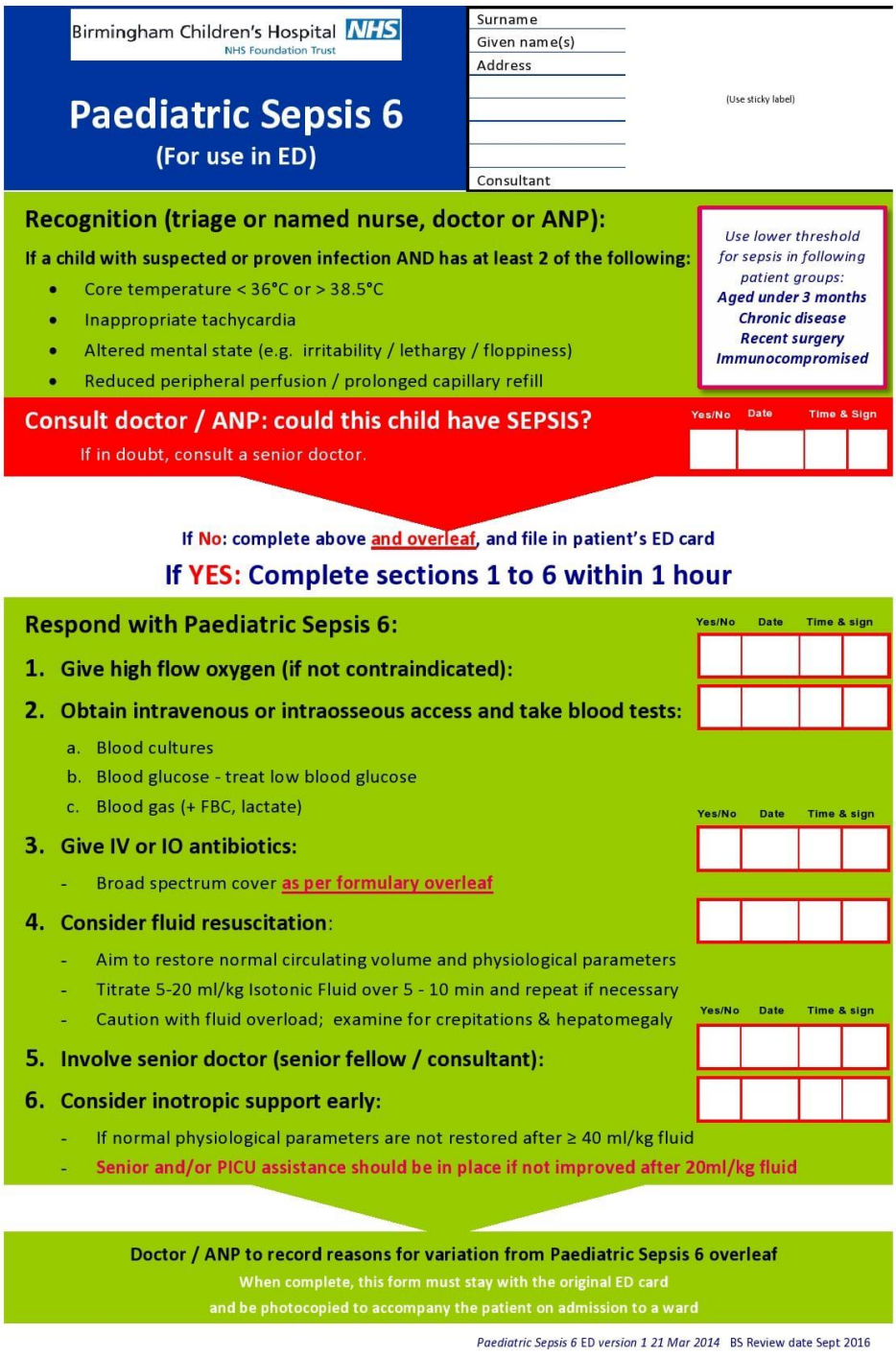
Aims: To audit the performance in a paediatric ED against our modified Sepsis Six standards.

Methods: We retrospectively analysed the initial management of those children attending the ED of a tertiary children's hospital over a six-month period, who presented with possible sepsis. Of 131 children treated via a sepsis pathway, 44 presented with febrile neutropenia.

Results: 77 (59%) of the 131 patients received IV/IO antibiotics within one hour of identifying possible sepsis; mean time to administration of antibiotics was 59.4 minutes. Only 24 (18.3%) of patients had a completed Sepsis Six pathway document. Of these, 18 (75%) received antibiotics within one hour, and mean time to antibiotic administration was 49.9 minutes.

Conclusions: We have had difficulty implementing a pilot sepsis pathway within a major children's hospital emergency department. However, we have shown some evidence of earlier antibiotic administration to children with suspected sepsis where

management has been based on our modified Sepsis Six framework.



Birmingham Children's Hospital NHS
NHS Foundation Trust

Paediatric Sepsis 6
(For use in ED)

Surname
Given name(s)
Address
(Use sticky label)
Consultant

Recognition (triage or named nurse, doctor or ANP):

If a child with suspected or proven infection AND has at least 2 of the following:

- Core temperature < 36°C or > 38.5°C
- Inappropriate tachycardia
- Altered mental state (e.g. irritability / lethargy / floppiness)
- Reduced peripheral perfusion / prolonged capillary refill

Use lower threshold for sepsis in following patient groups:
Aged under 3 months
Chronic disease
Recent surgery
Immunocompromised

Consult doctor / ANP: could this child have SEPSIS?

If in doubt, consult a senior doctor.

Yes/No	Date	Time & Sign

If No: complete above and overleaf, and file in patient's ED card

If YES: Complete sections 1 to 6 within 1 hour

Respond with Paediatric Sepsis 6:

Yes/No	Date	Time & sign

1. **Give high flow oxygen (if not contraindicated):**
2. **Obtain intravenous or intraosseous access and take blood tests:**
   a. Blood cultures
   b. Blood glucose - treat low blood glucose
   c. Blood gas (+ FBC, lactate)

Yes/No	Date	Time & sign

3. **Give IV or IO antibiotics:**
   - Broad spectrum cover as per formulary overleaf

4. **Consider fluid resuscitation**:
   - Aim to restore normal circulating volume and physiological parameters
   - Titrate 5-20 ml/kg Isotonic Fluid over 5 - 10 min and repeat if necessary
   - Caution with fluid overload; examine for crepitations & hepatomegaly

Yes/No	Date	Time & sign

5. **Involve senior doctor (senior fellow / consultant):**

6. **Consider inotropic support early:**
   - If normal physiological parameters are not restored after ≥ 40 ml/kg fluid
   - **Senior and/or PICU assistance should be in place if not improved after 20ml/kg fluid**

Doctor / ANP to record reasons for variation from Paediatric Sepsis 6 overleaf

When complete, this form must stay with the original ED card
and be photocopied to accompany the patient on admission to a ward

Paediatric Sepsis 6 ED version 1 21 Mar 2014 BS Review date Sept 2016

ESPID-0557
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

THERAPEUTIC APPROACH OF ACUTE OSTEOARTICULAR INFECTIONS IN CHILDREN IN SPAIN: NATIONAL MULTICENTER STUDY

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Background: Despite the potential severity of acute osteoarticular infections (AOI) in children, there are no well-established protocols for its management. Aim of the study: to evaluate different therapeutic approaches for AOI in children in Spain.

Methods: Medical records from children

Results: 641 patients were evaluated. 46% had osteomyelitis (OM), 36% septic arthritis (SA), 12% osteoarthritis and 5% spondylodiscitis. 95% of children initially received IV antibiotics, mostly cefotaxime+cloxacillin (60%;5 years), with a median 13.6(±8) days for OM and 11(±6,6) days for SA (p=0.014). 1st and 2ndG. cephalosporins were the most common oral antibiotics (50%) followed by amoxicillin-clavulanate (26%). Total treatment duration was 38(±31) days for OM and 28(±16) days for SA (p

Conclusions: In our setting, children still received a prolonged course of antibiotics as treatment for AOI. A high proportion of these antibiotics had too broad spectrum. There was a low rate of sequelae, even with a non-surgical approach.

ESPID-0738
Short Oral Presentation Session 7- SEVERE BACTERIAL AND VIRAL INFECTIONS

PREVIOUSLY HEALTHY CHILDREN AND THOSE WITH CO-MORBIDITIES EQUALLY REPRESENTED AMONG AUSTRALIAN INFLUENZA-RELATED ICU ADMISSIONS, 1997-2013

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Background: Influenza virus predictably causes an annual epidemic resulting in a considerable burden of illness in Australia. Children are disproportionately affected and can experience severe illness and complications, including death.

Methods: We conducted a retrospective descriptive study on paediatric influenza-related Australian ICU admissions between 01 January 1997 and 31 December 2013 using data collated in the Australian and New Zealand Paediatric Intensive Care (ANZPIC) Registry.

Results: Between 1997 and 2013, a total of 704 influenza-related ICU admissions were recorded (6.2 per 1,000 all-cause ICU admissions). Age at admission ranged between 0 days and 15.9 years (median=2.1 years), with 135 (19.2%) of those admitted aged <6 months. Approximately half of the cases (n=344, 48.9%) had co-morbidities, most commonly asthma and chronic lung disease. Compared with previously healthy cases, those with co-morbidities were older (median age 3.5 vs 4.3 years, p=0.01) and stayed in ICU longer (median stay 5.2 vs 6.5 days, p=0.04). Respiratory support requirements were similar for both groups, and overall 361 (51.3%) of admissions required invasive respiratory support for a median duration of 4.3 days (range 0.2 hours – 107.5 days). Death occurred more frequently among admissions with co-morbidities (n=18, 5.2%) compared to previously healthy children (n=9, 2.5%), however this was not significant (p=0.07).

Conclusion: Between 1997 and 2013, a substantial proportion of Australian paediatric ICU admissions were attributed to influenza. Influenza-related ICU admissions were evenly distributed among previously healthy children and those with co-morbidities.

ESPID-0334
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

COULD AN OUTER MEMBRANE VESICLE (OMV) CONTAINING MENINGOCOCCAL B VACCINE HELP PROTECT AGAINST GONORRHOEA INFECTION? A RETROSPECTIVE ECOLOGICAL STUDY FROM NORWAY

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Background

Components of meningococcal B vaccines, e.g. the outer membrane vesicle, could help protect against *Neisseria gonorrhoea*infection. An OMV vaccine, trialled in Norway from 1988 to 1992, was administered to 60% (n=149,000) of teenagers born in 1973 through 1976. We examined the association between gonorrhoea notification rates (1993-2009) in people ≥16 years, and vaccination coverage by birth cohort.

Methods

In this retrospective, ecological study, differences in gonorrhoea notification rates from the Norwegian Surveillance System for Communicable diseases (MSIS), between vaccinated cohorts (VC, born 1973-1976) and unvaccinated cohorts, born before (pre-VC, 1965-1972) and after (post-VC, ≥1977) were tested using Poisson log-linear regression.

Results

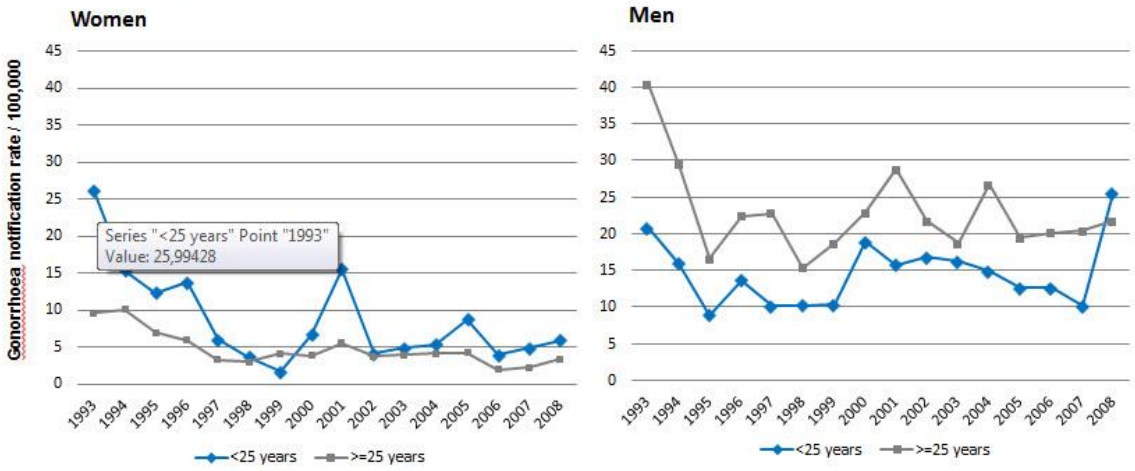
Among women, notification rates dropped until 1999, mostly in those aged <25 years (Figure 1). Among men, incidence dropped in those aged 20-30 from 1993-1995, before an overall incidence increase from 1995. In VC versus pre-VC, there was evidence of a limited age-specific effect in women (age 20-24 years, crude analysis) and men (age 20-24, adjusted analysis) [Figure 2, Table]. Rates in VC compared to post-VC were, overall, similar in women and lower in men.

Conclusions

This is the first formal attempt to address this question as data globally are limited. Our study suggests a limited age-specific vaccination effect. Within this ecological study design, any observable effect would have required prolonged vaccine

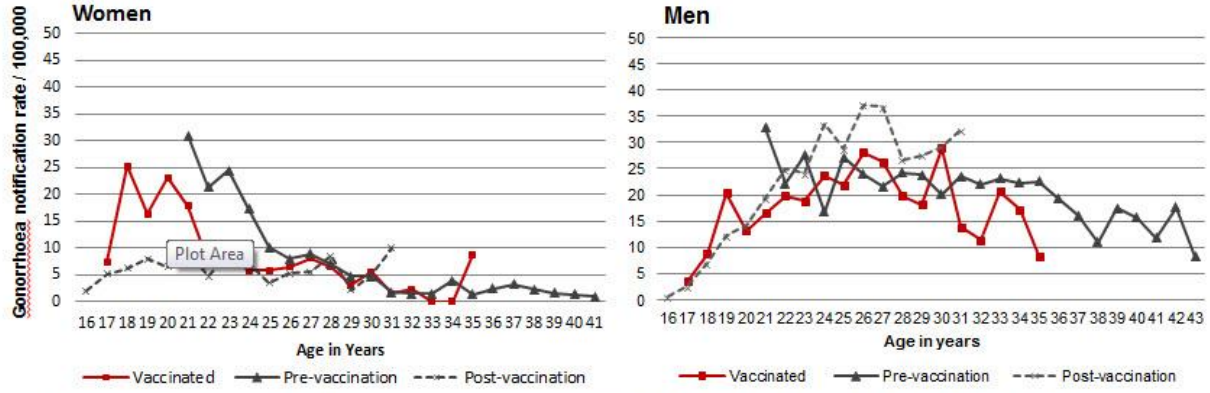
immunogenicity. Evaluation of new protein-based meningococcal B vaccines could prove useful in this regard.

Figure 1. Notification rate in women and men by age-group and year of diagnosis in those diagnosed from 1993 through 2008.



Notification rates dropped in all age groups in women until 1999, more markedly in those under 25 years of age. Among women from 1999 to 2008, incidence in each age group has been similar. In men, incidence dropped in all age-groups from 1993-1995, and has increased since 1995.

Figure 2. Notification rate in women and men by birth cohort and age in years in those diagnosed from 1993 through 2008.



Among young women (<25 years), there is some indication of an age-specific birth-cohort effect (see also Table). Women <25 years were diagnosed from 1993-1998 (pre-vaccination birth cohorts), from 1993-2001 (vaccinated birth cohorts) and from 1993-2008, (post-vaccination birth cohorts).

In men, trends are more mixed: incidence in pre-vaccinated and vaccinated cohorts is divergent until age 22 and after age 30 when rates in vaccinated cohorts appear to be lower (see also table 2 for analysis). In men, incidence in post-vaccination cohorts born after 1977 is higher overall than in other birth cohorts (dashed grey line).

Table. Gonorrhoea incidence rate (IR) and incidence rate ratio (IRR) by sex, agegroup and birth cohort, crude analysis and adjusted for year of diagnosis, 1993-2008, n=2601.

Age group	Birth Cohorts	IR[a]	Crude IRR[b]	(95%CI[c])	p value	Adjusted IRR[d]	(95%CI)	p value
Women								
16-20	Vaccinated (1973-1976)	17.9	ref.			ref.		
	Post-vaccination (≥1977)	5.2	0.3	(0.2-0.4)	0.000	0.4	(0.2-0.6)	0.000
20-24	Vaccinated (1973-1976)	12.5	ref.			ref.		
	Pre-vaccination (1969-1972)	21.7	1.7	(1.2-2.4)		1.4	(1.0-2.0)	
	Post-vaccination (≥1977)	7.3	0.6	(0.4-0.8)	0.000	1.1	(0.7-1.7)	0.179
25-29	Vaccinated (1973-1976)	6.0	ref.			ref.		
	Pre-vaccination (1965-1972)	7.5	1.2	(0.8-1.8)		1.1	(0.6-1.9)	
	Post-vaccination (≥1977)	5.0	0.8	(0.6-1.3)	0.106	0.9	(0.5-1.6)	0.924
30-34	Vaccinated (1973-1976)	1.9	ref.			ref.		
	Pre-vaccination (1965-1972)	2.7	1.2	(0.6-2.4)		1.6	(0.7-4.0)	
	Post-vaccination (≥1977)	6.7	3.1	(1.1-8.2)	0.069	2.8	(1.0-7.6)	0.105
>=35	Vaccinated (1973-1976)	8.9	ref.			ref.		
	Pre-vaccination (1965-1972)	2.0	0.2	(0.1-0.7)	0.012	0.2	(0.0-0.6)	0.005
Men								
16-20	Vaccinated (1973-1976)	13.8	ref.			ref.		
	Post-vaccination (≥1977)	5.2	0.4	(0.2-0.6)	0.000	0.4	(0.2-0.6)	0.000
20-24	Vaccinated (1973-1976)	18.4	ref.			ref.		
	Pre-vaccination (1969-1972)	22.7	1.2	(0.9-1.6)		1.5	(1.1-2.0)	
	Post-vaccination (≥1977)	22.4	1.2	(0.9-1.5)	0.186	0.7	(0.5-1.0)	0.007
25-29	Vaccinated (1973-1976)	22.8	ref.			ref.		
	Pre-vaccination (1965-1972)	23.9	1.1	(0.9-1.3)		1.0	(0.7-1.3)	
	Post-vaccination (≥1977)	31.9	1.4	(1.1-1.7)	0.044	1.5	(1.1-2.0)	0.009
30-34	Vaccinated (1973-1976)	18.3	ref.			ref.		
	Pre-vaccination (1965-1972)	22.2	1.2	(0.9-1.5)		1.3	(1.0-1.8)	
	Post-vaccination (≥1977)	30.3	2.1	(1.7-2.6)	0.000	1.6	(1.1-2.5)	0.034
>=35	Vaccinated (1973-1976)	8.4	ref.			ref.		
	Pre-vaccination (1965-1972)	16.8	2.0	(0.6-6.3)	0.231	1.7	(0.5-5.4)	0.363

a. IR incidence rate per 100,000 population
b. IRR incidence rate ratio to the reference category
c. 95%CI: 95% confidence interval

ESPID-0523
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

IMMUNOGENICITY AND SAFETY OF A BOOSTER DOSE OF PCV13 IN CHILDREN PRIMED WITH 2 OR 3-DOSES OF PHID-CV OR PCV13

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Background: While both 10-Valent Pneumococcal Non-Typeable Haemophilus Influenzae Protein D-conjugate vaccine (PHiD-CV) and 13-Valent Pneumococcal Conjugate Vaccine (PCV13) are broadly used PCVs, there is limited data on their interchangeability in terms of safety and immunogenicity.

Aim: To assess immunogenicity and safety of booster dose of Pfizer´s PCV13 in GSKs' PHiD-CV primed children.

Methods: Two phase III, open-label, multicenter studies were conducted. In the Czech Republic (CZ), 12-15-month-old children received booster dose of PCV13 after 3-dose-priming with either PHiD-CV or PCV13. In Slovakia (SK) 11-12-month-old children received PCV13 following 2-dose-priming with either PHiD-CV or PCV13. Primary objective was to assess non-inferiority of post-booster OPA titers for 19A.

Results: 98 subjects in CZ, 89 in SK.

Table 1: Immunogenicity: OPA titers for serotype 19A one month after booster dose

(TVC – preliminary data)

Schedule (Country)	Group	N	G_Mean	95% CI
	PHiD-CV	39	1918.0	(1406.4, 2615.6)
2+1 (SK)	PCV13	50	2373.6	(1898.9, 2967.0)
	PHiD-CV	53	2738.6	(2081.3, 3603.4)
3+1 (CZ)	PCV13	45	3004.9	(2391.4, 3775.7)

Table 2: Reactogenicity: Number of subjects reporting AE/SAE (TVC)

	PHiD-CV	PCV13	Total

AE			
Czech Republic	14 (26.4%)	25 (55.6%)	39 (39.8%)
Slovakia	15 (38.5%)	20 (40.0%)	35 (39.3%)
SAE			
Czech Republic	1	3	4
Slovakia	2	1	3

Conclusion: Similar robust immunological response in OPA, including for serotype 19A, was observed in PHiD-CV and PCV13 primed children when boosted with PCV13. Results suggest interchangeability of both vaccines in terms of safety and immunogenicity, including for 19A.

Disclosure: Investigator initiated trial with financial support of GSK Biologicals SA

ESPID-0836
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

SAFETY AND TOLERABILITY OF MENINGOCOCCAL SEROGROUP B BIVALENT RLP2086 VACCINE IN HEALTHY ADOLESCENTS AND YOUNG ADULTS AGED 10–25 YEARS

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Background and Aims: *Neisseria meningitidis* serogroup B (MnB) is a leading cause of meningococcal disease globally. Bivalent rLP2086 (Trumenba®), a factor H binding protein-based vaccine, recently received accelerated approval by the US FDA for prevention of invasive MnB disease in individuals 10-25 years old. This large, randomized, controlled, phase 3 study assessed safety and tolerability of bivalent rLP2086.

Methods: Subjects received bivalent rLP2086 at months 0, 2, and 6, or hepatitis A virus vaccine (HAV) at months 0 and 6 and saline at month 2. The primary safety endpoints were the percentages of subjects reporting serious adverse events (SAEs) throughout the study and medically attended AEs within 30 days of each vaccination.

Results: Of 5712 subjects randomized (bivalent rLP2086, n=3804; HAV/saline, n=1908), 4882 subjects (85.5%) completed the 3-dose series and 6-month follow-up. Demographic characteristics were similar between the 2 groups. SAEs were reported by 1.6% of bivalent rLP2086 recipients and 2.5% of HAV/saline recipients during the study. Medically attended AEs were reported by 7.0%, 5.5%, and 5.3% of bivalent rLP2086 recipients, and 6.1%, 6.1%, and 5.0% of HAV/saline recipients after vaccinations 1, 2, and 3, respectively. Reactogenicity events, mostly mild or moderate in severity, were more commonly reported by bivalent rLP2086 recipients (Table).

Table. Subjects Reporting ≥1 Serious Adverse Event Throughout the Study, ≥1 Medically-Attended Adverse Event and ≥1 Reactogenicity Event after Each Vaccination – Safety Population

	Group 1 Bivalent rLP2086			Group 1 HAV/saline		
Interval Endpoint	**N[a]**	**n[b] (%)**	**(95% CI)[c]**	**N[a]**	**n[b] (%)**	**(95% CI)[c]**
≥1 Serious Adverse Event						
Throughout the Study	3796	59 (1.6)	(1.2, 2.0)	1908	48 (2.5)	(1.9, 3.3)
≥1 Medically-Attended Adverse Event Within 30 Days						
Vaccination 1	3796	267 (7.0)	(6.2, 7.9)	1908	117 (6.1)	(5.1, 7.3)
Vaccination 2	3529	194 (5.5)	(4.8, 6.3)	1806	110 (6.1)	(5.0, 7.3)
Vaccination 3	3313	177 (5.3)	(4.6, 6.2)	1710	94 (5.5)	(4.5, 6.7)
≥1 Reactogenicity Event[d] Within 7 Days						
Vaccination 1	3796	832 (21.9)	(20.6, 23.3)	1908	165 (8.7)	(7.4, 10.0)
Vaccination 2	3529	455 (12.9)	(11.8, 14.0)	1806	55 (3.1)	(2.3, 3.9)
Vaccination 3	3313	265 (8.0)	(7.1, 9.0)	1710	43 (2.5)	(1.8, 3.4)

[a]N = number of subjects who are in safety population for the specified analysis interval. The values in this column are used as the denominators for percentages.

[b]n = Number of subjects with at least 1 event for the specified analysis interval.

[c]Exact 2-sided confidence interval (CI) based upon the observed proportion of subjects using the Clopper and Pearson method.

[d]Reactogenicity events were defined as any adverse event with an onset within 7 days after vaccination that matched a predefined preferred term list consistent with local and systemic reactions.

Conclusions: The safety profile demonstrated in this large phase 3 study was consistent with earlier studies that supported accelerated approval in the US. Bivalent rLP2086 is safe and well-tolerated in healthy individuals aged 10-25 years.

ESPID-0033
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

IMMUNOGENICITY OF 13-VALENT PNEUMOCOCCAL CONJUGATED VACCINE IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background and Aim

There are only a few studies on immune response to pneumococcal vaccines in patients with inflammatory bowel disease (IBD); all of them assessed polysaccharide vaccines only. The aim of the study was to evaluate the immunogenicity and safety of 13-valent pneumococcal conjugated vaccine (PCV13) in IBD pediatric patients compared with healthy controls.

Methods

This was a multi-center, prospective and controlled study on children and adolescents aged 5-18 years with IBD with no history of pneumococcal immunization or documented pneumococcal infection. The subjects for the study belonged to one of the following groups: patients with IBD on no immunosuppressive therapy (Group A), those on TNF agents or immunomodulators (Group B) and healthy controls (Group C). The study population received one intramuscular injection of PCV13. The primary outcome measure was adequate vaccine response defined as post-vaccination titer $\geq$0.35 μg/mL to all 13 serotypes. Geometric mean titers and geometric mean titer rises were measured for all serotypes. The evidence of local and systemic adverse effects for five days after the vaccine was registered.

Results

A total of 178 subjects (122 patients and 56 controls) completed the study course. There was no significant difference in the rate of adequate vaccine response between IBD patients and controls measured 4-8 weeks after vaccination (90.4% vs. 96.5%, p=0.5281). Children in group A had higher GMTRs than children in group B (p = 0.0369). There were no serious adverse events related to PCV13 during the study.

Conclusion

PCV13 is both immunogenic and safe in pediatric patients with IBD.

ESPID-0640
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

IMPACT OF HIV STATUS ON NASOPHARYNGEAL CARRIAGE FOLLOWING INFANT IMMUNIZATION WITH THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D-CONJUGATE VACCINE

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Background and Aims: The 10-valent pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine (PHiD-CV) administered according to a 3+1 schedule was shown to be immunogenic and well tolerated in infants in South Africa, irrespective of their HIV status.[1,2] Here, we present bacterial nasopharyngeal carriage (NPC) results in the same children up to 2 years of age.

Methods: In this phase III, open, controlled, single center study (NCT00829010), a subset of 284 South African infants stratified by HIV status (83 HIV-infected subjects, 101 HIV-uninfected subjects born to HIV-infected mothers, 100 HIV-uninfected subjects from uninfected mothers) was enrolled to receive PHiD-CV at 6, 10 and 14 weeks of age and a booster dose at 9–10 months of age. Between 6 weeks of age and 24–27 months of age, 8 nasopharyngeal swabs were collected and cultured using routine microbiological methods to identify bacterial pathogens.

Results: The prevalence of NPC of vaccine-type pneumococci was in similar ranges across groups (Table). No major differences in NPC of *Streptococcus pneumoniae* (any serotype), *H. influenzae* (non-typeable), and *Staphylococcus aureus* were recorded between groups. While higher than in PHiD-CV studies in other countries, NPC rates were in line with studies conducted in Africa.

Conclusions: HIV infection status of infants did not alter bacterial NPC rates following a 3+1 vaccination course with PHiD-CV.

Funding: GlaxoSmithKline Biologicals SA

[1]Madhi, ESPID 2012; [2]Madhi, APCP 2012

TABLE

Occurrence of *Streptococcus pneumoniae* in nasopharyngeal swabs (total vaccinated cohort)

CHILD AGE	HIV STATUS					
	HIV-infected children		Uninfected children from HIV+ mothers		Uninfected children from uninfected mothers	
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
Any vaccine serotype*						
6–12 weeks (pre-vaccination)	83	**15.7** (8.6; 25.3)	101	**12.9** (7.0; 21.0)	100	**14.0** (7.9; 22.4)
18 weeks (1 month post-primary vaccination)	81	**30.9** (21.1; 42.1)	98	**25.5** (17.2; 35.3)	98	**26.5** (18.1; 36.4)
9–10 months (at booster visit)	76	**34.2** (23.7; 46.0)	95	**20.0** (12.5; 29.5)	98	**26.5** (18.1; 36.4)
10–11 months	77	**32.5** (22.2; 44.1)	96	**15.6** (9.0; 24.5)	98	**23.5** (15.5; 33.1)
12–13 months	77	**24.7** (15.6; 35.8)	94	**23.4** (15.3; 33.3)	98	**28.6** (19.9; 38.6)
15–18 months	75	**25.3** (16.0; 36.7)	94	**17.0** (10.1; 26.2)	98	**27.6** (19.0; 37.5)
16–19 months	75	**28.0** (18.2; 39.6)	94	**21.3** (13.5; 30.9)	98	**20.4** (12.9; 29.7)
24–27 months	73	**26.0** (16.5; 37.6)	92	**16.3** (9.4; 25.5)	97	**19.6** (12.2; 28.9)
Any serotype						
6–12 weeks (pre-vaccination)	83	**27.7** (18.4; 38.6)	101	**23.8** (15.9; 33.3)	100	**25.0** (16.9; 34.7)
18 weeks (1 month post-primary vaccination)	81	**58.0** (46.5; 68.9)	98	**63.3** (52.9; 72.8)	98	**59.2** (48.8; 69.0)
9–10 months (at booster visit)	76	**72.4** (60.9; 82.0)	95	**64.2** (53.7; 73.8)	98	**66.3** (56.1; 75.6)
10–11 months	77	**64.9** (53.2; 75.5)	96	**66.7** (56.3; 76.0)	98	**63.3** (52.9; 72.8)
12–13 months	77	**67.5** (55.9; 77.8)	94	**64.9** (54.4; 74.5)	98	**68.4** (58.2; 77.4)
15–18 months	75	**69.3** (57.6; 79.5)	94	**68.1** (57.7; 77.3)	98	**70.4** (60.3; 79.2)
16–19 months	75	**78.7** (67.7; 87.3)	94	**72.3** (62.2; 81.1)	98	**63.3** (52.9; 72.8)
24–27 months	73	**79.5** (68.4; 88.0)	92	**64.1** (53.5; 73.9)	97	**64.9** (54.6; 74.4)

**Pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.*

N, number of swabs cultured at the considered visit; %, percentage of positive swabs at the considered visit; 95% CI, 95% confidence interval.

ESPID-0780
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

S. PNEUMONIAE SEROTYPE 1 BURDEN IN THE AFRICAN MENINGITIS BELT: IS THERE A LACK OF FUNCTIONALITY IN SPECIFIC ANTIBODIES?

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Background: *S. pneumoniae* serotype 1 (Sp1)constitutes an important cause of seasonal endemic meningitis in all age groupsin the African meningitis belt. Despite a higher meningitis incidence, the Burkinabe population has Sp1-specific antibody seroprevalence similar to that reported inUK. We aimed to establish whether pneumococcal immunity (functionalactivity, IgG avidity, IgM) naturally present in Burkina Faso differs from that seen in UK individuals and to compare natural and vaccine-induced immunity.

Methods:Samples collected from pneumococcal-vaccine naive Burkinabe and UK subjects were matched for age (1-39 years) and anti-Sp1 IgG level, then analyzed for OPA to 3 serotypes (1,5,19A) and compared to post-vaccine samples. Furthermore,Burkina samples were assessed for IgG avidity and serotype-specific IgM concentrations.

Results:169 matched sera from both populations were selected. A greater proportion of Burkinabe subjects aged 1-19 years had functional Sp1 activity (OPA>0.8) compared to UK subjects (12% vs 2%, p

Conclusions: Despite a substantially higher pneumococcal meningitis incidence, no decreased functional immunity to Sp1 could be evidenced in the Burkinabe population compared to UK. Furthermore naturally induced antibodies were less functional than vaccine induced antibodies.

ESPID-0913
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

IMMUNOGENICITY/SAFETY OF DTAP-IPV-HB-HIB VACCINE VERSUS INFANRIX® HEXA CONCOMITANT WITH PREVENAR 13® (PCV13), AT 3, 5, AND 11-12 MONTHS OF AGE

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Objective: Assess immunogenicity and safety of a fully liquid, ready-to-use, hexavalent DTaP-IPV-HepB-PRP-T vaccine (Hexaxim®, also trade-named as Hexacima® and Hexyon®) administered in a 2+1 schedule (at 3 & 5 months of age + 11-12 months of age). EudraCT#: 2012-001054-26

Methods: Phase III, randomized, active-controlled, observer-blind, multicenter Finnish/Swedish study. Infants received DTaP-IPV-HepB-PRP-T (N=271) or licensed hexavalent control (Infanrix® hexa). Participants in each study arm were concomitantly administered PCV13. Blood samples were collected pre-Dose 1, post-Dose 2, pre-Dose 3 and post-Dose 3 and analyzed via validated serological assays. Non-inferiority of DTaP-IPV-HepB-PRP-T to control vaccine was tested by comparison to predefined seroprotection (SP) and vaccine response (VR) rates 1 month post-Dose 3. Safety was assessed via study site observation and parental monitoring/reporting of solicited (predefined) and unsolicited adverse events.

Results: Non-inferiority of DTaP-IPV-HepB-PRP-T to control post-Dose 3 was demonstrated for each antigen.

Primary Objective: Noninferiority of seroprotection/vaccine response rates of DTaP-IPV-HepB-PRP-T vs. Control (1 month post-Dose 3)					
	DTaP-IPV-HepB-PRP-T (N=249)	Control (N=248)	DTaP-IPV-HepB-PRP-T minus Control		
	%	%	%[95% CI] †	δ%	Noninferior?
Anti-Diphtheria≥ 0.1 IU/mL	100	99.2	0.8 (-0.82; 2.92)	10	Yes
Anti-Tetanus ≥ 0.1 IU/mL	100	100	0 (-1.53; 1.54)	10	Yes
Anti-PT Vaccine response*	98.0	99.6	-1.6 (-4.30; 0.58)	10	Yes
Anti-FHA Vaccine response*	100	99.6	0.4 (-1.16; 2.30)	10	Yes
Anti-Polio 1 ≥ 8 (1/dil)	100	100	0 (-1.53; 1.54)	5	Yes
Anti-Polio 2 ≥ 8 (1/dil)	100	100	0 (-1.54; 1.54)	5	Yes
Anti-Polio 3 ≥ 8 (1/dil)	99.6	99.6	0 (-1.87; 1.89)	5	Yes
Anti-Hep B ≥ 10 mIU/mL	96.4	99.6	-3.2 (-6.34; -0.69)	10	Yes
Anti-PRP ≥ 1.0 µg/mL	93.5	85.2	8.2 (2.77; 13.8)	10	Yes
* Vaccine response for PT and FHA = post-Dose 3 Ab concentrations ≥ 4 × LLOQ, if pre-Dose 1 Ab concentrations < 4 × LLOQ; Post-Dose 3 Ab concentrations ≥ pre-Dose 1 Ab concentrations, if pre-Dose 1 Ab concentrations ≥ 4 × LLOQ ‡ If lower bound of 95% CI >-δ then the null hypothesis H0 rejected and conclude noninferiority					

Secondary Objective: post-Dose 3 GMC or GMT (95% CI)		
	DTaP-IPV-HepB-PRP-T (N=249)	Control (N=248)
Anti-Diphtheria	1.70 (1.54; 1.87)	1.20 (1.07; 1.34)
Anti-Tetanus	2.23 (2.01; 2.47)	2.37 (2.16; 2.60)
Anti-PT	90.9 (84.9; 97.4)	129 (119; 139)
Anti-FHA	148 (138; 158)	167 (155; 179)
Anti-Polio 1	1749 (1494; 2047)	3279 (2869; 3746)
Anti-Polio 2	1729 (1454; 2058)	2954 (2520; 3462)
Anti-Polio 3	1213 (1005; 1463)	1906 (1594; 2279)
Anti-Hep B	1370 (1069; 1757)	5015 (4178; 6020)
Anti-PRP	9.73 (8.12; 11.7)	5.64 (4.66; 6.81)

For PCV13, the SP rate was high for each antigen and similar for both groups. All vaccines were well tolerated.

Conclusions: These findings confirm the suitability of the new hexavalent vaccine for administration via 2+1 schedule; DTaP-IPV-HepB-PRP-T is safe and elicits protective responses against 6 targeted diseases. Study funding: Sanofi Pasteur.

ESPID-0915
Short Oral Presentation Session 8- PNEUMOCOCCAL and MENINGOCOCCAL vaccination

EFFECT OF 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON MENINGITIS AND INVASIVE DISEASE AFTER 3 YEARS OF ROUTINE IMMUNIZATION IN BRAZIL

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BACKGROUND:
Routine infant immunization with 10-valent pneumococcal conjugate vaccine (PCV-10) began in Brazil in March 2010, administered at 2, 4, 6 with a booster at 12-15 months of age. We assessed PCV-10 effectiveness on rates of invasive pneumococcal disease (IPD) notifications.

METHODS:
Pneumococcal meningitis cases confirmed by culture, antigen detection methods and/or bacteriology notified to the national surveillance system for notifiable diseases (SINAN) and all IPD cases from the national reference laboratory (Adolfo Lutz Institute/IAL) for the years 2008-2013 were cleaned and combined by means of record-linkage. An interrupted time-series analysis was conducted to estimate rates of IPD in the postvaccination period, based on rates from prevaccination period, adjusting for seasonality and secular trends. The year 2010 was excluded from the analysis. Vaccine coverage was estimated as 82%, 88%, and 92% for the years 2011, 2012 and 2013.

RESULTS:
PCV-10 significantly reduced rates of IPD for vaccine-target age-groups (Figure 1 and Table). Figure 2 presents yearly variations on the number of vaccine- and non-vaccine-type cases for children 2-23 months of age with serotyping information.

CONCLUSION:
After 3 years of PCV-10 vaccination in Brazil, IPD reduced significantly. No herd effect was observed in unvaccinated individuals. Continuous monitoring is essential to evaluate the sustainability of the effect of PCV10 and the need for changes in the vaccine schedules.

Figure 1. Rates of invasive pneumococcal disease of Brazilian infants aged 2-23 months, 2008-2013.

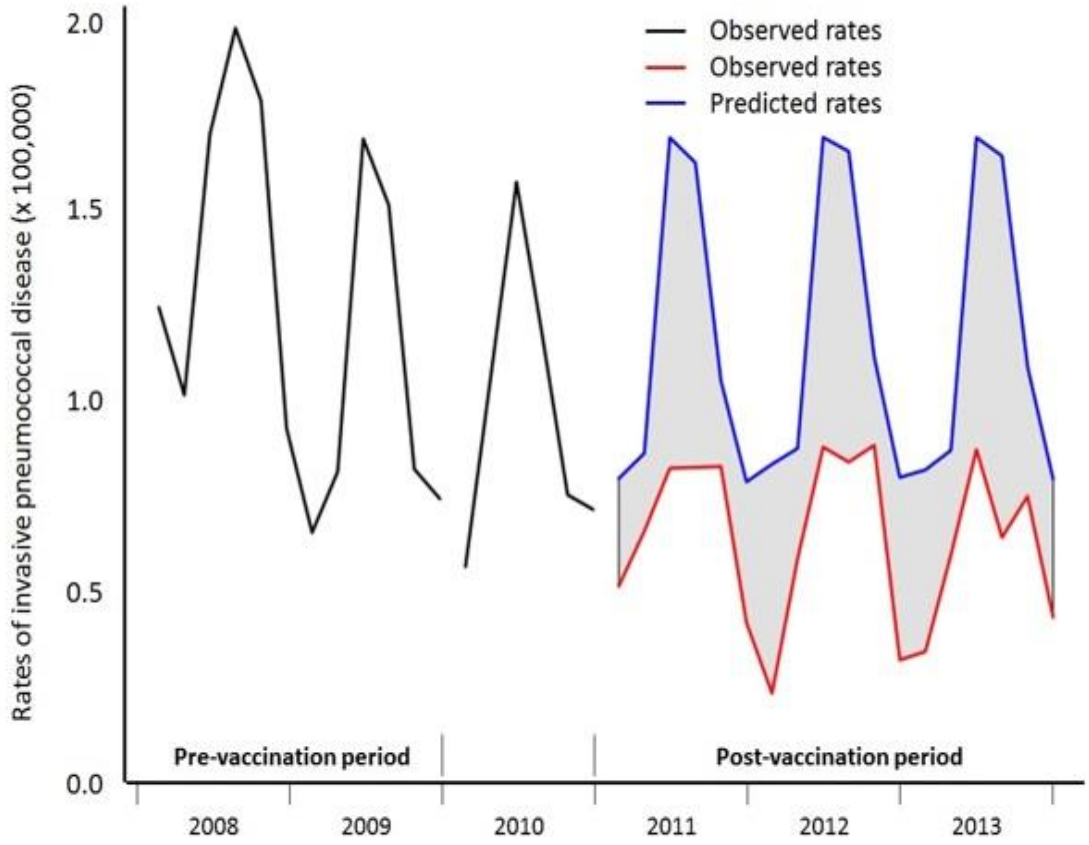
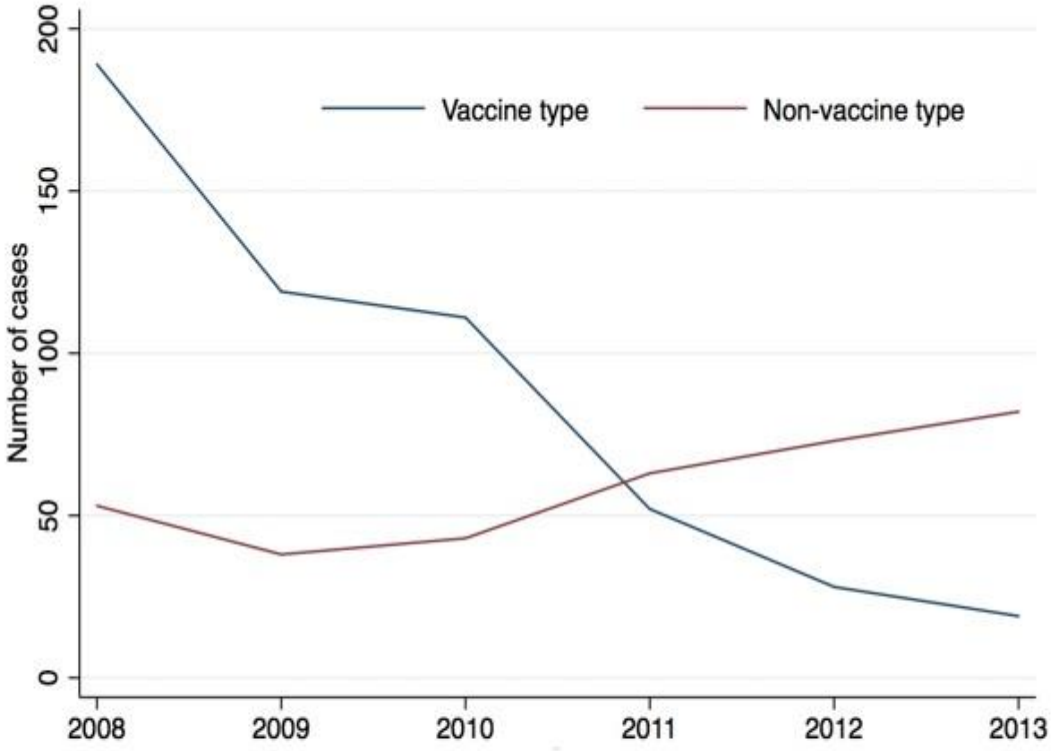


Table. Effectiveness of PCV-10 vaccination on pneumococcal meningitis and invasive disease by age-groups in Brazil. Interrupted time series analysis, 2008-2013.

Age-groups	Effectiveness		
	%	95%CI	p-value
2-23 mo	-44,2	-72,5; -15,8	0,000
2-11 mo	-34,7	-58,9; -10,4	0,002
12-23 mo	-61,1	-82,7; -39,6	0,000
2-4 years	14,7	-85,7; 115,1	0,347
5-9 years	-4,7	-66,0; 56,7	0,660
10-17 years	6,2	-72,9; 85,2	0,465

Figure 2. Trends of vaccine- and non-vaccine type pneumococcal invasive disease of Brazilian infants aged 2-23 months, 2008-2013.



ESPID-0134
Short Oral Presentation Session 9- ROTAVIRUS and PERTUSSIS vaccination

IMMUNIZATION OF PREGNANT WOMEN AGAINST PERTUSSIS: THE EFFECT OF TIMING ON ANTIBODY AVIDITY

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Background: The Centers for Disease Control and Prevention recommend tetanus-diphteria-acellular pertussis (Tdap) immunization during pregnancy, preferably at 27-36 weeks gestation.

Aims: First, to assess the relative avidity index (RAI) of umbilical cord immunoglobulin G (IgG) to pertussis toxin (PT) for newborns of women immunized with Tdap during late pregnancy as compared to unimmunized women. Second, to assess whether there is a preferential period of gestational Tdap immunization that provides the highest RAI of umbilical cord IgG to PT.

Methods: RAI of IgG to PT was assessed via an adapted ELISA using NH_4SCN as a dissociating agent.

Results: We found that newborns of women immunized with Tdap during late pregnancy (n=52) had higher mean RAI of umbilical cord IgG to PT than those of unimmunized women (n=8), 73.77 % ± 12.08 (95% CI, 70.41-77.13) vs. 50.23 % ± 21.32 (95% CI, 32.41-68.06), p< .001. Further, the RAI of umbilical cord IgG to PT was significantly higher in newborns of women immunized at $27\text{-}30^{+6}$ weeks gestation (n=20) when compared with newborns of women immunized at 31-36 weeks (n=22) and > 36 weeks (n=7), 79.53 %±5.61 (95% CI, 76.91-82.16) vs. 71.56%±12.58 (95% CI, 65.98-77.14) vs. 63.93% ± 17.98 (95% CI, 47.31-80.56), p<0.03.

Conclusion: Gestational Tdap immunization between 27-30^{+6} weeks resulted in the highest avidity of IgG to PT conveyed at delivery as compared with immunization beyond 31 weeks gestation. Future studies should be conducted to confirm our findings to optimize pertussis-controlling strategies.

ESPID-0135
Short Oral Presentation Session 9- ROTAVIRUS and PERTUSSIS vaccination

PERTUSSIS RESURGENCE ASSOCIATED WITH PERTACTIN-DEFICIENT AND GENETICALLY DIVERGENT BORDETELLA PERTUSSIS ISOLATES IN ISRAEL

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Background: Despite the addition of two teteanus-diphteria-acellular-pertussis (Tdap) booster doses in 2005 and 2008, the Israeli Ministry of Health surveillance data reveals a marked increase in the incidence of pertussis. We aim to assess the rate of positivity in the laboratory diagnosis and changes in *B. pertussis* genotype and phenotype following the introduction of two Tdap boosters.

Methods: For polymerase chain reaction (PCR), *B. pertussis* detection was based on the amplification of Insertion Sequence 481. Pulse field gel electrophoresis (PFGE) utilized the *Spe*I restriction enzyme. The Pertactin (Prn) protein was detected by western immunoblot

Results: There was a change in the *B. pertussis* PCR positivity, 40/408 (9.8%), 66/491 (13.4%), 111/504 (22%) and 87/572 (15.2%) for 2010, 2011, 2012 and 2013, $p<0.001$, respectively. A similar trend was evident for positive- culture specimens. Several PFGE restriction patterns from 2009-2012 were identified and referenced to our 2007-2008 profiles. Profile A decreased from 54% (n=44) to 26% (n=10), $p<0.006$, whereas B increased from 41% (n=34) to 50% (n=18), $p>0.43$, respectively. Profiles C and D disappeared and new profiles, E (n=2, 5%), F (n=1, 3%), G (n=3, 8%), H (n=1, 3%), and I (n=2, 5%) emerged. The proportion of Prn negative isolates increased significantly over 2005-2006, 2011-2012 and 2013-2014, 1/15 (6.6%) vs. 1/17 (7.1%) vs. 11/33 (33.3%), $p<0.03$.

Conclusions: The increase in pertussis laboratory detection is associated with changes in *B. pertussis* genetics and the circulation of isolates not expressing Prn. Studies should explore whether these divergent strains are caused by high Tdap coverage.

ESPID-0376
Short Oral Presentation Session 9- ROTAVIRUS and PERTUSSIS vaccination

PREVENTING PERTUSSIS IN PREMATURE INFANTS: ANTIBODY CONCENTRATIONS FOLLOWING MATERNAL ANTENATAL PERTUSSIS VACCINATION

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INTRODUCTION & AIMS

Antenatal pertussis vaccination provides direct and indirect protection to unvaccinated infants. Premature babies are at increased risk of pertussis and may not benefit from maternal vaccination (MV) due to decreased placental antibody transfer. We aimed to assess antibody concentrations in premature infants whose mothers had been vaccinated in pregnancy.

METHODS

This was a sub-study of a premature infant vaccine trial. Mothers received DTaP (Repevax®: diphtheria, tetanus, acellular pertussis and polio, Sanofi Pasteur MSD) vaccine as part of their routine antenatal care.

Infants had IgG concentrations measured for pertussis toxin (PT), filamentous haemagglutinin (FHA), Fimbriae types 2&3 (Fim), diphtheria and tetanus before and after their primary immunisations.

RESULTS

A total of 32/206 (16%) premature infants' mothers received DTaP vaccine (median gestation at administration 28.4 weeks; IQR 28.0-29.4 weeks). The median birth gestation was 32.5 weeks (IQR 29.7-33.7). MV was associated with higher IgG GMCs at 2 months for PT (3.4 vs 1.4IU/ml), FHA (16.9 vs 2.7IU/ml), Fim2&3 (33.6 vs 3.0IU/ml), tetanus (1.0 vs 0.11IU/ml) and diphtheria (0.15 vs 0.02IU/ml); p

Following primary vaccination, lower antibodies against FHA and diphtheria were seen in the MV group (p=0.008 and 0.024 respectively). Responses to concomitant vaccines did not differ between groups.

CONCLUSION

Even in infants born prematurely antenatal DTaP vaccination can result in higher antibody concentrations at 2 months of age. Women at risk of premature delivery should receive DTaP vaccination promptly.

ESPID-0771
Short Oral Presentation Session 9- ROTAVIRUS and PERTUSSIS vaccination

SEVENTH YEAR POST-ROTAVIRUS VACCINATION IN BELGIUM: SUSTAINED DECREASE OF ROTAVIRUS-POSITIVE STOOL SAMPLES IN HOSPITALISED CHILDREN.

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Background and aims:

In Belgium, rotavirus vaccination has been reimbursed since November 2006 and the coverage is more than 85%.

This analysis aims to assess and compare the impact of mass rotavirus vaccination on rotavirus related hospitalisations in children ≤2-year-old pre-vaccination and up to 7 years post-introduction of the vaccine in 11 paediatric wards in Belgium.

Methods:

All rotavirus detection tests collected from hospitalised children ≤2-year-old were analysed. The absolute number of rotavirus positive tests pre-vaccine (01/06/2004-31/05/2006) were compared with data at launch (01/06/2006-31/05/2007), and post-launch (01/06/2007-31/05/2014). Data are presented as a percentage reduction (95% Confidence Interval - CI) per year post-vaccination considering the annual average pre-vaccination period as reference.

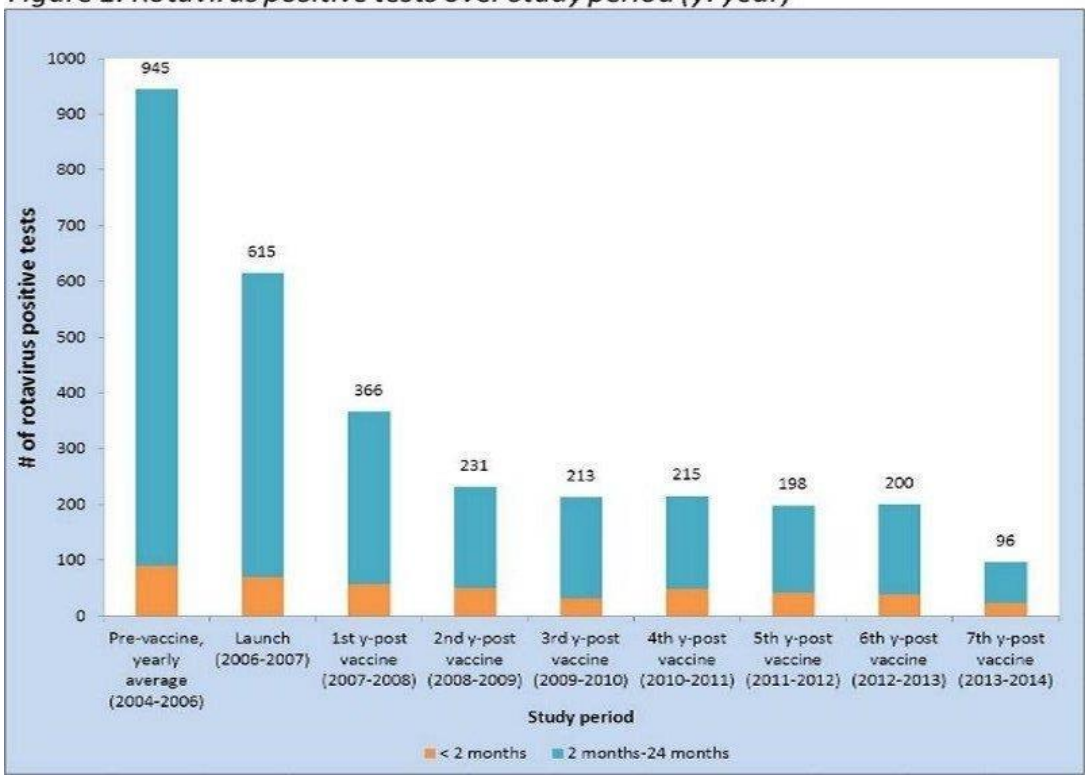
Results:

Between June 2004 and May 2014, 26,393 rotavirus detection tests were performed in children ≤ 2-year-old. 4,024 tested positive. The number of rotavirus positive tests dropped from 945 on average during pre-vaccine period to 96 during the 7th year post-vaccine, a reduction of 90% (95% CI: 88%-92%) (figure 1). We observed a reduction in nosocomial rotavirus infections from 141 cases pre-vaccine to 17 during the 7th year post-vaccine, a reduction of 88% (95% CI:83%-93%). A reduction of 50% of Acute Gastroenteritis (AGE)-driven hospitalisation days is observed during the 7th year post-vaccine, from 11,881 AGE-driven hospitalisation days pre-vaccine to 5,897.

Conclusions:

Sustained significant declines in number of rotavirus and all-cause AGE-related hospitalisations are seen in young children 7 years after the introduction of mass rotavirus vaccination in Belgium.

Figure 1: Rotavirus positive tests over study period (y: year)



ESPID-0693
Short Oral Presentation Session 9- ROTAVIRUS and PERTUSSIS vaccination

INTUSSUSCEPTION RISK AFTER PENTAVALENT ROTAVIRUS VACCINATION IN FINNISH INFANTS

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Background: An association between rotavirus immunisation and intussusception (IS) has been shown in some studies. In Finland, rotavirus vaccination programme was implemented in 9/2009 with 2, 3, and 5 months schedule. By the end of 2013, over 700 000 doses, of which 240 000 1st doses, were given. Nationwide registers allow us to evaluate the association between rotavirus vaccination and IS.

Methods: Cases of IS diagnosed during 1999-2013 were identified from the National Hospital Discharge Register. All cases under 250 days of age diagnosed during 2009 - 2013 were confirmed by reviewing medical charts. Self-controlled risk interval method was used to assess the risk of IS during 1-21 days compared to 22-42 days post-vaccination.

Results: In non-verified register data the relative incidence of IS at 2 months of age between the post and pre vaccination era was 9.1 (95%CI 2.0-84.3). After case verification, the incidence of IS in the risk period after the 1st dose relative to the control period was 2.0 (95% CI 0.5 – 8.4; p= 0.34) The number of excess IS cases per 100 000 first vaccine doses was therefore estimated to be 1.03 (95% CI 0.0-2.5), i.e. one IS case per 96 000 first doses of rotavirus vaccine (95% CI 54 600 to ∞). No risk was observed after the 2nd and 3rd dose.

Conclusion: Although the finding is not statistically significant, it excludes a 10-fold risk of IS associated with RotaShield vaccine with confidence. The benefits of rotavirus immunisation programme outweigh possible small risks of intussusception.

ESPID-1076
Short Oral Presentation Session 9- ROTAVIRUS and PERTUSSIS vaccination

IMPACT OF THE NATIONAL ROTAVIRUS VACCINATION PROGRAMME 1 YEAR AFTER ITS INTRODUCTION IN ENGLAND AND WALES: A TIME SERIES ANALYSIS

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Background:
A monovalent oral rotavirus vaccine was introduced into the infant immunisation programme in England and Wales in July 2013. This study aimed to estimate the impact of the rotavirus immunisation programme on laboratory-confirmed rotavirus infections and hospital admissions for all-cause acute gastroenteritis (AGE) during the first year post-introduction.

Methods:
Time series analysis using national laboratory-confirmed rotavirus infection reports (n=201,591) between July 2000 and June 2014 and Hospital Episodes Statistics (HES) for all-cause AGE (n=2,251,424) between July 2007 and June 2014 for England and Wales. Adjusted rate ratio (RR) was calculated by comparing the rate of reported laboratory-confirmed rotavirus infections and all-cause AGE hospital admissions before and after the implementation of the infant rotavirus immunisation programme.

Results:
In children under 1 year of age, the target group for vaccination, there was a 77% (RR 0.23, 95% CI 0.16 to 0.32,p<0.0001) decline in laboratory-confirmed rotavirus infections and a 26% (RR 0.74, 95% CI 0.65 to 0.84, p<0.0001) decline in all-cause AGE hospital admissions in 2013-2014 compared to the pre-vaccination era. Reductions were also observed in older children and adults, suggesting indirect benefits from rotavirus vaccination. In total, we estimated 10,884 laboratory-confirmed rotavirus infections and 50,427 all-cause AGE hospital admissions were averted in 2013-2014 which could be attributable to the infant rotavirus immunisation programme.

Conclusions:
During the first post-vaccination year, we observed a substantial decline in rotavirus

disease burden, most pronounced in the target age group, but with evidence of herd protection across all age groups.

ESPID-0644
Short Oral Presentation Session 10- Viral vaccines

COMPARISON OF SIX YEAR EFFICACY BETWEEN ONE OR TWO DOSES OF LIVE VARICELLA VIRUS- CONTAINING VACCINES: A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Background: We are conducting a follow-up (NCT00226499) of an initial randomized, multicenter trial evaluating the 10-year efficacy of one-dose of the live attenuated varicella vaccine (*Varilrix*™, GSK Vaccines) and 2-doses of the combined measles-mumps-rubella-varicella (MMRV) vaccine (*Priorix-Tetra*™, GSK Vaccines) versus a control group for the prevention of varicella disease. We present here efficacy results for 6-years post-vaccination.

Methods: Children aged 12-22 months from 10 European countries received either (i) 2 doses of MMRV or (ii) first-dose combined measles-mumps-rubella (MMR) and second-dose monovalent varicella vaccine (MMR+V) or (iii) 2 doses of the MMR vaccine (active control), 42-days apart. Vaccine efficacy against all and moderate-or-severe varicella (confirmed by detection of viral DNA or epidemiological link) was assessed from 6-weeks post-dose-2 up to year-6 for the MMRV and MMR+V groups, and calculated with 95% confidence interval. Cases were graded for severity (modified Vasquez scale: mild≤7; moderately severe=8-15; severe≥16); herpes zoster cases were also recorded.

Results: 5289 children (mean age=14.2 [standard deviation=2.5] months) (MMRV=2279, MMR+V=2266, MMR=744) formed the efficacy cohort. 815 cases were confirmed. Efficacy of two-dose MMRV against all and moderate-or-severe

varicella was 95.0% and 99.0%, respectively. Efficacy of one-dose varicella vaccine against all and moderate-or-severe varicella was 66.9% and 90.2%, respectively (Table). All 4 confirmed cases of herpes zoster (MMR+V=2, MMR=2) were mild; 3 tested positive for the wild-type virus.

Conclusions: Two doses of the MMRV vaccine and one dose of the varicella vaccine remain efficacious through at least 6-years post-vaccination.

Table: Vaccine efficacy of two doses of MMRV and one dose of varicella vaccine (MMR+V) compared to an active control (MMR)

Vaccine Group	N	n	Vaccine efficacy (%) 95% CI
Vaccine efficacy against all varicella cases from 6 weeks post-dose-2 to year 6			
MMRV	2279	71	95.0 (93.6-96.2)
MMR+V	2266	419	66.9 (61.8-71.5)
MMR	744	325	-
Vaccine efficacy against moderate or severe varicella cases from 6 week post-dose-2 to year 6			
MMRV	2279	6	99.0 (97.8-99.6)
MMR+V	2266	58	90.2 (86.9-92.8)
MMR	744	166	-

N = number of children included in each group

n = number of children with varicella infection in each group

% = Vaccine efficacy (Cox regression model)

95% CI = 95% confidence interval

MMR+V = first-dose combined measles-mumps-rubella (MMR) and second-dose monovalent varicella vaccine

MMRV = 2-doses of the combined measles-mumps-rubella-varicella vaccine

MMR = control group with combined measles-mumps-rubella vaccine

ESPID-0412
Short Oral Presentation Session 10- Viral vaccines

QUALITY OF THE IMMUNE RESPONSE TO HEPATITIS B VIRUS VACCINE IN CHILDREN WITH CELIAC DISEASE AND THE ROLE OF GLUTEN.

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AIMS: To investigate the quality of the immune response to hepatitis B virus (HBV) vaccine in children with celiac disease (CD) in comparison with a population of healthy controls. To analyze if gluten intake can affect this immune response.

MATERIAL AND METHODS: We developed a prospective observational study. All the participants (346 controls and 214 CD patients) had been complete vaccinated with HBV vaccine in the first year of life. Antibody titers were measured by ELISA.

RESULTS:

1.- A statistically significant relationship was found, by logistic regression, between anti-HBs titers and age of serological investigation in the control group.

2.-The percentage of non-responders to HBV vaccine (anti-HBs < 10 mUI/mL) was higher in children with CD than in controls (68.7% versus 60.7%) with statistic signification in those younger than 5 years old (50% versus 30.1%). The percentage of children with undetectable titers of anti-HBs was higher in children with CD than in controls (14.02% versus 8.38%) with statistical signification in all patients and in those younger than 10 years old.

3.-An Spearman correlation showed no relationship between anti-HBs titers and the time that had lasted gluten intake in children with CD.

CONCLUSSIONS:

1.-Anti-HBs titers decreased with time. When evaluating serological response to HBV vaccine, time elapsed since vaccination should be consider.

2.-Patients with CD have an impaired response to HBV vaccine. This response should be evaluated at diagnosis.

3.-Gluten intake has no role in the genesis of a suboptimal immunological response to HBV in CD patients.

ESPID-0530
Short Oral Presentation Session 10- Viral vaccines

ROLE OF HLA GENES IN THE IMMUNE RESPONSE TO HEPATITIS B VIRUS VACCINE IN CELIAC AND HEALTHY CHILDREN.

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AIMS: To investigate the role of the HLA genes DQ2, DQ8, DR3 and DR7 in the genesis of an immunological response to hepatitis B virus (HBV) vaccine in children with celiac disease (CD) and healthy controls.

MATERIAL AND METHODS: We developed a prospective observational study in 393 children (188 CD patients and 204 controls) who were complete vaccinated with HBV vaccine in the first year of life. Antibody titers were measure by ELISA. HLA haplotypes were studied by oligonucleotide hybridization. In controls, only DQ genes were studied.

RESULTS: summarized in table 1.
Table 1: Percentage of responders and non-responders to HBV vaccine and percentage of children with anti-HBs titers= 0.00 and >0.00 mUI/mL, related to presence of HLA-DQ genes. Statistic signification.

Gen		Responders[1]	Non-responders[2]	p value	Anit-HBs= 0.00 mUI/mL	Anti-HBs > 0.000mUI/mL	p value
DQ2	YES	80 (30.19%)	185 (69.81%)	0.088	37 (13.96%)	228 (86.04%)	**0.002**
	NO	50 (39,06%)	78 (60.94%)		5 (3.91%)	123 (96.09%)	
DQ8	Yes	15 (25%)	45 (75%)	0.148	5 (8.33%)	55 (91.67%)	0.521
	No	115 (34.53%)	218 (65.47%)		37 (11.11%)	296 (88.89%)	
DR3	YES	26 (22.41%)	90 (77,59%)	**0.000**			
	NO	39 (47.56%)	43 (52.44%)				
DR7	YES	13 (23.64%)	42 (76.36%)	0.088			
	NO	52 (36.36%)	91 (63.64%)				

[1] Anti-HBs ≥10 mUI/mL; [2] Anti-HBs < 10 mUI/mL

CONCLUSSIONS:

HLA DQ2 and DR3 expression is associated with a worse immune response to HBV vaccine in these groups of children.

ESPID-0317
Short Oral Presentation Session 10- Viral vaccines

INFLUENZA VACCINATION DURING PREGNANCY: A SYSTEMATIC REVIEW OF FOETAL SAFETY

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Background & aims

Pregnant women are considered the most important risk group for influenza vaccination. Despite this, the potential risk of harm from the vaccine on the foetus is a key factor in low uptake of the vaccine. This systematic review aimed to synthesize the best available evidence on the safety of influenza vaccination during pregnancy on foetal development.

Methods and results

A search up to March 2014 resulted in 23 included studies. A mixture of narrative summary and meta-analysis was performed. Foetal death outcomes in later pregnancy ranged from OR 0.34 to 2.95, with 95% CIs crossing or below the null value. Spontaneous abortion < 24 weeks ranged from HR 0.45 to OR 1.23, with 95% CIs crossing or below the null value. Congenital malformations for women vaccinated during their first trimester ranged from OR 0.67 to 1.21 and imprecise CIs crossed the null value. Premature birth meta-analysis estimates of retrospective studies for influenza A (H1N1) vaccines were OR 0.88 (95% CI, 0.74 to 1.04) and HR 1.00 (0.93 to 1.07), and for trivalent vaccines OR 0.88 (95%CI, 0.74 to 1.04).

Conclusions

Results do not indicate that maternal influenza vaccination is associated with an increased risk of premature birth, foetal death, spontaneous abortion, or congenital malformations. Statistical imprecision and clinical and methodological heterogeneity mean it is not possible to totally exclude adverse effects. Studies investigating first trimester vaccination should be the highest priority to allow more precise estimates, especially for spontaneous abortion, and congenital abnormality outcomes.

ESPID-0163
Short Oral Presentation Session 10- Viral vaccines

LONG-TERM IMMUNOGENICITY/SAFETY OF THE HUMAN PAPILLOMAVIRUS (HPV)-16/18 AS04-ADJUVANTED VACCINE ADMINISTERED TO 10-14-YEAR-OLD GIRLS: 9-YEAR OPEN FOLLOW-UP OF A RANDOMIZED TRIAL

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Background and aims: Girls who received 3 doses of HPV-16/18 AS04-adjuvanted vaccine at age 10-14 years in a phase III, randomized, controlled, observer-blinded trial (NCT00196924) and participated in a follow-up study (NCT00316706) were invited for this open-label extension study (NCT00877877), with total follow-up of 10 years after first vaccination. This extension study evaluated long-term immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine. We present results until 9 years after first vaccination.

Methods: Humoral immune responses were determined by enzyme-linked immunosorbent assay annually. Serious adverse events (SAEs) are reported throughout the study.

Results: Approximately 9 years after first vaccination, in the Month 108 according-to-protocol immunogenicity cohort (N=394), all but 2 subjects analysed were seropositive for HPV-16 and HPV-18 antibodies. Geometric mean titres (GMTs) were 1949.2 EL.U/mL [95%CI: 1776.8-2138.5] for HPV-16 and 739.1 EL.U/mL [95%CI: 669.9-815.3] for HPV-18 among those who were baseline seronegative for the type analysed. GMTs were 65.4- and 32.6-fold higher, respectively, than those induced by natural infection (NCT00122681), and 4.7- and 3.1-fold higher than post-vaccination antibody levels observed at equivalent timepoints (Month 107-113) in women vaccinated at age 15-25 years for whom vaccine efficacy was demonstrated (NCT00518336). During the 9-year follow-up period, in the total vaccinated cohort,

92/557 (16.5%, 95%CI: 13.5-19.9) subjects reported 145 SAEs; none were vaccine-related, led to study withdrawals or were fatal to participants.

Conclusions: Sustained high immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine was demonstrated up to 9 years after first vaccination of adolescent girls. No significant safety concerns were identified.

Funding: GlaxoSmithKline Biologicals SA

ESPID-0144
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

ACCURACY OF A NEW TECHNIQUE OF URINE COLLECTION FOR THE DIAGNOSIS OF URINARY TRACT INFECTION IN INFANTS

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Background and aims: An uncontaminated sample of urine is mandatory for diagnosis of urinary tract infection (UTI). Obtaining appropriate samples from young infants usually require invasive methods, as catheterization. A new, non-invasive, technique for obtaining clean-catch urine in less than 60 seconds was recently described by our group. The technique is based on selective stimulation of bladder and lumbar area (video available elsewhere). Success rate is 86%.
Our aim was to evaluate the sensitivity, specificity and contamination rate of cultures obtained from this new, non-invasive technique.

Methods: We designed a cross-sectional study. Sixty infants were recruited. All infants were younger than 90 days. They had been admitted for fever without a source. Each patient provided two matched samples of urine obtained through 2 different methods: clean-catch standardized stimulation technique and bladder catheterization – as gold standard. Samples (n=120) were cultured following standard laboratory methods. Sensitivity, specificity and contamination rates were calculated.

Results: Average age of patients was 44 days, and 70% of them were male. Clean-catch technique sensitivity was 96.9% (CI 95%: 82.4% - 99.8%). Specificity was 89.4% (CI 95%: 65.4% - 98.1%). Contamination rate in samples obtained by clean catch was 5%. Contamination rate in samples obtained by catheterization was 8.3%. No adverse events were reported.

Conclusions: Sensitivity and specificity were high. Contamination rate was lower than catheterization contamination rate. This technique is an accurate and safe method for UTI diagnosis.

ESPID-0375
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

DOES 2 ML BLOOD SAMPLE VERSUS 1 ML INCREASE YIELD OF ORGANISMS IN PEDIATRIC BACT/ALERT BLOOD CULTURE SYSTEM IN NEONATES WITH PRIOR EXPOSURE TO ANTIBIOTICS?

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Background: Blood culture to isolate the offending pathogen remains the gold standard for definitive diagnosis of neonatal sepsis. Previously antibiotic treated neonates may have low colony counts and so may have spuriously negative blood culture.

Aims and Objectives: To compare blood culture yield of 1ml versus 2 ml sample for previously antibiotic treated neonates.

Methods: This observational analytical study was conducted at Sir Ganga Ram Hospital, New Delhi, India between May 2010 to July 2012**.**All extramural neonates of more than 30 weeks gestation admitted in NICU having clinical features and signs of neonatal sepsis and with prior exposure to antibiotics were enrolled. With all sterile precautions, paired blood culture samples of 2 ml and 1 ml were taken and cultured in automated BacT/Alert bottles.

Results

A total of 140 neonates who previously received antibiotics were enrolled. Blood culture positivity was 35.7% (50/140).Forty blood cultures were positive in either 1ml or 2 ml blood sample. 30 blood cultures were common in both 2 ml and 1 ml blood samples while 10 were positive in 1 ml blood samples and another 10 in 2 ml blood samples (kappa level of agreement=0.65).Mean time to culture positivity in 1 ml vs 2 ml blood culture samples was 0.24 days (95% CI : 0.15- 0.33 days) vs 0.39 days (95% CI :0.24-0.54 days) ,(p= 0.038).

Conclusion: In previously antibiotic treated neonates, increasing volume of blood in BacT/ALERT system neither led to increase in yield of organisms nor decrease in isolation time.

ESPID-0386
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

RAPID IDENTIFICATION OF MICROORGANISMS BY FILMARRAY® BLOOD CULTURE IDENTIFICATION PANEL IMPROVES CLINICAL MANAGEMENT IN CHILDREN.

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Background and aims

Blood cultures are a common investigation for children admitted to hospital. When blood cultures first become positive a Gram stain cannot differentiate pathogens from contaminants. In routine practice it takes a further 24 hours before the organism is identified. FilmArray® Blood Culture Identification Panel (FA-BCIP) is an automated nested multiplex PCR that can detect 24 pathogens within one hour. We aimed to assess whether results from FA-BCIP lead to changes in clinical management.

Methods

We prospectively studied children having blood cultures taken at our tertiary children's hospital. Blood cultures were monitored using the BacT/ALERT® system and organisms identified using standard methods. FA-BCIP was performed when growth was initially detected in first positive blood cultures per episode, between 1st January and 30th June 2014. Assessment of whether the FA-BCIP result altered clinical management was made by a consultant in Paediatric Infectious Diseases. This focused on earlier changes to antimicrobials and earlier discharge from hospital.

Results

FA-BCIP was done on 117 positive blood cultures; 74 (63%) grew significant organisms, 43 (37%) grew contaminants (assessed by infection consultants). FA-BCIP results were judged to alter clinical management in 63 of the 117 episodes (54%). Antimicrobials were started /altered in 23 episodes and de-escalated/ withheld /stopped in 29 episodes. Ten children were discharged earlier which saved 14 bed days.

Conclusions

Rapid identification of micro-organisms in paediatric blood cultures by FA-BCIP, led to changes in clinical management for half of the episodes. This improved antimicrobial stewardship and allowed early discharge from hospital.

ESPID-0464
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

RISK PREDICTION MODELS FOR THE DIAGNOSIS OF SERIOUS BACTERIAL INFECTIONS IN THE CHILDREN'S EMERGENCY DEPARTMENT, AND COMPARISON USING NET RECLASSIFICATION IMPROVEMENT

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Background
Improving the early recognition of serious bacterial infections (SBI) in the children's Emergency Department (ED) is a clinical priority while supporting clinicians to confidently rule out SBI may reduce unnecessary admissions and antibiotic use.

Methods

A prospective study of clinical and biomarker variables for the diagnosis of SBI in febrile children presenting to the Alder Hey Children's Hospital ED. A diagnostic model was derived using multinomial logistic regression, and internally validated. External validation of a previously published model was undertaken followed by net reclassification improvement (NRI) using a model extended with biomarkers Procalcitonin and Resistin.

Results

1101 children were studied, and 264 (24.0%) had SBI. Median age was 2.4 years. A multinomial logistic regression model discriminated well between pneumonia and no SBI (C statistic 0.88), and between other SBIs and no SBI(C statistic 0.82). External validation of a previously published model revealed similar performance

characteristics (C statistic 0.85 and 0.76 for pneumonia and other SBIs respectively). The addition of Procalcitonin and Resistin resulted in improved classification of both pneumonia and other SBIs. There was a significant improvement in the classification of non-events (NRI 1.4% and 9.2%, for pneumonia and other SBIs respectively).

Conclusions

A diagnostic model combining clinical and biomarker variables discriminated well between pneumonia, other SBIs and no SBI in febrile children of all ages in the ED. Extending an existing model using a combination of biomarkers had particular value in ruling out SBI.

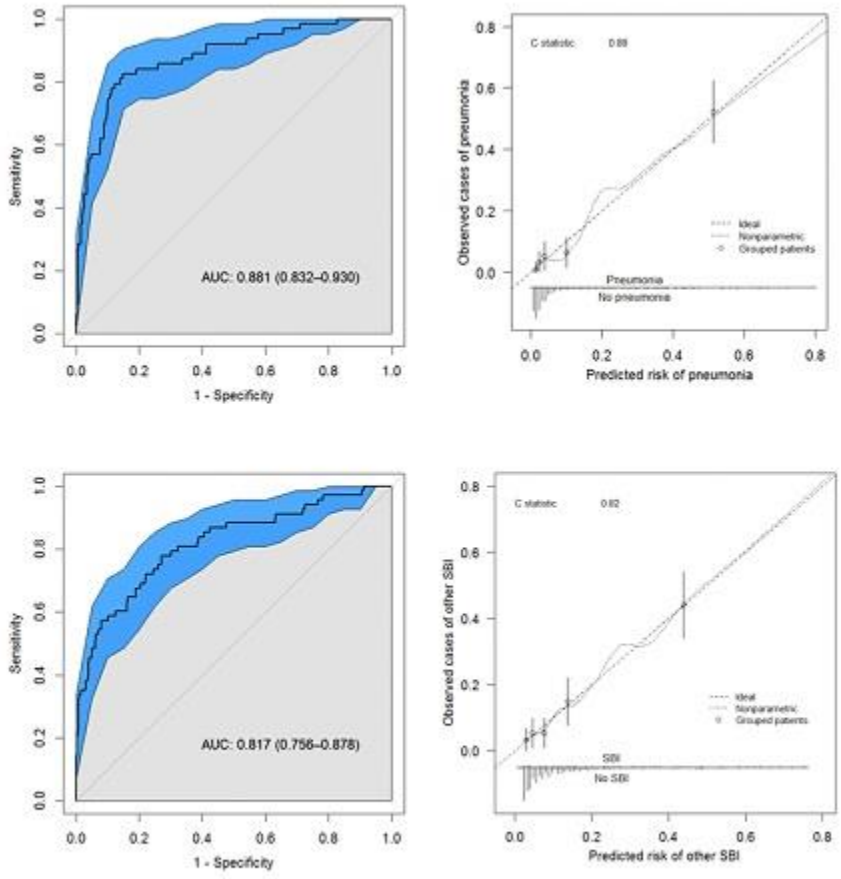

Figure: ROC curve (left) and calibration plot (right) for the derived multivariable model for the diagnosis of pneumonia (top), and other SBIs (bottom).

		Model with biomarkers (PCT,RTN)	
		Model <=10%	Model >10%
Pneumonia =1 (n=108)	Model <=10%	14	5
	Model >10%	2	87
Pneumonia =0	Model <=10%	666	6
	Model >10%	18	147
Other SBI =1 (n=156)	Model <=10%	18	3
	Model >10%	10	125
Other SBI =0	Model <=10%	484	2
	Model >10%	79	272

Table 1: Reclassification table comparing a previously published model with the model extended by the inclusion of Procalcitonin (PCT) and Resistin (RTN), at a risk threshold of 10%.

Pneumonia	%	LCI	UCI
NRI	4.2	-0.7	9.1
NRI for events	2.8	-2.0	7.6
NRI for non-events	1.4	0.3	2.6
Other SBI			
NRI	4.7	-0.2	9.6
NRI for events	-4.5	-9.0	0.0
NRI for non-events	9.2	7.2	11.2

Table 2: Summary NRI at a risk threshold of 10%.

ESPID-0989
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

CHAMPAGNE, ROSÉ, OR A BLOODY MARY? – A PROSPECTIVE AUDIT OF LUMBAR PUNCTURES IN A TERTIARY NEONATAL UNIT

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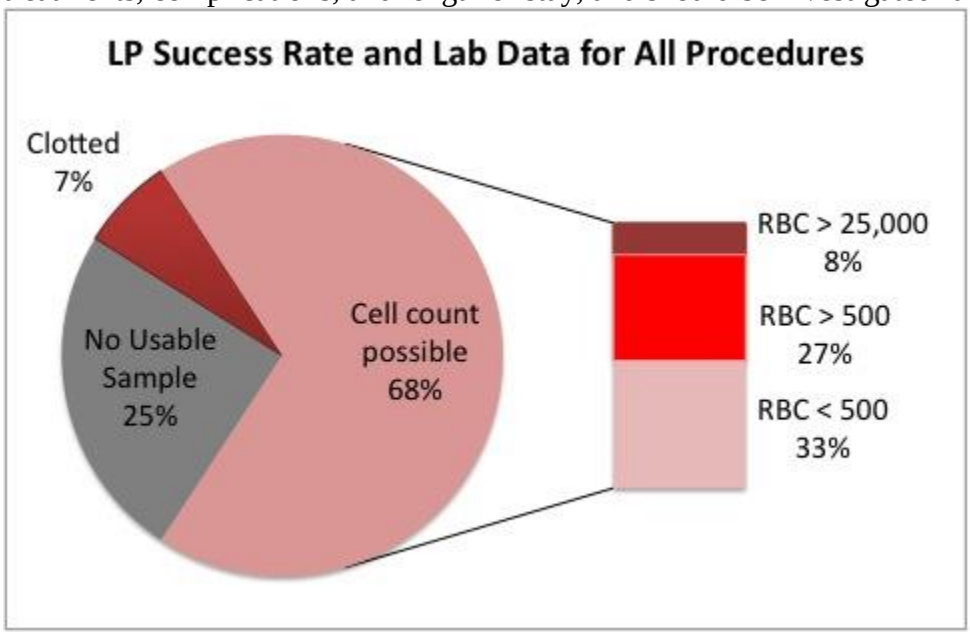
Background and Aims: Published success rates for neonatal lumbar puncture (LP) are 48 - 60%, and lower in preterm babies. We audited our LP practice in 2014, following the introduction of guidelines for early-onset infection from the National Institute for Health and Care Excellence (NICE).

Methods: Demographic, procedural and laboratory data for all LPs (neonatal and postnatal wards) were collected prospectively over 54 days. Medical notes were reviewed for additional LPs and subsequent management/complications.

Results: 47 patients (31% preterm) had 52 separate indications for LP, requiring 73 procedures, each involving up to 5 attempts at LP. Compared with audit data from 2010 (pre-NICE guidance), the estimated number of LPs per year had increased by 27%. 81% of indications were raised CRP (> 25 mg/L), and for 92%, antibiotics were commenced pre-LP. 25% of indications required >1 procedure, and 48% of procedures involved >1 attempt. The overall rate of non-traumatic LP (<500/μl RBC) was 33%. During first procedures, an interpretable sample was obtained for 55% of indications, rising to 82% after multiple procedures. Babies without an interpretable sample were usually treated cautiously with 14-21 days of antibiotics. For half of these babies, this necessitated an additional length of stay (median 9 days).

Conclusions: LP success rates were comparable with those previously published. Methods to enhance LP success could potentially reduce unnecessary procedures,

treatments, complications, and length of stay, and should be investigated further.



ESPID-0901
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

LIPOCALIN 2 IS A SENSITIVE AND SPECIFIC MARKER OF SERIOUS BACTERIAL INFECTION IN CHILDREN

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Background

Bacterial infection is the leading cause of death in children globally. Clinical algorithms to identify children who are likely to benefit from antimicrobial treatment remain suboptimal. Biomarkers that accurately identify serious bacterial infection (SBI) could improve diagnosis and management.

Methods

We evaluated Lipocalin 2 (LCN2) and neutrophil collagenase (MMP-8) as candidate biomarkers in 40 healthy controls, and 151 febrile children categorised after intensive investigation as having confirmed, probable or possible SBI, or viral infection. The diagnostic performance of LCN2 and MMP-8 to predict SBI was estimated by the area under the receiver operating characteristic curve (AUROC) and compared to the performance of C-reactive protein (CRP).

Results

Concentrations of plasma LCN2 and MMP-8 were lowest in controls, and increased stepwise with likelihood of SBI. The AUROC (95% CI) for LCN2, MMP8 and CRP to predict SBI was 0.88 (0.82-0.94); 0.80 (0.72-0.87) and 0.88 (0.84-0.94), respectively. The diagnostic performance of LCN2 in combination with CRP was significantly superior to either marker alone: AUROC 0.92 (95% CI: 0.88-0.96). This was not influenced by renal impairment.

Conclusions

The potential for LCN2 to improve rapid, early identification of children with SBI could benefit clinical decision-making for children presenting with febrile illness, and improve antibiotic coverage in the easily missed minority of children with an SBI. The potential for LCN2 to improve antibiotic management decisions in febrile children should be evaluated in clinical trials.

ESPID-0547
Short Oral Presentation Session 11- DIAGNOSTIC TOOLS

MENINGOCOCCAL ANTIGEN TYPING SYSTEM (MATS) ESTIMATES HIGH PREDICTED 4CMENB STRAIN COVERAGE IN 15 COUNTRIES.

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Background and aims: 4CMenB is a multicomponent vaccine indicated for immunization against *Neisseria meningitidis* serogroup B (MenB) invasive disease. To date (January 2015), 4CMenB is approved for use in the European Union, Canada, Australia, Uruguay, Brazil and Chile. A worldwide assessment of 4CMenB strain coverage is important to predict vaccination impact on the disease burden. The

Meningococcal Antigen Typing System (MATS) was specifically developed to fulfil this need.

Methods: A total of 3007 epidemiologically representative MenB isolates from 15 countries were selected by the respective public-health institutes (Figure 1). MATS data were generated for all the isolates while molecular typing was performed for a subset thereof (2679 and 2571 isolates with available sequence type and 4CMenB antigen molecular typing information, respectively).

Results: Clonal Complex (CC) 41/44, CC32 and CC269 were the most prevalent clones. MATS estimate of coverage by country ranged from 66% to 91% (Figure 1). Overall, it was predicted that 36%, 31% and 11% of strains would be covered by one (mostly factor H binding protein (fHbp) or Neisseria heparin binding antigen (NHBA)), two (mostly fHbp+NHBA) or three (mostly PorA+fHbp+NHBA) 4CMenB antigens, respectively. Strains expressing fHbp and NHBA variants identical or very similar to the antigen variants of 4CMenB were mostly predicted to be covered by MATS.

Conclusions: Comparison of these results with post-launch data will provide an important tool to assess changes in vaccine strain coverage, and help evaluate the impact and effectiveness of 4CMenB.

Country	Years	No of isolates	Predicted coverage [95% CI]
United States	2000 to 2008	442	91% [72, 96]
Greece	2008 to 2010	52	88% [60, 96]
Italy	July 2007 to June 2008	54	87% [70, 93]
Norway	July 2007 to June 2008	41	85% [76, 98]
France	July 2007 to June 2008	200	85% [69, 93]
Poland	Jan 2010 to Dec 2011	196	84% [79, 91]
Germany	July 2007 to June 2008	222	82% [69, 92]
Brazil	2010	99	81% [71, 95]
Australia	2007 to 2011	373	76% [63, 87]
Czech Republic	2007 to 2010	108	74% [58, 87]
E&W	July 2007 to June 2008	535	73% [57, 87]
Spain	2008 to 2010	300	69% [48, 85]
Ireland	July 2009 to June 2013	111	68% [61, 83]
Austria	July 2008 to June 2011	118	68% [56, 73]
Canada	2006 to 2009	157	66% [43, 78]

ESPID-0759
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

TEN YEARS OF NEONATAL LISTERIOSIS IN THE UK

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Background and aims: Listeriosis is the third most common cause of early-onset neonatal infection in the UK, causing significant morbidity and mortality.

Methods: Listeriosis was identified prospectively from 25 neonatal units in the UK participating in the neonatal infection surveillance network (neonIN) between 2004 and 2014.

Results: 20 cases were identified with a median gestational-age of 33 weeks (27-38 weeks) and a median birth-weight of 1896g (700-3210g). The incidence was 3.3 per 100,000 live births.

Neonatal listeriosis was confirmed in 18 cases (17 blood cultures and 1 cerebrospinal fluid) and presumed in 2 cases (positive maternal cultures). 19 infants presented within 24 hours of age whereas 1 infant presented at 10 days of age.

18 (90%) mothers were symptomatic, 7 (45%) had an antenatal microbiological diagnosis. 19 (95%) infants were symptomatic.

Maternal/labour complications	**18 mothers**
Meconium-stained liquor	13 (72%)
Abnormal cardiotocography	12 (67%)
Reduced foetal movements	8 (44%)
Pyrexia	5 (28%)
Pre-term labour	6 (33%)
Neonatal signs	**19 infants**
Respiratory distress	18 (95%)
Lethargy	7 (37%)
Rash	4 (21%)

2/6 women from the data available received a penicillin pre-delivery. 18/19 infants with early-onset infection received a penicillin a median of 1 hour (1-28 hours) post-birth. 18/20 infants completed the treatment with Amoxicillin. 5 (25%) infants died and 5 had neurodevelopmental impairment.

Conclusions: The majority of infected babies were treated promptly with appropriate antibiotics. Over half of infected women were symptomatic but not treated prior to delivery, suggesting that opportunities still exist for early recognition and treatment in pregnancy.

ESPID-0659
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

PERINATAL HCV TRANSMISSION RATE IN HIV/HCV COINFECTED WOMEN

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Background: It is estimated that about 10% of children from HIV/HCV coinfected pregnant women (CPW) are finally HCV-infected. Maternal HIV coinfection is the most important risk factor associated to HCV transmission. However, HCV perinatal transmission rates on the HAART era are not well known.

Methods: Prospective study within the Madrid cohort of HIV-infected pregnant women (2000-2012). CPW were included in the study and epidemiological and clinical variables were analyzed. The rate of HCV transmission was determined.

Results: Among all patients registered in the Madrid cohort there were 348 (31.8%) CPW. Data from 264 (76%) paired coinfected mother and children were analyzed. Most (83.7%) patients were Spanish and 58.3% of infections in CPW were caused by parenteral drug use. Although 79.5% of women were on antiretroviral treatment during pregnancy, only 64.2% were HIV suppressed at the time of delivery and 52.7% had a CD4 count >500cell/mm^3. HCV genotype (G) 1 was the most common (62.5%), followed by G3 (17.5%), G4 (15%) and G2 (5%). Cesarean section was performed in 68.6% of CPW and only 9/83 (10.8%) of vaginal deliveries had known RNA-positive HCV viremia. HCV was transmitted to 4.9% (95% CI, 2-9.8) of the perinatally exposed children followed-up up to over 18 months of age, the HIV transmission rate was 1.2% (95% CI, 0.41-3.5) and no infants were coinfected.

Conclusions: The HCV transmission rate in the studied cohort appeared to be lo low compared to that found in the literature. HCV transmission from CPW might be decreasing in the HAART era.

ESPID-0746
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

FEASIBILITY OF LARGE RANDOMISED CONTROLLED TRIALS (RCT) IN EUROPEAN NEONATAL INTENSIVE CARE UNITS (NICU): THE NEOMERO1 TRIAL

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Background: Late onset sepsis (LOS) is the most commonly treated disease in neonates and young infants. However, RCT on its treatment are rare and date back over 20 years. Furthermore, studies were mostly single centre or single country trials evaluating antibiotics not in current use. One of the major issues for such studies is their feasibility.

We aimed to describe the feasibility issues in NeoMero 1 - an open label RCT of meropenem vs predefined standard of care in LOS.

Results: NeoMero1 was the largest multicentre trial in LOS conducted between 01.09.2012 to 31.12.2014 and involving 6 countries with 18 actively recruiting sites. The median forecasted number of patients per site was 16 (IQR 7; 40). A total of 272 patients, equally distributed between treatment arms, were recruited. More than 95% of enrolled patients completed all visits and contributed to unique biobank of PK (blood and CSF), microbiological (blood and stool) and genetic samples. The median percentage of recruited vs forecasted patients was 30% (IQR 20%; 75%). Reasons for non-recruitment were enrolment criteria not met and informed consent not given (both 32%), and the need for treatment with meropenem (12%). The discrepancy between forecasted and recruited patients could be due to the changing epidemiology of LOS, strict inclusion criteria, and limited experience in predicting patient's numbers by individual sites.

Conclusion: We have performed a successful multinational RCT in LOS in European NICUs. Networking and good cooperation between paediatric infectious diseases specialists and neonatologists is essential for similar studies in the future.

ESPID-0632
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

WHAT IS THE BEST AUC/MIC RATIO FOR VANCOMYCIN (VAN) IN PREMATURE NEONATES?

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Background and aims: Van AUC/MIC≥400 has been associated with treatment success in adult *Staphylococcus aureus* pneumonia. In neonate true Van AUC value and AUC/MIC association with *coagulase negative staphylococci* (CoNS) sepsis are not known. We simulated doses for 80% and 90% probability of target attainment (PTA) of AUC/MIC>400 and AUC/MIC>300 and correlated these with recommended doses and clinical outcome.

Methods: Neonates with Van Ctroughs performed for therapeutic drug monitoring (TDM) were included. Treatment and bacteriological outcome were collected retrospectively. A 1000-subject Monte Carlo simulation (MCS) was performed using Anderson (Anderson et al 2006) model and TDM results to estimate the PTA of AUC/MIC>300 and AUC/MIC>400.

Results: In total 186 TDM points in 76 neonates (mean±SD PMA 30.9±4.8 weeks, current weight 1316.8±843.1 gram) were included; 57 neonates had Gram-positive sepsis; 95% caused by CoNS with median (range) MIC of 1µg/mL (0.19-3). 39 /57 had successful outcome. Using Anderson model lead to higher clearance and lower AUC compared to the TDM model. With currently recommended doses the achievement of PTA AUC/MIC >400 or AUC/MIC >300 was 40% and 60%, respectively. Simulated doses required for 80% PTA of AUC/MIC >400 resulted in Ctrough values ≥14 mg/L for neonatal CoNS Van MIC distribution. AUC/MIC value was not associated with outcome.

Conclusions: Currently recommended Van dosing may be suboptimal in achieving the target of AUC/MIC>400 in neonates. Prospective clinical and experimental studies are needed to define appropriate PKPD target and doses for Van treatment of neonatal CoNS sepsis.

ESPID-0862
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

WHAT IS THE SIGNIFICANCE OF COAGULASE NEGATIVE STAPHYLOCOCCI IN THE BLOOD CULTURES OF NEONATES IN A NEONATAL INTENSIVE CARE UNIT?

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BACKGROUND AND AIMS:

Coagulase negative Staphylococci (CoNS) are the commonest organisms recovered in late-onset sepsis in neonatal intensive care units (Stoll, *et al* 2002). Determining the clinical significance of CoNS bacteraemias can be challenging as CoNS are normal skin commensals. We recorded patient demographics, sub-species distribution and quantitative susceptibilities of CoNS isolates to ascertain pathogenicity.

METHODS:

Infants with blood cultures positive for CoNS were identified between January 2012 and January 2013. True bacteraemia was defined as a blood culture positive for CoNS, in an infant treated for ≥ 5 days with intravenous antibiotics, in the presence of ≥3 clinical manifestations (definition supported by published clinical tools for diagnosing neonatal sepsis)(Modi, *et al* 2009, Vergnano, *et al* 2011). Isolates were speciated by mass spectrometry, and minimum inhibitory concentration (MIC) to vancomycin determined.

RESULTS:

76 CoNS blood culture isolates were collected from 59 patients. No significant difference was found between *Staphylococcus epidermidis* and non-*Staphylococcus epidermidis* isolates in those cases defined as true bacteraemia. Increasing MIC and gestational age showed no relationship towards true bacteraemia.

Covariate		True bacteraemia	Contaminant	OR	*p*-value
	<28/40	11	9	1.00	0.4

Gestational age at time of blood draw	28/40 – 31^{+6}/40	8	17	0.38	
	32/40 – 36^{+6}/40	6	6	0.81	
	≥ 37/40	7	12	0.48	
MIC	<1.5	12	17	1.00	0.9
	1.5 - 4	20	27	1.09	
Species	*S. epidermidis*	15	23	1.00	0.6

CONCLUSIONS:

Sub-speciation between *Staphylococcus epidermidis* and non-*Staphylococcus epidermidis* did not correlate with increased propensity for true bacteraemia in neonates.

ESPID-0984
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

KLEBSIELLA HOSPITAL-ACQUIRED INFECTION (HAI) IN NEONATES IN EUROPE-DATA FROM THE NEONIN SURVEILLANCE NETWORK (NEONIN:HTTP://WWW.NEONIN.ORG.UK)

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On behalf of the Neonatal Infection Surveillance Network (neonIN)

Background & Aims: The emergence and spread of resistance in *Klebsiella* HAI is complicating the treatment of serious nosocomial infections within neonatal units (NNUs). We aim to describe the epidemiology of invasive *Klebsiella* infections across European countries participating in a neonatal infection surveillance network.

Methods: neonIN is an international web-based surveillance database for culture proven neonatal infections. *Klebsiella* cases between 2004 and 2014 were extracted. Late-onset sepsis (LOS) was defined as occurring after 48-hours from birth. Repeated growth of the same organism was considered the same episode if occurring within 7-days.

Results: There were 158 episodes from 33 NNUs. The incidence and prevalence by country is shown in table-1, while details of the pathogens and the demographics

appear in table-2. Overall, *K. pneumoniae* was the commonest subspecies (59, 37.3%) followed by *K. oxytoca* (55, 34.8%). Early-onset sepsis was rare (3 *K. pneumoniae episodes*). *Klebsiella* was isolated together with other pathogens in 15% (24) of cultures. *K. aerogenes* infection occurred in more premature neonates (median 25 vs 28 weeks gestation-age, p=0.05). Resistance to 3rd generation cephalosporins (11/88, 12.5%) and aminoglycosides (21/126, 16.7%) was detected while all tested isolates were susceptible to quinolones (62/62, 100%) and carbapenems (67/67, 100%).

Table 1	UK	Greece	Estonia	p-value
Number of Units	20	7	5	-
Total number of infection-episodes (IE)	3050	136	163	-
Incidence of IE (NNU admissions)	39.2/1000	63/1000	50.3/1000	<0.001
Incidence of GNS (NNU admissions)	7.3/1000	26.0/1000	13.3/1000	<0.001
Incidence of *Klebsiella* spp (NNU admissions)	1.6/1000	9.3/1000	4.0/1000	<0.001

IE: infection episodes, GNS: Gram-negative sepsis

Table 2	UK n=125	Greece n=20	Estonia n=13	p-value
Predominant *Klebsiella* spp n (%)	*K. pneumoniae* 43 (34.4%)	*K.pneumoniae* 12 (60.0%)	*K.oxytoca* 9 (69.2%)	-
Sex (male)	65 (53%)	14 (70%)	5 (38.5%)	0.173
Gestational Age at birth (weeks)	26 (25 – 30)	33.5 (28-36.5)	29 (24 – 35)	<0.001
Birth weight (g)	821 (666 – 1140)	1730 (1000-2230)	1480 (846 – 2740)	<0.001
PNA (days)	34 (16 – 69)	23.5 (9.5– 70.5)	15 (10– 50)	0.257
CRPmax (mg/dL)	108 (53-160)	69 (11-147)	89 (51-136)	0.16
CVC in situ n (%)	77 (61.6%)	5 (25%)	3 (23.1%)	<0.001
Treated for meningitis	13 (10.4%)	1 (5%)	1 (7.5%)	0.920

Median (IQR)
PNA: post-natal age at the time of infection, CRPmax (mg/dL): maximum CRP within 48 hours of culture taken

Conclusions: *Klebsiella* infections are an important cause of HAI in preterm infants. However the disease burden and epidemiology varies by country; knowledge of local antibiotic susceptibility is therefore required to direct appropriate empiric antibiotic therapy in LOS and to guide effective infection-control measures.

ESPID-0946
Short Oral Presentation Session 12- CONGENITAL AND PERINATAL INFECTIONS

INCREASING MIC IS ASSOCIATED WITH HIGHER MORTALITY IN GENTAMICIN TREATED NEONATAL GRAM NEGATIVE INFECTIONS

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Introduction and aims

Gram negative (GN) infections in neonates are associated with high mortality and morbidity. Early treatment with appropriate antibiotics is vital and gentamicin is the most frequently used antibiotic on neonatal units (NNU). Antimicrobial breakpoints are predominantly determined by adult data and the relationship between minimum inhibitory concentrations (MIC) and outcome in neonates is unclear.

We aimed to determine the antibiotic susceptibility of isolates causing neonatal infections and relate this to clinical outcomes

Methods

Bacterial isolates from invasive GN infections from 7 UK NNUs were centralised and MICs for 8 antibiotics plus ESBL status were determined by E-Test. EUCAST breakpoints were applied. MIC was correlated with outcome using multivariable regression analysis.

Results

128 episodes from 121 patients were analysed. The median birth gestation and median postnatal age was 27 weeks (IQR 24.9-32.0) and 18 days (IQR 5-43) respectively. Pathogens included *E.coli* (46%), *Klebsiella sp.* (19%) and *Enterobacter sp.* (17%). 10 day attributable mortality was 17% (21/121) with the highest mortality in *P. aeruginosa* infections (43%).

Increasing gentamicin MIC was associated with increased 10 day attributable mortality in gentamicin treated patients (OR per $\log_e$ increase in MIC: 2.17; 95% CI 1.18-4.01, p=0.013), including in those with 'susceptible' isolates (MIC≤4) (OR per $\log_e$ increase in MIC: 2.93; 95% CI 1.05-8.20, p=0.041).

Conclusion

Neonatal mortality from GN infections remains high and can be related to the gentamicin MIC of the causative pathogen, even for isolates deemed susceptible. Improved knowledge of population-specific MICs may be important for guiding empirical treatment.

Moderated E-Poster Walk Presentations

ESPID-0093
MODERATED E-POSTER WALK 1 - Viral Infections

MIDDLE EAST RESPIRATORY SYNDROME CORONA VIRUS (MERS-COV) INFECTION IN SAUDI CHILDREN DURING CORONA VIRUS EPIDEMIC, MARCH-MAY,2014

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Background and aims:

From March to May 2014, 416 cases of MERS-CoV infection were reported by Command and Control Center of Saudi Ministry of Health (CCC of SMH). The majority of affected patients were adults. Data on the clinical presentation and outcome of pediatric cases were lacking. Therefore, this study was conducted to identify demography, clinical presentation and outcome of MERS-CoV infection in 12 reported pediatric patients.

Methods:

Review of all data of CCC of SMH to extract and analyze demographic characters, clinical presentation and outcome of reported pediatric cases with confirmed MERS-CoV infection.

Results:

A total of 12 pediatric cases with confirmed MERS-CoV were reported. Five cases were from Riyadh, 3 from Jeddah, 3 from Madina, and one case from Mecca. The median age of patients was 12.4 (range: 9 months-17 years). There were 8 males and 4 females. Nine cases were contacts to other adult patients diagnosed with MERS-CoV. Five patients were symptomatic and 7 cases were asymptomatic. All symptomatic patients had comorbidities; 9- month male with nephrotic syndrome admitted to ICU and died, 2-year female with congenital anomalies admitted to ICU and died, 10-year male with traffic accident acquired MERS-CoV in hospital and admitted to ICU, 11-year male with brain tumor acquired infection in hospital and died, and 13-year male with bronchial asthma.

Conclusions:

MERS-CoV infection rate was lower in children than adults. The majority of childhood MERS-CoV infection was secondary infection found during screening contacts of adult patients. Severe symptomatic disease occurred in children with comorbidities.

ESPID-0211
MODERATED E-POSTER WALK 1 - Viral Infections

ENTEROVIRUS INFECTION IN INFANTS

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Background: Enterovirus (EVs) infections are common in infants. They are often found causing mild symptoms but they can also cause severe disease. There are more than 100 recognized types, classified in four species: from A to D. The information regarding to types and its relation with clinical data is very scarce.

Methods: This study includes < 3 m-old children with fever without source attended from March 2010 to December 2012 in an Emergency Department of a pediatric hospital (Hospital Sant Joan de Déu, Barcelona) in whom an EV infection was confirmed by real-time PCR in blood or cerebrospinal-fluid. Clinical and epidemiological data was prospectively collected.

Results: 699 children were tested for EV infection and it was confirmed in 195 (27.8%). In 152 of 195 (77.9%) patients, EVs could be typed. The most common type was Echovirus-5 (E-5;32, 21.1%), followed by Echovirus-11 (E-11; 18, 11.8%), Echovirus-21 and 25 (E-21, EC-25;11 each one, 7.2%) and Coxackievirus-B4 (CV-B4;6, 6.6%). 33/64 (52%) patients had meningitis. CV-B4 tended to cause meningitis more often than other types ($p=0.07$). Most of the patients had low-grade fever, but E-21 caused high-grade fever more often ($p<0.05$). E-5 was associated with exanthema and the shortest hospital stay ($p<0.05$). None of them presented an association with bacterial coinfection.

Conclusions: In our setting, the most common EV types causing infection in < 3 m-old children were Echovirus-5 and Echovirus-11. Echovirus-21 was associated with high-grade fever. Coxsackievirus-B4 tended to cause meningitis more often than other types and Echovirus-5 often appeared with exanthema.

ESPID-0531
MODERATED E-POSTER WALK 1 - Viral Infections

IMPORTANCE OF VIRAL DIAGNOSIS IN SEVERE LOWER RESPIRATORY TRACT INFECTIONS IN PRESCHOOL CHILDREN AND INFANTS

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Introduction: Lower respiratory tract infection (LRTI) is a major cause of morbidity and viruses are encountered in more than 60% of the cases. We aim to determine the impact of viral detections on hospitalization cost and use of antibiotics in children with severe LRTI.
Methods: We did a retrospective study from 2011 to 2014. We selected children from 0-5 years. We compared two groups: children with specified viral infection and children with unspecified viral infection.
Results: We recorded 39969 admissions in our clinic with 18,6% being diagnosed as LRTI. From this group 48% had the diagnosis of viral infection. Only 2% (n=67) had a viral determination. The etiology was: VSR 70%, Influenza 11%, Parainfluenzae 4,5%, HMPV, Rhinovirus, Bocavirus, Adenovirus - 3%. The mean hospitalization was 6 days for the first group and 5 days for the second. The hospitalization cost was 20 % higher in the first group. For both groups 90% of the children received an antibiotic. The most used group of antimicrobials for both groups was: Cephalosporins 47%, followed by Aminopenicillins 44%.
Conclusion: In our study the viral diagnosis haven`t shortened the length of stay or influenced antibiotic treatment, on the contrary in the viral specified group the cost was higher. Our study suggests that if the clinician attitude towards therapy doesn`t change, the use of viral determination in clinical practice is limited.
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ESPID-0593
MODERATED E-POSTER WALK 1 - Viral Infections

GENITAL HPV INFECTION AND ASSOCIATED RISK FACTORS IN PREPUBERTAL CHILDREN AND ADOLESCENTS

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Background and aims: The aim of the study was to compare the prevalence of HPV genital infection among prepubertal children, sexually active and inactive adolescents.

Methods: Vaginal or/and cervical specimens were obtained from 95 girls aged 2-21 years; 38 sexually active adolescents (group A), 28 sexually inactive adolescents (group B) and 29 prepubertal children (group C) and tested for HPV infection with a multiplex molecular assay and for cytological abnormalities.

Results: HPV genital infection was detected in 38.9% of participants; 52.6% of adolescents in group A, 25% in group B and 34.5% in group C. Multiple HPV infection was detected in 26.3%, 3.5% and 13.8% of groups A, B and C respectively. High- and low-risk HPV strains were detected in 31.5% and 8.4% of participants respectively; high-risk HPV genotypes in 47.4% of group A, 25% of group B and 24.1% of group C. Sexual activity was associated with increased risk for genital HPV infection (OR:2.39, 95%CI:1.07-5.33) and especially from high risk types (OR:3.41, 95%CI:1.19-9.78). Adolescents with low and high grade squamous intraepithelial lesions were found to be infected with high risk HPV types. Family history of skin HPV infection was associated with genital HPV in sexually active adolescents (OR:2.01, 95%CI:1.17-3.46).

Conclusions: There is a high prevalence of genital low- and high- risk HPV infections in girls prior to sexual activity indicating a significant non-sexual way of transmission. Timeline and target population of HPV vaccination may need to be reappraised, in view of nonsexual transmission of HPV so early in childhood.

ESPID-0611
MODERATED E-POSTER WALK 1 - Viral Infections

CHARACTERISTICS OF CHILDREN WITH KAWASAKI DISEASE REQUIRING INTENSIVE CARE: A CASE-CONTROL STUDY IN A TAIWAN TERTIARY CARE CHILDREN'S HOSPITAL

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Background and Aims

Kawasaki disease (KD) is usually self-limiting, but some patients developed serious complications requiring intensive care. We aim to ascertain the clinical presentations and outcomes of these patients.

Methods

From October 2004 to October 2014, children with KD who had stayed in pediatric intensive care units (ICU) for acute stage treatment were defined as case patients; for each case, three age/gender-matched patients, if identified, with KD without ICU stay were selected as control subjects. Clinical data were retrospectively collected and analyzed.

Results

Among 1065 KD patients we identified 28 cases and 79 controls. ICU patients had longer fever duration (9.0 vs. 6.9 days) and tended to have a leukocyte count > 20000/mm^3, hemoglobin level < 10 g/dL, platelet count < 150000/mm^3, band cell percentage > 10%, peak serum C-reactive protein levels > 200 mg/L, serum albumin value < 3 g/dL, and to present multi-organ systems involvement. Time from symptom onset to the diagnosis of KD was longer (8.4 vs. 6.8 days) in ICU patients. Shock (46%, n=13) was the most common reason for ICU admission. ICU patients were more likely to need a second dose of intravenous immunoglobulin (IVIG) or steroid, and to develop coronary artery lesions at acute stage. No in-hospital mortality was observed.

Conclusions

Patients with KD requiring ICU care tend to have multi-organ involvement, have uncommon presentations and clinical course with a late diagnosis, and have an IVIG-refractory disease.

ESPID-0815
MODERATED E-POSTER WALK 1 - Viral Infections

CLINICAL OUTCOMES IN CHILDREN WITH HERPES SIMPLEX VIRUS ENCEPHALITIS RECEIVING STEROID THERAPY

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Clinical outcomes in children with herpes simplex encephalitis receiving steroid therapy

Background and aims: We aimed to compare the prognosis of pediatric herpes simplex virus (HSV) encephalitis with or without steroid therapy.

Methods: We retrospectively screened our hospital archive of 2009 to 2014 for patients diagnosed as HSV encephalitis based on clinical, neuroradiological features, and cerebrospinal fluid HSV polymerase chain reaction. Clinical outcomes were noted and compared in patients who received adjuvant steroid therapy with those who did not.

Results: Five patients (1 male, 4 females; aged 1-10 years) were included. Fever, focal seizures and encephalopathy were present in all patients. Overall symptom duration before hospital admission was ≤5 days. All patients received acyclovir treatment for at least 14 days. Two of them (10-year-old, and 18-month-old) received steroid therapy early during the disease, while three patients did not receive it. Follow-up duration was 2 months-5 years. All patients had neuroradiological sequelae of encephalitis. Cognitive, motor function and seizure frequency were better in patients who received steroid therapy.

Conclusion: Steroid is not used routinely in HSV encephalitis, but there are a few case reports with favorable outcomes, where steroids were used for deteriorating disease. Adjuvant steroid therapy seems effective in decreasing morbidity in pediatric HSV encephalitis. Prospective studies are needed to confirm case based observations of steroid efficacy in HSV encephalitis.

ESPID-0853
MODERATED E-POSTER WALK 1 - Viral Infections

HUMAN BOCAVIRUS (HBOV) AND ITS ROLE IN ACUTE GASTROENTERITIS (AG): FOLLOW-UP STUDY IN HEALTHY COHORT OF CHILDREN IN GIPUZKOA.

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Background: The causative role of HBoV in AG remains uncertain. Most studies assessed its prevalence in the absence of defined healthy control. We investigated the prevalence of HBoV in one cohort of healthy children followed since their birth until 2 years of age.

Methods: Prospective follow–up study from January2011-December2013. 159 healthy full-term newborn were included. Every 4 month, two pediatricians visited the children of whom one stool sample (SS) was taken.Besides, one extra SS was collected if the chidren had AG. Common enteric bacteria and viruses were examined using coprocultive, ELISA and PCR.

Results: 98 children fullfilled the follow-up with 6 visits each one. We obtained 780 SS from asymptomatic children and 148 samples from children with AG. HBoV was detected in 62 samples (6,7%) and 18/62 (29%) of them were children with symptoms of AG (average age 9,9±1,9months).The percentage of HBoV infections was significantly higher in children with AG than in healthy subjects (12,2%vs.5,6%;p<0,005). Many [12/18(66,6%)] of cases occurred during November-February. 8/18 children were coinfected with either rotavirus (5/18) and campylobacter (3/18). Coinfections were significantly higher in patients with AG (44,4%vs.9,5%;p<0,0039).The clinical course was autolimited and only one child required hospitalization for dehydration. The specie more frecuently detected was the HBoV1.

Conclusion: The majority of children with HBoV and AG had uncomplicated illness and were younger than 1year. Despite the higher prevalence of HBoV in stool samples from children with AG, our study cannot support a causative role of HBoV in AG because of the high percentage of coinfections.

ESPID-0995
MODERATED E-POSTER WALK 1 - Viral Infections

RESPIRATORY SYNCYTIAL VIRUS (RSV) CIRCULATION IN FIVE CONSECUTIVE YEARS IN ITALY

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Background and aims: Knowledge of RSV types and genotypes is important for the development of effective preventive and therapeutic measures. Aim of this study was to evaluate RSV circulation in consecutive years and correlate genotypes with clinical manifestations.

Methods: Nasopharyngeal swabs positive for RSV collected in children with respiratory infections during the winter periods from 2009-2010 to 2013-2014 were evaluated by means of PCR and sequencing methods in order to identify A and B RSV types and genotypes.

Results: A total of 165 swabs were evaluated: RSV-A predominated (131 cases) in all the seasons with the exception of 2010-2011. Only two different A genotypes were identified (A/NA1, 62 cases, and A/ON1, 69 cases). A/NA1 was identified in the first three study periods, but it was replaced by A/ON1 since 2012-2013. Among B strains, genotype BA9 (26 cases) and BA10 (8 cases) were detected. The first was identified in all the seasons, whereas BA10 only desultorily. No difference in virulence between A and B types was found. Genotype A/ON1 was significantly less frequently associated with lower respiratory tract involvement than A/NA1 ($p<0.05$), whereas no difference in virulence between the two different B genotypes was evidenced.

Conclusions: Different RSV strains can be temporary predominant and are frequently replaced by other genotypes. The recently emerged A/ON1 strain seems to be less virulent than the previously dominating A strains. These data highlight the need for the periodical evaluation of RSV circulation and genetic variations in order to develop new preventive and therapeutic measures.

ESPID-0303
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

LONG-TERM EFFECT OF EDUCATION ON PARENTS' INFORMATION, MOTIVATION AND BEHAVIORAL SKILLS FOR FEVER MANAGEMENT

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Background and Aims: Parents are often anxious when dealing with a febrile child and may lack the knowledge to determine the appropriate interventions. Although educational interventions for parents of febrile children have been examined, few have evaluated the comprehensive elements of parents' knowledge, attitudes, skills, and social influence of fever management. This study aims to evaluate the effects of aparental Fever-Education program based on Information-Motivation-Behavioral Skills Model.

Methods: A pre-post test experimental design was conducted. Parents of 3-month to 6-year old febrile children who visited a pediatric clinic were randomly assigned to face-to-face (FF, n=67) or telephone-counseling (TC, n=66) groups. Parents of the FF group received a face-to-face fever-education with a brochure during the clinic visit, while TC group received telephone fever-education after completing the 3-day questionnaire. Parental knowledge, attitude, social norms, skills and self-efficacy for fever management were evaluated by a 23-item Parental Fever Management Scale (PFMS) at baseline, 3-day, and 6-month after the clinic visit.

Result: At 3 days, the FF group showed significant increases in all PFMS scores (p

Conclusions: A structured Fever-Education program significantly improved parents' knowledge and behavioral skills. Face-to-face education is preferred, but telephone-counseling with brochure was effective. Further studies would determine whether these measures change behavior under the strong social norms.

ESPID-0316
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

ASSESSING VACCINE ATTITUDES AND BELIEFS AMONG MEDICAL STUDENTS IN UKRAINE: FINDINGS FROM A SURVEY CONDUCTED AT BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

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BACKGROUND/AIMS: Ukraine has the lowest immunization rates of any European country. Potential reasons for low immunization rates include physician inadequacy in advocating for vaccination, vaccine shortages, and public mistrust of vaccinations. This study sought to determine beliefs and fund of knowledge about vaccines and vaccinations in medical students at Bogomolets National Medical University, one of the premier medical educational institutions in Ukraine.

METHODS: We created a 30-question survey, which was administered in June 2014 to 463 medical students in their clinical (third through sixth) years at Bogomolets. The written survey contained questions regarding vaccine safety, contraindications, beliefs in the need to vaccinate, and the adequacy of vaccine education at the students' medical school.

RESULTS: Of the surveys distributed, 95% (438) were eligible for analysis. Of the survey respondents, 39% (175) stated they were satisfied with the vaccine education provided by their medical school. We found varying rates of opinions and knowledge regarding vaccines and clinical indications. Only 8% (36) of respondents stated the media describes vaccines as very safe. 86% (371) of respondents felt vaccines are beneficial, and 69% (302) felt the polio vaccine is still necessary. Forty-five% (183) were unsure if vaccines cause autism. Only 4% (7) indicated they would never defer vaccinations in an afebrile child with a cold. Forty-six% (187) were either very hesitant or somewhat hesitant about administering vaccines.

CONCLUSIONS: Medical students participating in the survey are not adequately prepared to improve vaccination rates and decrease the heavy burden of vaccine preventable disease in Ukraine.

ESPID-0509
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

MOLECULAR-GENETIC STUDIES OF PSEUDOMONAS AERUGINOSA ISOLATED IN CYSTIC FIBROSIS

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Pseudomonas aeruginosa plays a key role in the progression of the lung disease in cystic fibrosis (CF).

For the period 2006-2012 a total of 168 strains of *P. aeruginosa* from the sputa of 106 CF patients were studied to determine the frequency distribution of genes encoding virulence factors with pathogenetically different meaning. Using PCR the following genes were amplified: algD (encoding alginate), pilB (fimbrial protein PilB of type IV pili), nan1 (neuraminidase), lasB (elastase LasB), plcH (hemolytic phospholipase C), exoS (exoenzyme S) , exoU (exoenzyme U), exoT (exzoenzyme T) and exoY (exzoenzyme Y). For nan1 amplification nucleotide sequencing was performed.

The genes for algD and plcH were wide spread - 85.7% and 71.4% resp. Frequencies of genes for type III effector proteins with cytotoxic properties: exoS - 52.4%, exoU - 28.6%, exoT - 100% , and exoY - 85.7%. The genes for pilB and nan1 were identified in 9.5% and 38.1% respectively. *P. aeruginosa* strains with nan1 gene were isolated from 32 patients with frequent exacerbations and serious clinical condition.

The pathogenesis of *P. aeruginosa* respiratory infections is defined by an elaborated "arsenal " of cell-associated and extracellular virulence factors. The main factor for the adhesion was the slime composed of alginate. Frequency of nan1-positive strains was moderate and in direct correlation with the prevalence of patients in good clinical condition in this study. Molecular genetic evidence of this gene can be used as an indirect measure for assessing the progression of pulmonary disease in CF patients.

ESPID-0537
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

STATUS OF MEASLES AND RUBELLA ELIMINATION IN THE WHO EUROPEAN REGION

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All 6 WHO Regions have goals for eliminating measles and 3 for rubella. The 53 countries of the European Region have committed to measles and rubella elimination by 2015. The European Regional Verification Commission (RVC) for Measles and Rubella Elimination, an independent panel of experts, conducts annual reviews of reports submitted by national verification committees (NVC) to assess the status of interruption of endemic transmission of these diseases in each country. Essential criteria supporting interruption include absence of endemic transmission in the presence of high-quality surveillance systems and genotyping evidence. By the end of 2014, 50 countries had established a NVC. For 2013, the RVC concluded that measles and rubella endemic transmission had been interrupted in 22 and 24 countries, respectively. However, 7 of these countries had immunity gaps in the population thereby at risk of re-establishing transmission. The elimination status of some countries (8 for measles, 10 for rubella) could not be verified due to poor quality or incomplete data. Additionally, adequate documentation of virus transmission pathways was generally lacking because of missing genomic sequence data and insufficient linking of clinical, epidemiological and laboratory data. Ten countries could not be assessed: 7 countries did not submit reports and 3 countries' reports were deemed inadequate for assessment. The status of measles and rubella elimination in the Region was similar to that in 2012, with regards to number of countries with interrupted endemic transmission and ability to document virus transmission pathways. However, the overall quality and timeliness of reports had improved.

ESPID-0621
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

PREVALENCE OF MATERNALLY TRANSFERRED ANTI-MEASLES ANTIBODIES IN SRI LANKAN INFANTS

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Introduction: Primary protection against measles during early infancy is provided by maternally transferred antibodies and it gradually decreases with time. Measles vaccination schedule was changed in Sri Lanka with the introduction of triple combined vaccine (MMR) in October 2011. Fourteen months after this change, an outbreak of measles was reported in which approximately 40% of the total infected was infants below 1 year of age.

Objectives: Determining sero-prevalence of anti-measles IgG antibodies in newborns and 6-12 months old infants, thereby determining the waning-off of these antibodies.

Method: Blood samples were collected from 6-12 month old infants (n=280) at Medical Officer of Health (MOH) area clinics and from newborns (n =100) at De Soysa Maternity Hospital, Colombo after obtaining ethical clearance and participants' written consent. Sera was separated. Serum antibody levels were measured using commercial ELISA kits following manufacturers' instructions.

Results: ELISA results showed that 97% of newborns were sero-positive whereas only 10.7% of 6-12 month old infants were sero-positive for measles antibodies. There was significant negative correlations between the age of the infants and the antibody levels in 6-12 month old infants ($r= -0.413$; $P<0.0001$). All infants were sero-negative by the completion of nine months of age.

Conclusions: Prevalence of anti-measles antibodies at birth was higher in the newborns but, majority of the infants were unprotected by completion of 9 months with the decay of maternal antibodies and were susceptible for infection. Vaccination timing may have to be reconsidered.

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ESPID-0687
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

EPIDEMIOLOGIC AND ECONOMIC IMPACT OF NON-FUNDED VARICELLA VACCINATION, WITH MEDIUM-HIGH VACCINE COVERAGE, IN SPAIN.

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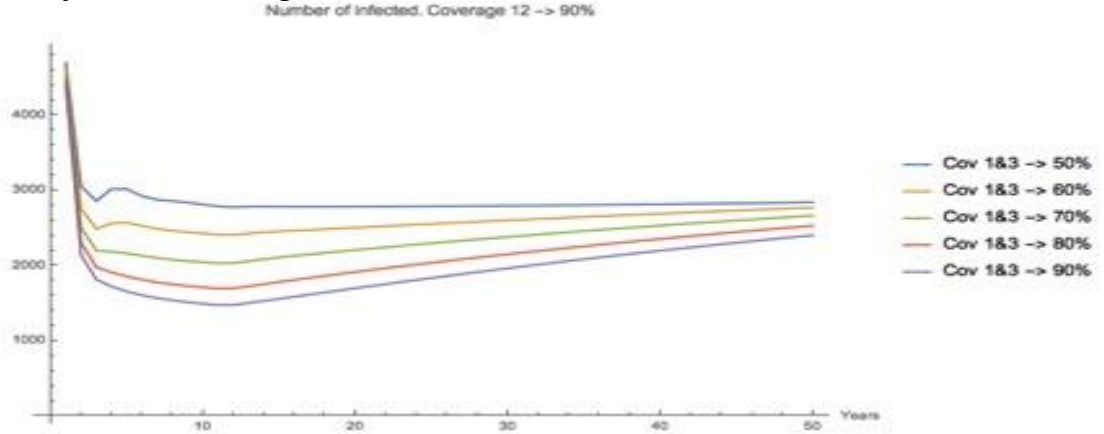
BACKGROUND AND AIMS: Varicella vaccination in Spain is not recommended by Public Health, however the Spanish Paediatric Association does. Vaccine coverage of about 50% in children was achieved. The Spanish Medicine Agency retired the vaccine for the potential shift of the disease to older ages. AIM: To assess the impact of this partial vaccination supported by parents.

METHODS: The transmission of the disease was modelled by a compartmental system consisting of 5 states (susceptible-latent 1st week-latent 2nd week-infected-recovered) and 5 age groups (0-6 months; 6-12 months; 1-3 years; 3-12 years; older than 12). Vaccine program: Two doses at 12 months and 3 years of age, with coverage 50-70%, **and** a Public Health catch up of susceptible at 12-years-old with coverage 90%. Birht cohort of Valencia 47500 children. 2-dose vaccine effectiveness 97%, 1% loss of efficacy from years 15-23.

RESULTS: The catch up program avoided the shift disease to older ages, even with a 1% loss of vaccine effectiveness (figure 1).This program was cost saving from the Public health and the societal perspective, where parents pay for the vaccine (Table 1) at any vaccine coverage.



CONCLUSION: A free vaccination program pay by parents does not to produce any epidemiological harm and is cost saving for the society.

Coverage	Payers perspective	Total Cost	Difference Payers perspective vs base case	Difference Total Cost vs base case
Base Case 0%	4,389,925	12,822,330		
50	2,181,501	9,570,811	-2,208,424	-3,251,519
60	1,735,576	9,147,873	-2,654,349	-3,674,457
70	1,301,485	8,752,787	-3,088,440	-4,069,543
80	912,521	8,493,597	-3,477,404	-4,328,733
90	630,673	8,574,043	-3,759,252	-4,248,287

ESPID-0730
MODERATED E-POSTER WALK 2 - EPIDEMIOLOGY AND PUBLIC HEALTH 1

THE IMPACT OF VARICELLA VACCINATION ON THE BURDEN OF HERPES ZOSTER: MODELLING THE EFFECT OF EXOGENOUS AND ENDOGENOUS BOOSTING

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Background and aim:

Two immune system processes inhibit reactivation of varicella-zoster virus (VZV) as herpes zoster (HZ): asymptomatic endogenous reactivation and periodic exogenous exposure to circulating VZV. The weighting of each process may be of importance when considering public health impact of routine childhood varicella vaccination on HZ. We analyzed the effect of varying assumptions on relative weighting of exogenous and endogenous boosting following introduction of varicella vaccination.

Methods:

Age-structured dynamic transmission model was adapted and fitted to the seroprevalence of varicella in France without vaccination with an empirical contact matrix. Two-dose vaccination schedule was introduced at 12-/18-month-old, with vaccine efficacy and coverage of 65%/95% and 90%/80%, respectively. Exogenous boosting was based on several assumptions: immunity duration against HZ, age-dependent boosting and HZ reactivation rates calibrated to reproduce HZ incidence. Maximum value of endogenous boosting was considered the same as for exogenous boosting and obtained by multiplying the force of infection at steady pre-vaccination state with age-dependent boosting rates. The model tested various weighting of exogenous and endogenous boosting (100%/0%, 75%/25%, 50%/50%, 25%/75%, 0%/100%).

Results:

Pre-vaccination HZ incidence was 3.96/1,000 population and similar for all scenarios. In presence of vaccination, the model predicted various effects on HZ in terms of long term impact, duration and magnitude of temporal HZ increase (Table).

Conclusions:

Assumptions on relative weighting of exogenous and endogenous boosting effects may have an important and varied impact on HZ burden following introduction of universal childhood varicella vaccination.

Table: Effects of exogenous and endogenous boosting on herpes zoster burden post varicella vaccination introduction.

Parameters	Exogenous-Endogenous (%)				
	100-0	75-25	50-50	25-75	0-100
Decrease in HZ by year 80 (%)	62.6	63.6	64.6	65.5	66.3
HZ above pre-vaccine rate (total years)	21	10	3	2	0
Max HZ increase (%)	3.7	1.8	0.8	0.2	0
Max HZ increase (at year)	8	3	2	1	NA

HZ: herpes zoster.

ESPID-0430
MODERATED E-POSTER WALK 3 - EPIDEMIOLOGY AND PUBLIC HEALTH 2

AN OBSERVATIONAL STUDY OF KAWASAKI DISEASE INCIDENCE IN CHILDREN AND ADOLESCENTS

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Background and aims A very low but increasing UK incidence of Kawasaki disease in those <5 years was reported to 2000.We estimated the incidence in a wider age range, and investigated trends across study years and between seasons.

Methods A case definition for use with UK primary care records was developed. The THIN database of electronic patient records was searched to identify those with an entry indicating Kawasaki disease. These records were compared to the case definition and a date of onset assigned. The incidence, age-sex distribution, and trend in seasonal and temporal distribution were estimated for cases aged <20 years between 2008 and 2012 inclusive.

Results The annual incidence of Kawasaki disease was 2.8 per 100,000 population (95% CI 1.9, 4.1) under 20 years and 9.1 (95% CI 7.3, 11.2) under five years, with more males (55%) and a fifth of cases diagnosed after five years of age. The highest incidences were at 6-12 months and 36-48 months. There was no trend in incidence over the study years (p=0.10 adjusted for sex and month), or between seasons (p=0.65 adjusted for year and sex). Inclusion of cases diagnosed as probable or possible Kawasaki disease increased the incidence to 3.0 per 100,000 (95% CI 2.0, 4.3).

Conclusions An algorithm allowing case ascertainment of Kawasaki disease from primary care records provided an updated incidence with no significant increase over the study period or differences between seasons. Some inconclusive discharge diagnoses suggest a lack of confidence in diagnosing the condition.

ESPID-0489
MODERATED E-POSTER WALK 3 - EPIDEMIOLOGY AND PUBLIC HEALTH 2

HAND-FOOT AND MOUTH DISEASE: CREATION OF A NATIONAL SENTINEL SURVEILLANCE SYSTEM IN FRANCE

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Background and aims. Hand foot and mouth disease (HFMD) and herpangina (HA) are usually benign illnesses. Rare fatal neurological complications with cardio-pulmonary failure associated with enterovirus 71 (EV-A71) justifies reinforcing the surveillance and investigation of HFMD in Europe.

Methods. A citywide sentinel system for HFMD previously set up in Clermont-Ferrand, France showed its feasibility during 4 years. From the 1st April 2014, epidemiological, clinical and virological surveillance have been extended to a national scale.

Results. Epidemiological surveillance consists in weekly reporting the number of HFMD/HA cases over the total number of consultations by all volunteers paediatricians. Clincal-virological surveillance relies on 47 paediatricians selected by stratified sampling on French regions. After parental consent, throat or buccal swabs were taken from children presenting with HFMD/HA and prospectively sent along with a standardized report form to the national reference centre for EVs. EV molecular detection and genotyping were performed with prospective feed-back on results. The first eight months of existence of this surveillance have proved its efficiency in identifying two epidemic waves of HFMD. As of 31st December 2014, a total of 628 children were enrolled; 497 (79%) presented with an enterovirus infection. Five EV-A71 infections were detected. However, to ensure the sustainability of this surveillance, enrolment of children should be simplified.

Conclusions. This is the first sentinel system for HFMD in a European country at a national scale. This should provide accurate information on epidemiological trends of HFMD in France and allow early detection of epidemics and upsurge of EV-A71 infections.

ESPID-0798
MODERATED E-POSTER WALK 3 - EPIDEMIOLOGY AND PUBLIC HEALTH 2

COST-EFFECTIVENESS EVALUATION OF A TODDLER MENINGITIS ACWY CONJUGATE VACCINATION (MENACWY) IN TURKEY

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Background and aim:

Neisseria meningitidis causes up to 1,700 invasive meningococcal disease (IMD) cases annually in Turkey. No vaccination is currently in place. We assessed the cost-effectiveness of a 1-dose MenACWY-TT vaccination among 1-year Turkish toddlers compared with no vaccination.

Methods:

An annual population static model reproduced variable epidemiologic IMD patterns over a 100-year time-horizon, based on observed IMD incidence among under 16-year old population adjusted by a random parameter (+/-20%) accounting for annual variability. Vaccination effectiveness was calculated from IMD serogroup and age distribution, estimated serogroup specific vaccine effectiveness, duration of protection, and vaccination coverage. IMD and associated sequelae related lifetime costs and quality adjusted life-years (QALYs) were assigned to each model-projected IMD. Costs and QALYs were extracted from international literature and adapted to the Turkish setting, applying a 3.5% discount rate. A vaccine price of 17,5$ was assumed and the incremental cost-effectiveness ratio (ICER) comparing MenACWY-TT toddler vaccination with no vaccination was calculated. Univariate sensitivity analyses on ICER were conducted varying IMD incidence, costs, QALYs and vaccine parameters (+/-20% base case). The vaccine price to reach 3-x gross domestic product/capita ($32,916: cost-effectiveness threshold) was determined.

Results:

MenACWY-TT toddler vaccination was modelled to prevent 198 cases annually on average. Vaccination was cost-effective ($11,055/QALY discounted; $4,933 undiscounted) and remained cost effective for a vaccine price up to $31.1/dose ($59.3 undiscounted) compared with no vaccination. The base case ICER ranged from $6,545/QALY to $17,819/QALY over the sensitivity analyses.

Conclusions:

Implementing MenACWY-TT among Turkish toddlers was modeled to be cost-effective.

ESPID-0905
MODERATED E-POSTER WALK 3 - EPIDEMIOLOGY AND PUBLIC HEALTH 2

UK PREPAREDNESS FOR CHILDREN WITH EBOLA INFECTION

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Introduction

No child with Ebolavirus disease (EVD) has been diagnosed in the UK, but practicalities of assessment, diagnosis, transport and care for children with EVD were previously not established. The Ebola outbreak prompted development of a paediatric clinical pathway, which balances paediatric specialist care and staff safety.

Methods

A new paediatric pathway was developed for the UK NHS through a process of consensus-building mediated by weekly NHS England teleconferences.

Outcome

A UK child with confirmed EVD should be transferred by a designated team to, and cared for in, a bed isolator (Trexler tent) at a national specialised High Level Isolation Unit (HLIU), rather than be cared for at a paediatric centre. Paediatric clinical staff should be mobilised to the HLIU. The Department of Health has recommended that level 3 critical care is not part of normal care, but sedation and intubation may be needed for safe delivery of care for children in a bed isolator, for instance during central line insertion. Level 3 care should not be initiated in children with EVD outside the HLIU. Whether parents can remain with their child during transfer and subsequent admission depends on public health concerns, the best interests of the child and the EVD status of the parent.

Conclusion

Planning for care of a child with EVD has prompted discussion around ethical and practical challenges. There is a balance between a cautious approach, based on public health concerns, and the best care for the individual child.

ESPID-0970
MODERATED E-POSTER WALK 3 - EPIDEMIOLOGY AND PUBLIC HEALTH 2

FIRST DESCRIPTION OF NASOPHARYNGEAL CARRIAGE OF KINGELLA KINGAE (KK) IN PRE-SCHOOL CHILDREN

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BACKGROUND AND AIMS: Kingella kingae (KK) has become recognised as the cause of a significant proportion of paediatric bone and joint infections. However there are few data concerning the normal life cycle of this organism in humans and although oropharyngeal carriage has been reported, no information is available about its presence and behaviour in the nasopharynx.

METHODS: In winter 2011-12, up to 5 nasopharyngeal swabs taken at 4-6 weekly intervals were collected from each of 150 children attending pre-school nurseries in Bristol, UK into STGG broth and stored at -80ºC. DNA was extracted from broth samples and KK was identified by qPCR targeting the rtxA and rtxB genes using published primers. Samples were considered positive if above threshold after <=35 PCR cycles.

RESULTS: 21/640(3.3%) samples were positive for either one or both rtxA & B (11 both, 5 rtxA only, 5 rtxB only). Of the 20 colonised children (12M, 7F, 1 no data; Age range 0.9-4y; rhinitis score range 0(min)-3(max)), only one had more than one positive sample (two on sequential visits) suggesting that duration of carriage may usually be less than 4-6 weeks. The number of cycles of amplification ranged from 29 to 35 meaning that absolute density of colonisation varied over approximately 100 fold with the large majority towards the lower end of this range.

CONCLUSIONS: KK nasopharyngeal carriage is found in a minority of healthy pre-school children and appears to be at relatively low density most of the time and relatively transient.

ESPID-1054
MODERATED E-POSTER WALK 3 - EPIDEMIOLOGY AND PUBLIC HEALTH 2

PROGRAM OF SCREENING AND DIAGNOSING OF CONGENITAL CHAGAS DISEASE IN CATALONIA(2010-2012)

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Introduction:
In Catalonia (Spain) has been implemented a systematic screening program for prevention of congenital transmission of *Trypanosoma cruzi* in Latin American pregnant women in 2010.
Methods:
We analyzed the reported cases to the *Register volunteers of congenital Chagas disease in Catalonia* during 2010-2012, in which positive women and their children are included. The diagnosis of infection is performed with two serological tests in pregnant women, and parasitological test at birth or two serological test from 9 months old in children.
Results:
The coverage rate estimated program has fluctuated between 69% and 86%, in 2010 and 2012, respectively.
During 2010-2012, 19,438 infants were born from women, who come from endemic areas. The mothers of 353 children were infected with *T. cruzi*. The prevalence rate was 1.8%.
From 277 infants that have been completely followed-up, 11 have been diagnosticated positively implying a rate of congenital transmission (TTC) of 4%.
A follow-up has been done of 103 from 318 (32.4%) reported cases in children under 18 years (5.1%, 51.2% and 54.2% in 2010, 2011 and 2012, respectively). In 9 from 103 cases were positive to *T. cruzi*.
Conclusions:
The estimated coverage of the program is high and has improved since its implementation in 2010.
The TTC was 1.8%, the range of the transmission rate in non-endemic countries (range 0-7.3%).
It is necessary to intensify the network of pediatric surveillance in order to keep the follow up of newborns and improve the control of other children.

ESPID-0284
MODERATED E-POSTER WALK 4 - HIV/AIDS

CHARACTERIZATION OF ASYMPTOMATIC CHILDREN INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS AT BIRTH

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Background: Mother-to-child HIV transmission remains very high in Cameroon. Therefore follow-up of numerous HIV-infected infants is a critical issue in the country. Here, we investigated on HIV-infected infants remaining asymptomatic in the absence of anti-retroviral therapy (ART). The first goal was to obtain an estimate of the prevalence of infants with an HIV controller like status.

Method: HIV-infected infants, aged 6 months to 17 years were enrolled upon signed a proxy-consent. The enrollment took place from April 2011 to February 2013. From the medical file of 359 HIV vertically-infected infants, 41 were found naive of anti-retroviral therapy and free of clinical symptoms. From the selected infants, CD4 counts and viral load were recorded. Non-exposed children were enrolled as control group.

Results: Of the 359 infants, 41 were ARV-naive and free from HIV clinical symptoms. Five of them (12%) exhibit a viral load < 1200 RNA copies/ml. Their CD4 counts were not statistically different from those of a control group (p=0.33). Furthermore, ten years after contamination, three children did exhibit a viral load < 5500 RNA copies/ml. Altogether, this suggests the existence of pediatric HIV controllers (pHIC) with a frequency much higher (>10%).

Conclusion: Our preliminary cross-sectional study highly suggests the existence of pediatric HIV controllers **like** in Cameroon despite all disfavoring living conditions. However, a longitudinal study would be required to confirm this hypothesis. The development of an HIV vaccine applicable to infants of countries with high incidence should benefit from the immunological analysis explaining the HIV controller (HIC) status.

ESPID-0329
MODERATED E-POSTER WALK 4 - HIV/AIDS

FIRST HIV-2 INFECTION IN A CHILD IN TURKEY

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The prevalence of HIV-2 infection remains highest among West African countries. In Turkey, there is no any pediatric HIV-2 case to date.

Herein, we present a 10 years-old girl with HIV-2 infection due to maternal transmission. Her father was a sailor in a commercial shipping company working for West African countries. She was treated as HIV-1/AIDS diagnosis before transferred to our hospital.

Case: A two-years-old girl was admitted to another hospital with multipl molluscum contagiosum lesions. Her Anti-HIV 1/2 serology was positive, Western-Blot immunobloting and HIV-1 PCR were negative. The HIV-2 PCR was not available in those years, in Turkey. The physicians were suspected HIV infection strongly because of the low level of CD-4 lymphocytes. Lamivudin, stavudin and lopinavir/ritonavir combination therapy was started. She transferred to our hospital because of parental incompliance to follow-up. Her therapy was changed to lamivudin, zidovudin and darunavir/ritonavir combination because of severe gastrointestinal disturbances with previous therapy. Her HIV-1 PCR was negative in our hospital but HIV-2 PCR analysis was positive which was performed in a reference laboratory. Her mother refused her own anti-retroviral therapy, and she has died after 2 years of follow-up. Her relatives told that the mother was never compliant to her daughter's anti-retroviral therapy. The daughter's anti-retroviral therapy re-arrenged and she is very compliant in last 6 months follow-up.

Conclusion: The most important feature of HIV-2 infection is its natural resistance to NNRTI drugs. However, its diagnosis is quite harder than HIV-1 infection because of technical insufficiences in our country.

ESPID-0700
MODERATED E-POSTER WALK 4 - HIV/AIDS

PERINATAL HIV EXPOSURE AFFECTS INFANT COGNITION AT 6 MONTHS BUT NOT CHANGES IN COGNITIVE SCORES BETWEEN 6 AND 12 MONTHS

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Background and aims: Limited data exist on cognitive development of infants perinatally exposed to HIV. We examined the effect of perinatal HIV exposure on cognitive outcomes of infants at 6 and 12 mo in northern Uganda.

Methods: Assessments were performed on 181 infants [32.6% perinatally exposed to HIV] at 6 mo using the Mullen Early Learning Scales (MELS), and at 12 months using the MELS & Home Observation for Measurement of the Environment (HOME) scales. Maternal education, dietary diversity, and other prenatal characteristics were assessed at median (IQR): 19.4 (16.23-21.6) weeks of gestation. Separate regression models were used to assess the effect of perinatal HIV exposure on infant MELS composite standard (MELS CS) scores at 6 mo, 12 mo, and on the rate of change in these scores between the two time points.

Results: Overall, (mean±SD) MELS CS scores were 111.6±16.5 and 101.5±15.1 points at 6 and 12 mo respectively. MELS CS scores declined at a rate of -1.70±3.14 points per month. Controlling for infant age and prenatal dietary diversity, perinatal HIV exposure was associated with a 6.7 point decline in MELS CS scores at 6 mo (p=0.01). HOME scores, but not HIV exposure, predicted MELS CS scores at 12 mo. Maternal education, but not HIV exposure or HOME scores, predicted the rate of change in MELS CS scores between 6 and 12 mo.

Conclusion. Perinatal HIV exposure affected cognitive scores at 6 mo, but not at 12 mo, nor the change in cognitive scores between 6 and 12 mo.

ESPID-0922
MODERATED E-POSTER WALK 4 - HIV/AIDS

ESTABLISHMENT AND REPLENISHMENT OF THE VIRAL RESERVOIR IN PERINATALLY HIV-1 INFECTED CHILDREN INITIATING ART LESS THAN ONE YEAR OF AGE

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Background & Aims: Invertical transmission, previous studies suggest that early initiation of cARTmay prevent the establishment of viral reservoirs and accelerates the reservoirdecline. Only long-term viral remission after treatment discontinuation will beevidence of a functional cure. The aim was to analyse the impact of early cARTinitiation and treatment discontinuation on the size of the latent HIV-1reservoir in paediatric patients perinatally HIV-1 infected with sustainedvirological suppression.

Methods: Study included 23 HIV-1 infectedchildren (median age = 8.0 years) who initiated veryearly treatment within 12 weeks after birth (14 patients), or early treatment betweenweek 12-48 (9 patients). Samples were collected after 1 year of sustainedplasma viral suppression (VL≤50 copies/ml, median time on virologic control =4.5 years [IQR: 3.3-6.9]). Samples and associated clinical data were obtainedfrom HIV-BioBank-HGM and coRISpe. To evaluate the size of proviralreservoir, $CD4^+$ T cell-associated totalHIV-1 DNA was quantified by ddPCR.

Results: There is strong positive correlation between the time to onset of treatmentand amount of total cell-associated HIV-1 DNA/10^6 $TCD4^+$ cellsand, in a lesser extent, between cell-associated HIV-1 DNA and time required toachieve virologic control. Patients who underwent transient treatment discontinuationshowed an irreversible increase in the size of the viral reservoir.

Conclusions: Initiation of cART during the first 12 weeks of life in perinatally infectedchildren limits the size of the viral reservoir. Treatment

discontinuationsshould be carefully considered, as they may lead to a fast replenishing of theviral reservoir.

ESPID-0961
MODERATED E-POSTER WALK 4 - HIV/AIDS

HOW EFFECTIVELY ARE WE CONTROLLING KNOWN RISK FACTORS FOR MOTHER-TO-CHILD TRANSMISSION OF HIV – A THREE-YEAR STUDY AT A SECONDARY CARE HOSPITAL

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Background/aims: Mother-to-child transmission (MTCT) of Human Immunodeficiency Virus (HIV) is the primary route of infection in children. The aim of this study was to inquire how recommended preventive measures are being adopted.

Methods: Review of the clinical files of children born to HIV-infected mothers from January 2011 to December 2013.

Results: We identified forty-one children born to HIV-infected mothers (mean annual prevalence of 0.5% of all births). Thirteen women were diagnosed during pregnancy (one in the third trimester). Three women did not adhere to antiretroviral therapy (ART) during pregnancy, the remaining were on ART for more than four weeks before delivery. Thirty-eight women were on ART during labor. Of the remaining three, one had a viral load 1.000cp/ml at the time of delivery in three women. Rupture of membrane lasted >4h in fourteen women. The mode of delivery was cesarean section in twenty-six women and vaginal in the remaining. Late preterm birth occured in six newborns. Thirty-three newborns were started on antiretroviral monotherapy for four weeks, the remaining were on triple antiretroviral therapy. No infant was breastfed. HIV infection was excluded in all infants, with a minimum follow-up of twelve months.

Conclusions: Preventive measures of MTCT are effective in reducing infection rates. Cooperation between obstetric and paediatrics departments is crucial in the attempt to eliminate MTCT. A considerable number of diagnoses were made during pregnancy, emphasizing the importance of screening opportunities in women.

ESPID-0039
MODERATED E-POSTER WALK 5 - HOST-PATHOGEN INTERACTIONS

PROCALCITONIN LEVELS IN PFAPA SYNDROME

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Background: To assess procalcitonin (PCT) levels during febrile attacks in children diagnosed with the Periodic Fever, AphthousStomatitis, Pharyngitis, Adenitis Syndrome (PFAPA).

Methods: C-reactive protein (CRP) and PCT values were recorded during 87 febrile episodes in 35 patients with PFAPA syndrome and 35control patients with diagnosis of septicemia.

Results: We compared CRP and PCT levels in bothgroups. Mean CRP and PCT values of patients in the PFAPA group were 76.88 ±47.63 mg/L and 0.18 ± 0.10 ng/mL, respectively. In the control group, the mean CRP value was 34.64 ± 18.61mg/L, and PCT was 2.12 ± 1.95 ng/mL. CRP levels did not differ significantly between the two groups ($p > 0.05$). PCT levels were significantly lower in the PFAPA group ($p < 0.001$).

Conclusion: During febrile episodes in patients diagnosed with PFAPA syndrome, CRP values increased, while PCT values remained within normal levels. Concomitant assessment of CRP and PCT, in addition to clinical diagnostic criteria, may help distinguish febrile attacks from infections.

ESPID-0091
MODERATED E-POSTER WALK 5 - HOST-PATHOGEN INTERACTIONS

GRANULOMATOUS HERPES SIMPLE VIRAL ENCEPHALITIS.

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Background: Herpes simple virus (HSV) encephaltis can manifest with diverse clinical presentations including classic adult, neonatal and diphasic chronic granulomatous herpes encephalitis.
Aim & Methods: We report a 14 year old boy admitted with an acute onset non-fluent expressive dysphasia and focal epilepsy of frontal lobe origin after three days history of fever and lethargy. He had had an episode of viral meningitis in infancy and there was no family history of immunodeficiency.
Cerebrospinal fluid (CSF) analysis by PCR testing was positive for HSV1 while HSV1 IgG were detected in serum. MRI scan showed areas of cortical and subcortical signal change associated with swelling and a prominent lesion in the left inferior frontal gyrus in Broca's area.
The patient received twentyone days of intravenous acyclovir and his neurological state gradually returned to normal. However, two months later, he re-presented with severe anxiety and episodic headaches, associated with worsening EEG, suggestive of moderate cerebral impairment. CSF and blood PCR were negative for HSV1. The repeat MRI revealed diffuse bilateral leptomeningeal and superficial cortical inflammatory enhancing lesions and neuropathology demonstrated graulomatous inflammation of brain tissue. The immunological workup was unremarkable apart from abnormal Toll-like receptor (TLR) functional testing for TLR 7/8. Abnormalities of the latter have been associated with HSV1 susceptibility.
Conclusion: HSV encephalitis in children, associated with underlying defect in innate immunity can be complicated by chronic granulomatous inflammation.

ESPID-0598
MODERATED E-POSTER WALK 5 - HOST-PATHOGEN INTERACTIONS

CHARACTERISATION OF CIRCULATING CLOSTRIDIUM DIFFICILE STRAINS AND MUCOSAL INFLAMMATORY RESPONSE IN CHILDREN WITH DIARRHOEA IN MERSEYSIDE, UK.

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Background & aims

The prevalence of *Clostridium difficile* (*C. difficile*) is increasing amongst 'low risk' groups, such as children. We aimed to characterise the epidemiology of and host response to *C. difficile* in children.

Methods

A total of 197 faecal samples were tested from children with diarrhoea (78 children <2yrs and 119 children 2-16yrs). Faecal samples were cultured and tested for the presence of *C. difficile* antigen (GDH) and toxin, using Quik Chek Complete. Isolates were characterised using PCR ribotyping. Stool supernatants were analysed using MSD VPLEX faecal cytokine assays, and plasma samples tested for IgG to ToxinB by ELISA.

Results

A total of 20 samples (26%) from <2yr and 12 samples (11%) from >2yr group were culture and antigen positive for *C. difficile*. Of these, 10 (50%) of the <2yr samples and 9 (75%) of the >2yr samples were toxigenic. Most common ribotypes were: 020(7 isolates), non-typeable 1 (10 isolates), 014 and 017 (2 isolates). Compared with circulating adult strains, greatest overlap was seen between hospitalised adults and children >2yrs. Mean Th1/Th2 ratios (IFNγ,IL12,IL2/IL13,IL4,IL6) and plasma Toxin B IgG(inverse log optical density) were increased in children >2yrs; 0.70 versus 0.004, 3.27 versus 1.35 respectively. Mean Th1/Th2 ratios were also increased in stool bacterial co-infection (6.40 versus 0.22).

Conclusions

Children with diarrhoea frequently harboured toxigenic isolates of C. *difficile*. Overlap with adult ribotypes from the same area suggests children as a community reservoir for *C. difficile*. The host response in children may partly explain lower morbidity from infection.

ESPID-0824
MODERATED E-POSTER WALK 5 - HOST-PATHOGEN INTERACTIONS

FAMILIAL MEDITERRANEAN FEVER MASQUERADING AS ACUTE INFECTION

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Background and Aim: Familial Mediterranean Fever (FMF) typically presents with recurrent episodes of fever and serositis caused in most cases by mutations in the responsible gene *MEFV*. The aim of this study was to identify patients with atypical initial presentation mimicking acute infections. **Patients-Methods**: We retrospectively analysed data from patients with FMF with known mutations of the *MEFV* gene followed-up during an 8-year period. **Results**: Among 23 patients with FMF, 10 (43.5%) had been initially diagnosed as suffering from acute infection, of whom 5 underwent surgery for presumed appendicitis, two were hospitalized for acute gastroenteritis, two were diagnosed as septic arthritis of the knee and one presented with acute pericarditis that subsequently recurred. In all cases history revealed recurrent febrile episodes with variable or no periodicity. History and follow-up pointed to an autoinflammatory syndrome. In all patients FMF diagnosis was confirmed with genetic analysis and all were treated with colchicine. In 3 out of 10 cases with atypical presentation molecular analysis revealed M694V/E148Q and M694I/E148Q genotype. **Conclusion**: Atypical presentation in FMF patients can be misleading. FMF should be suspected in patients with atypical "infectious" presentation, especially in patients coming from areas with considerable incidence of the disease, and detailed history can lead to the correct diagnosis.

ESPID-1062
MODERATED E-POSTER WALK 5 - HOST-PATHOGEN INTERACTIONS

ROBUST INNATE IMMUNE RESPONSES CORRELATE WITH IMPROVED CLINICAL OUTCOMES IN INFANTS WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) ACUTE RESPIRATORY INFECTION (ARI)

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Background and aims:
By 2 years of age 95% of children have been infected with RSV, yet only ~2% are hospitalized. The viral and host innate immune responses in the great majority of children who do not require hospitalization are not well understood. We compared the systemic neutrophil and monocyte responses in infants with mild (outpatients) vs. severe (hospitalized) RSV ARI.

Methods:
We enrolled 105 previously healthy infants (median age 4.3 mo) with mild (n=23) or severe (n=56) RSV ARI, and healthy controls (HC; n=26). Blood samples were analyzed by flow cytometry to define the numbers and phenotypic activation (mean fluorescent intensity, MFI) of monocytes and neutrophils. RSV loads were measured by RT-PCR in nasal wash samples, and severity determined by the need for hospitalization and a standardized clinical disease severity score (CDSS).

Results:
Total numbers of monocytes and neutrophils were increased in infants with severe RSV ARI ($p<0.01$), but comparable between mild RSV ARI and HC. In contrast, expression of neutrophil (CD11b MFI) and monocyte (HLA-DR MFI) activation markers was reduced only in severe RSV ARI ($p<0.001$). Further, CDSS inversely correlated with neutrophil ($r=-0.26$; $P=0.024$) and monocyte activation ($r=-0.48$; $P<0.0001$), but not with absolute cell counts. No correlation was observed between any of these parameters and RSV loads.

Conclusions:
Activation of blood neutrophils and monocytes was not impaired in infants with mild compared with severe RSV ARI. These data suggests that robust rather than weak innate immune responses are associated with improved clinical outcomes in infants with RSV infection.

ESPID-0035
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

SEROPROTECTION RATES AMONG INDIAN CHILDREN AT 4-6 YEARS AND 9-12 YEARS AFTER PRIMARY MEASLES AND MMR VACCINATION

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Objective: To find out seroprotections rates among Indian children against measles, mumps, rubella infections in at 4-6 years and 9-12 years of age, who received primary measles(9-12 months) and MMR(15-18 months) vaccination.

Design: Cross sectional, observational study

Setting: Pediatric out-patient department(OPD) at a tertiary-care referral hospital.

Participants: Children attending pediatric OPD for vaccination at 4-6 years and 9-12 years; having documented evidence(immunization card) of received measles vaccine at 9-12 months and MMR vaccine at 15-18 months, fulfilling predefined inclusion and exclusion criteria's.

Methods: Children were enrolled after taking informed consent from their parents. Antibody estimation was done by using commercially available(quantitative IgG specific) ELISA kits.

Results: A total of 80 children(53 males, 27 females) were enrolled in study; 50 in group-1(4-6 years) & 30 in group-2(9-12 years). The protective antibody titers were 80%, 86%, 96% at 4-6 years and 83.3%, 96.7%, 96.7% at 9-12 years for measles, mumps & rubella respectively. Geometric mean concentration(GMC) of IgG antibodies in group 1 and group 2 for measles were 0.63 & 0.75, for mumps 84.63 & 114.60 & for rubella 78.96 & 88.37 respectively.

Conclusions: One dose measles vaccine at 9 months and single dose of MMR vaccine at 15-18 months was able to provide seroprotection against measles, mumps, rubella in 80%, 86%, 96% at 4-6 years and 83.3%, 96.7%, 96.7% at 9-12 years respectively. Incorporation of MMR2 at or before 5 years could improve these titers and help in eradication of these diseases.

ESPID-0090
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

THE PREVENTIVE EFFECT OF PERTUSSIS VACCINE ADMINISTERED TO THE MOTHERS IN POSTPARTUM PERIOD FROM DEVELOPMENT OF PERTUSSIS IN INFANTS WITHIN FIRST 8-10 MONTHS

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Background: The aim of this study was to assess the preventive effect of acellular pertussis vaccine administered to the mothers in postpartum period from development of pertussis in infants.

Materials and Methods: The mothers followed postpartum in Istanbul University Perinatology Service between December 2013 and April 2014 was informed about cocoon strategy. Total number of 405 mothers was enrolled in study and 205 of them accepted to be vaccinated. The complaint of cough lasting than two weeks in infants was asked at monthly controls or via telephone. Infants who had pertussis like symptoms were taken throat culture for pertussis PCR. The antibody response after vaccination was compared between infants of thirty vaccinated mothers and thirty unvaccinated mothers.

Results: The rate of acceptance of vaccination was 45%. There was significant difference between vaccinated and unvaccinated group in terms of education level of parents, occupation of parents and siblings going to kindergarten ($p<0.05$). The pertussis PCR was evaluated in eighty percent of infants complaining cough and 17.4% of them was positive. All of six infants complaining cough and whose mother vaccinated resulted in negative PCR whereas four of seventeen infants whose mother unvaccinated resulted in positive PCR. The antibody level of infants whose mother vaccinated was significantly higher (403.26 IU/ml) than infants whose mother unvaccinated (94.76 IU/ml) in 5.59 ± 1.19 (4-8) month ($p<0.05$).

Conclusion: The pertussis vaccine that is administered to the mothers within first three days of postpartum period can protect children against pertussis in first ten months.

ESPID-0536
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

RESPONSE TO A "BOOSTER" OF HEPATITIS B VIRUS VACCINE IN CELIAC CHILDREN NON-RESPONDERS TO A PRIMARY COURSE OF VACCINATION.

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AIMS: To evaluate the response to a "booster" of hepatitis B virus (HBV) vaccine in children with celiac disease (CD) non responders to a primary course of vaccination administered in the first year of life.

MATERIAL AND METHODS: We develop a prospective, observational study in 72 patients with CD whose anti-HBs titers at the moment of study were below 10 mUI/mL. All of them had been fully vaccinated in the first year of life. They were given and additional dose of HBV vaccine and titers were measured by ELISA after 6 months.

RESULTS: Are summarized in table 1

Table 1: Response to a booster of HBV vaccine according to the pre-"booster" anti-HBs titer.

PRE-"BOOSTER" TITER	POST "BOOSTER" TITER			
	≥ 10 mUI/mL	>0 and <10 mUI/mL	0,000 mUI/mL	TOTAL NON RESPONDERS
<0 and <10 mUI/mL	54 (91.52%)	4 (6.77%)	1 (1,69%)	5 (8.47%)
0,000 mUI/mL	7 (53.84%)	4 (30.76%)	2 (15.38%)	6 (46.15%)
Total	61 (84.72%)	8 (11.11%)	3 (4.16%)	11 (15.27%)

CONCLUSIONS:

1.-Children with CD have an impaired response to HBV vaccine

2.-A single booster dose of HBV vaccine is not effective to achieve an adequate immune response, especially in those children with anti-HBs= 0.000 mUI/mL.

3.-CD children with anti-HBs= 0.000 mUI/mL should be revaccinated with complete immunization scheme.

ESPID-0566
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

A PHASE III RANDOMIZED, DOUBLE-BLIND, CLINICAL TRIAL OF AN INVESTIGATIONAL HEXAVALENT VACCINE GIVEN AT 2, 3, 4, AND 12 MONTHS

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BACKGROUND

Combination vaccines simplify vaccination visits and improve coverage and timeliness. DTaP-HB-IPV-Hib is a new investigational, fully-liquid, combination vaccine containing a 5-antigen pertussis component and which is designed to protect against 6 infectious diseases.

METHODS

In this multicenter, double-blind, comparator-controlled, Phase III study conducted in Finland, Germany, and Belgium, healthy infants were randomized 1:1 to receive one of the following immunization regimens:

Group	Age	
	2, 3, 4 Months	**12 Months**
1	DTaP-HB-IPV-Hib Prevnar 13 (PCV13)* RotaTeq (RV5)	DTaP-HB-IPV-Hib ProQuad (MMRV)*
2	Infanrix-hexa (DTaP-HBV-IPV/Hib) Prevnar 13 (PCV13)* RotaTeq (RV5)	Infanrix-hexa (DTaP-HBV-IPV/Hib) ProQuad (MMRV)*

* Also administered at 13 months

RESULTS

A total of 628 subjects in Group 1 and 622 subjects in Group 2 were randomized. In a per-protocol analysis, immune responses to vaccine antigens 1 month after dose 3 and after the toddler dose were non-inferior in Group 1 as compared to Group 2. Group 1 responses to MMRV given concomitantly at 12 months were all non-inferior compared to Group 2.

Solicited adverse event (AE) rates after any dose, including fever, were similar in both groups. Most AEs were mild-to-moderate and did not lead to subject withdrawal. Vaccine-related serious adverse events occurred infrequently in Group 1 (0.3%) and Group 2 (0.2%).

CONCLUSIONS

The safety and immunogenicity of DTaP-HB-IPV-Hib is comparable to Infanrix-hexa when administered in the 2,3,4 and 12 month schedule. DTaP-HB-IPV-Hib has the potential to provide a new hexavalent option for pediatric combination vaccines, aligned with recommended immunizations in Europe.

ESPID-0567
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

A PHASE III RANDOMIZED, DOUBLE-BLIND, CLINICAL TRIAL OF AN INVESTIGATIONAL HEXAVALENT VACCINE GIVEN AT 2, 4, AND 11-12 MONTHS

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BACKGROUND

Combination vaccines simplify vaccination visits and improve coverage and timeliness. DTaP-HB-IPV-Hib is a new investigational, fully-liquid, combination vaccine designed to protect against 6 infectious diseases.

METHODS

In this multicenter, double-blind, comparator-controlled, Phase III study conducted in Sweden, Italy, and Finland, healthy infants were randomized 1:1 to receive one of the following immunization regimens:

Group	Age	
	2 and 4 months	**11-to-12 months**
1	DTaP-HB-IPV-Hib Prevnar 13 (PCV13) RotaTeq (RV5)* or Rotarix (RV1)	DTaP-HB-IPV-Hib Prevnar 13 (PCV13)
2	Infanrix-hexa (DTaP-HBV-IPV/Hib) Prevnar 13 (PCV13)* RotaTeq (RV5)* or Rotarix (RV1)	Infanrix-hexa (DTaP-HBV-IPV/Hib) Prevnar 13 (PCV13)

* Subjects administered RV5 received a 3rd dose at 5 months

RESULTS

A total of 656 subjects were randomized to Group 1 and 659 subjects to Group 2. Immune responses to all vaccine antigens post-toddler dose were non-inferior in Group 1 as compared to Group 2. Additionally, the post-dose 2 and pre-toddler Group 1 anti-PRP responses were superior. Group 1 responses to concomitant RV1 were non-inferior compared to Group 2.

Solicited adverse event rates after any dose were similar in both groups, except for higher rates of pyrexia (6.4%; 95% CI:1.5,11.3) and somnolence (5.8%; 95% CI:1.7,9.8) in Group 1. Vaccine-related serious adverse events occurred infrequently in Group 1 (0.3%) and Group 2 (0.5%).

CONCLUSIONS

The safety and immunogenicity of DTaP-HB-IPV-Hib is generally comparable to Infanrix-hexa when administered in the 2,4, 11-12 month schedule. Early Hib responses were superior vs. Infanrix-hexa. DTaP-HB-IPV-Hib could provide a new hexavalent option for pediatric combination vaccines, aligned with recommended immunizations in Europe.

ESPID-0685
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

HERD IMMUNITY WITH PARTIAL VARICELLA VACCINATION COVERAGE. EPIDEMIOLOGICAL MODEL.

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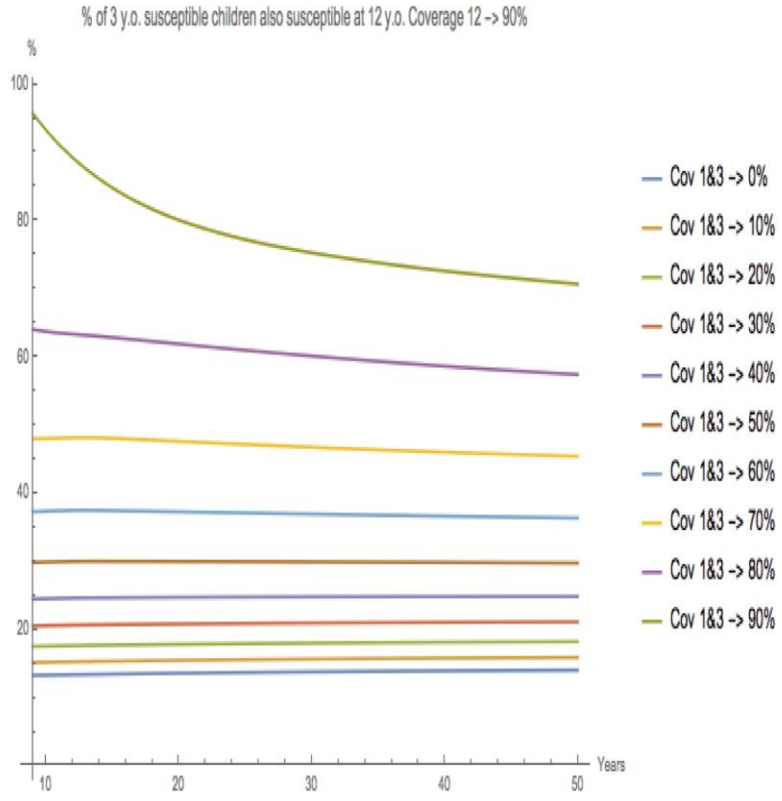
BACKGROUND: Varicella vaccination should decrease the impact of varicella and herpes zoster. Partial vaccine coverage was obtained in 2013 in Spain (30 to 70%) depending on areas. We expected to assess the coverage needed to obtain a herd immunity level that may sift disease to older ages.

METHODS: Mathematical model consisting of 5 states (susceptible-latent 1st week-latent 2nd week-infected-recovered) and 5 age groups (0-6 months; 6-12 months; 1-3 years; 3-12 years; older than 12) to study the transmission dynamics of the varicella in Valencia, Spain. Transmission depends on the age group, and on the week of the year. The model reproduces the varicella incidence per age groups very accurately. **Vaccine program:** Two doses at 12 months and 3 years of age, with coverage 0-100%, and catch up of susceptible at 12-years-old with coverage 90%.

RESULTS: With a vaccination coverage in children (1-3yoa) <=70%, the percentage of unvaccinated that reach susceptible at 12 years of age over the next 50 years is low (less than 50%) and the main effect of the vaccine is the direct protection (Figure). However, for coverage 80-90%, the herd immunity effect produces a remarkable increase in the percentage of susceptible individuals.

CONCLUSION: With vaccine coverage <=70% no major herd immunity is expected as the virus will circulate freely, and therefore it is not expected a shift of the disease

to older ages.



ESPID-0716
MODERATED E-POSTER WALK 6 - DTPP, MMRV and Hepatitis B Vaccines

VARICELLA-ZOSTER IMMUNIZATION AFTER PEDIATRIC LIVER TRANSPLANTATION: MAINTENANCE OF LONG TERM IMMUNITY

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Background and aims

Live-attenuated varicella-zoster-virus (VZV) vaccine is usually contraindicated in transplant recipients. We compare the maintenance of long-term immunity in liver transplant (LT) children immunized with VZV vaccine after LT to those seroprotected.

Methods

All eligible children at the Swiss Reference LT Center ≥1 year after LT received 2-3 doses of Varilrix® vaccine if VZV IgG was 2nd dose. Standardized phone calls evaluated safety. All patients had yearly antibody testing.

Results

99 children were included 3.0 years (IQR 1.0-8.0) after LT (50.5% boys; median age: 7.3 years; IQR 3.0-11.6). 48/99 were seropositive (median IgG: 622.0 IU/L, IQR 369.8-1664.5): 24 had chickenpox (16 before, 8 after LT), 11 were immunized (median: 11 months before LT), 7 had both disease and vaccination, 6 neither. On follow-up, 32/34 maintained or increased the antibody levels (median follow-up: 4.9 years, IQR 2.0-6.0; median IgG: 759.2 IU/L, IQR 294.0-1278.0; p=0.0246).

51/99 were seronegative: 5 had chickenpox after LT, 16 were immunized (median: 3 months before LT), 1 had both, and 29 neither. 48/51 children were immunized (median age: 4.5 years; IQR 2.7-8.8), 2.6 years (IQR 1.3-7.7) after LT. 47/48 (98%) children reached a protective level (median IgG: 1097 IU/L, IQR 618.5-1924.0; p

Conclusion

VZV vaccine in selected pediatric LT recipients seems to be safe and protective on long-term follow-up.

ESPID-0050
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

TOLL-LIKE RECEPTOR 2 SUBFAMILY GENE POLYMORPHISMS ARE ASSOCIATED WITH BACILLUS CALMETTE-GUÉRIN OSTEITIS FOLLOWING NEWBORN VACCINATION

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Background and aims. Toll-like receptors (TLR) 1,2, 6 and 10, which make up the TLR2 subfamily, are known to be associated withimmunity against tuberculosis. We evaluated whether polymorphisms in genesencoding TLR1, TLR2 and TLR6 were associated with osteitis in infants whoreceived the *Bacillus Calmette-Guérin* (*BCG*) vaccine soon after birth.

Methods. Blood samples from 132 adultsaged 21-49 who had *BCG* osteitis inearly childhood, were analysed in a controlled study for *TLR1* T1805G (rs5743618), *TLR2* G2258A (rs5743708)and *TLR6* C745T (rs5743810) gene single nucleotide polymorphisms.

Results. The frequencies of the variantgenotypes differed between the cases and controls: 11.4% versus 5.7% for *TLR2* G2258A (p=0.033) and 77.3% vs.61.6% for *TLR6* C745T (p=0.001). The *TLR2* and *TLR6* variant genotypes were associated with a higher risk of *BCG* osteitis, with adjusted odds ratios(aOR) of 2.154 (95%CI 1.026-4.521) and 1.907 (95%CI 1.183-3.075), respectively.The frequency of the *TLR1* T1805Gvariant genotype was 19.7% in the cases and 33.6% in the controls (p=0.003).The *TLR1* variant genotype wasassociated with a lower risk of *BCG*osteitis (aOR 0.554, 95%CI 0.336-0.911).

Conclusions. Gene polymorphisms thatregulate the function of the TLR2 subfamily play a role in the development of *BCG* osteitis in vaccinated infants.

ESPID-0374
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

INTER-RATER CONSISTENCY IN CAUSALITY ASSESSMENT OF SERIOUS ADVERSE EVENTS IN PAEDIATRIC VACCINE CLINICAL TRIALS; AN ONLINE SURVEY

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BACKGROUND:

Serious adverse events (SAEs) in clinical trials require reporting within 24 hours, including assessment of the causal relationship with the investigational product. In paediatric vaccine studies this classification is often challenging, but can impact on the perceived safety of an investigational vaccine. This on-line survey assessed the consistency of SAE classification for hypothetical vaccines and SAEs.

METHODS:

Members of the clinical advisory forum of experts (CAFÉ), a Brighton Collaboration online-forum, were emailed a survey link. Respondents were randomly assigned to either have two classification options (related/not related to study immunisation) or three options (possibly/probably/not related). The relevant clinical scenarios were i) leukaemia diagnosed 5 months post-immunisation with a live RSV vaccine, ii) juvenile idiopathic arthritis (JIA) 3 months post-immunisation with a Group A Streptococcal vaccine, iii) developmental delay diagnosed at age 10 months following infant serogroup B meningococcal vaccine administration and iv) developmental delay diagnosed at age 10 months after maternal immunisation with a group B streptococcal vaccine.

RESULTS:

The survey was completed by 140 respondents (72 two options, 68 three options). Across all respondents, SAEs were considered related to study immunization by 28% (leukaemia), 73.5% (JIA), 29% (developmental delay following infant immunization) and 42% (developmental delay following maternal immunization). Having only two options made respondents significantly less likely to classify the SAE as immunization related for two scenarios (JIA ($p = 0.0075$) and maternal immunization ($p = 0.045$))

CONCLUSIONS:

SAE causality classification is inconsistent amongst study physicians, and can be influenced by the classification systems available to them.

ESPID-0453
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

A REPORT ABOUT ON THE USE OF THE QUADRIVALENT HUMAN PAPILLOMAVIRUS VACCINE FOR THE TREATMENT OF JUVENILE-ONSET RECURRENT RESPIRATORY PAPILLOMATOSIS DUE TO HUMAN PAPILLOMAVIRUS TYPE 11

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Background and aims: Recurrent respiratory papillomatosis (RRP) is characterized by the growth of benign tumors on the larynx and other areas of the respiratory tract. Recently, it has been suggested that juvenile-onset recurrent respiratory papillomatosis (JoRRP) is caused by human papilloma virus(HPV) types 6 and 11.

Methods: We present a case of JoRRP that was treated with the quadrivalent HPV vaccine.

Results: An otherwise healthy 2-year-old boy presenting with a 1-month history of stridor was found to have a cauliflower-like upheaval lesion on the larynx upon fibroscopic examination. HPV type 11 was detected by using polymerase chain reaction in a sample of his vocal cords. As a consequence, he was diagnosed with JoRRP. His mother had been diagnosed with condyloma acuminatum during pregnancy and, therefore, the boy may have been infected via the vertical transmission of HPV. He required frequent laryngomicrosurgery almost every month to maintain breathing. We administered the quadrivalent HPV vaccine, following which, the intervals between each laryngomicrosurgery was extended. However, respiratory failure as a result of airway obstruction continued and, eventually, a tracheotomy was necessary.

Conclusions: Adjuvant therapy for the treatment of JoRRP (including interferon-α, cidofovir, and indole-3-carbinol) has been reported; however, the success of these therapies have not been proven. Recently, some reports have suggested that the quadrivalent HPV vaccine may prevent and treat JoRRP. The evidence from this current reportis not sufficient to confirm this effect, and a larger study is necessary to validate these earlier published findings.

ESPID-0664
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

SAFETY OF INTRANASAL QUADRIVALENT LIVE ATTENUATED INFLUENZA VACCINE (QLAIV) IN CHILDREN AND ADOLESCENTS - INTERIM RESULTS FROM A QUESTIONNAIRE STUDY

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Background: Following the publication of guidance issued by the EMA for enhanced safety surveillance of influenza vaccines, the DSRU conducted a cohort safety study in England during the 2014/2015 'flu season involving children and adolescents given intranasal quadrivalent live attenuated influenza vaccine (QLAIV, Fluenz Tetra®).

Aims: To measure the incidence of "reactogenicity" and other adverse events of interest (AEIs) following vaccination with QLAIV.

Methods: Participants were recruited during a mass vaccination programme through General Practices or schools in pilot areas in England. Responses to online or mailed questionnaires captured adverse events observed in the first 14 days post-vaccination. *(RECRef:14/WS/1067)*

Results: Interim data (collected between September and November 2014) included an evaluable cohort of 282 participants (Group1: 2-4years n=143; Group2: 5-10years n=103; Group3: 11-17years n=36) who each received one dose of QLAIV. Four events of hypersensitivity type reactions were reported (Group1: n=1(0.7%); Group2: n=2(1.94%); Group3: n=1(2.78%)) although on follow-up, none were true allergic reactions, serious or required hospitalisation. The most frequently reported AEI was nasal congestion in all age groups (Group1: n=67(46.9%); Group2: n=46(44.7%); Group3: n=15(41.7%)). Cough (Group1: n=31(21.7%); Group2: n=22(21.4%)), increased irritability (Group1: n=33(23.1%)), malaise (Group2: n=22(21.4%) Group3: n=8(22.2%)) and headache (Group3: n=9(25.0%)) were other frequently reported AEIs.

Conclusions: Interim safety data from this study are broadly comparable with the incidence of similar AEIs reported during randomised clinical trials although direct comparisons are not possible due to differences in study design. No apparent safety signal or unexpected difference in reactogenicity was detected from the small amount of data collected.

ESPID-0775
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

NATIONWIDE HPV VACCINATION COVERAGE AMONG 15 YEAR OLD GIRLS AFTER FIRST YEAR OF INTRODUCTION IN FINLAND

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In Finland, school-based vaccination against human papillomavirus (HPV) was introduced in November 2013. Target group is girls aged 11-12 years, catch-up among girls 13-15 years. Booster vaccination against diphtheria, tetanus, and pertussis (DTaP) is recommended to children aged 14-15 years since 2009.

Study focused on HPV catch-up, girls born 1998. Individual vaccination history from January 2012 to December 2014 was assessed linking Finnish Population Register with National Vaccination Register. Health care center/ municipality specific vaccination recording problems necessitated excluding 15.0% of birth cohort. Coverage was calculated by dividing vaccinated number by size of study population. Association between HPV and DTaP uptake, mother tongue and whether the girl had moved between 2012 and 2014 between municipalities was investigated with logistic regression.

Study population comprised 24593 girls. Coverage was 65.7% (first dose against HPV), 63.9% (second) and 58.2% (third); 87.2% against DTaP. HPV vaccination is more likely among girls vaccinated against DTaP (odds ratio: 2.50, 95% confidence interval: 2.31-2.70) and less likely among Swedish-speakers (0.77, 0.68-0.86), respectively foreign language speakers (0.72, 0.64-0.81), compared with Finnish-speakers and girls who moved between municipalities (0.64, 0.59-0.70).

DTaP booster is better accepted than recently introduced HPV vaccination series. Non-Finnish-speaking girls are less likely to be vaccinated against HPV. Girls moving during school-based vaccination campaign form another risk group for reduced HPV coverage. In future, after assuring that all vaccination record errors and reporting delays are eliminated, these groups should be particularly targeted to understand reasons behind not being vaccinated and ensure nationwide high HPV vaccination uptake.

ESPID-0809
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

ASSESSING THE IMPACT OF THE FIRST YEAR OF ROTAVIRUS VACCINATION IN THE UK

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Aims
The United Kingdom added rotavirus vaccine (Rotarix GlaxoSmithKline) to the national immunisation schedule in July 2013. We performed two years of active surveillance at our regional children's hospital to establish the baseline characteristics of disease burden pre-vaccine and now report the epidemiological trends one year after vaccine introduction.

Methods
During the 2012-2014 rotavirus seasons, children presenting to our regional paediatric emergency department with gastroenteritis symptoms (>2 loose stools and/or >1 episode of vomiting in the last 24 hours) had stool virology analysis (real-time PCR), severity assessment (Vesikari score) and clinical outcome recorded.

Results
Compared to pre-vaccine seasons, in the first year after vaccine introduction there were 42-47% ($p<0.001$) fewer attendances diagnosed with gastroenteritis, a 38-58% ($p<0.001$) reduction in gastroenteritis admissions and a total saving of 300-358 bed days' occupancy per year. There was a 73-78% reduction in number of samples testing positive for rotavirus. In those under 1 year old there was a 94% reduction in rotavirus positive cases and a 67-70% reduction among children too old to have been vaccinated.

Conclusions
In the first year after the introduction of universal vaccination against rotavirus we observed a profound reduction in gastroenteritis presentations and admissions. Although by early 2014 only those under 1 year old had been vaccinated, there were also many fewer cases than expected in older children. Extrapolating these findings to the UK population we estimate first year secondary healthcare savings of ≈£7.5 million. Ongoing surveillance will determine the long term impact of the rotavirus immunisation programme.

ESPID-0859
MODERATED E-POSTER WALK 7 - VARIOUS VACCINES

SINGLE DOSE HEPATITIS A IMMUNIZATION: 7.5 YEAR OBSERVATIONAL STUDY IN NICARAGUAN CHILDREN TO ASSESS PROTECTIVE EFFECTIVENESS AND IMMUNE MEMORY

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Background and Objectives*:* Universal vaccination of toddlers with two doses of hepatitis A virus (HAV) vaccine effectively eliminates hepatitis A. High vaccine costs impede, however, the implementation in endemic countries. Relying on the efficient immune priming of a first dose of virosomal HAV vaccine, we initiated in 2005 an observational pilot-study to assess protection and immune memory following a single dose.

Methods: Following a serosurvey in Q4-2003, 130 seronegative, 2-17 year old children of León, Nicaragua, received in January 2005 single doses of virosomal hepatitis A vaccine, followed by serological and clinical assessments after 3 months, and yearly from 2006 to 2012, to document serological changes and/or clinical signs indicative of intermittent HAV infections. Concurrent antibody screening of hepatitis patients at the community health-centers documented persistent HAV circulation. After 7.5 years a booster dose of an alum-adsorbed hepatitis A vaccine was administered.

Results*:* Between serosurvey and study start, 25 of initially seronegative children had contracted hepatitis A subclinically (anti-HAV levels >>8,000 mIU/mL). Immunisation resulted in the remaining children in anti-HAV levels of 25 to 572 mIU/mL. None of these children presented ever with hepatitis symptomatology. In 7 of them antibodies dropped and remained for years below detectable levels; in 1 case a serological breakthrough infection (7106 mIU/mL) was documented. Boosting resulted on average in a 44-fold increase of anti-HAV levels in 95 non-infected children followed-up until 2012.

Conclusions*:* In children one dose of virosomal hepatitis A vaccine initiates immune memory and may provide longterm protection in a hyperendmic setting.

ESPID-0408
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

OBSERVED VS. EXPECTED PCV13-TYPE IPD CASES IN CHILDREN AFTER THE DROP OF VACCINATION RATES IN MADRID REGION: HERACLES STUDY (2007-2014)

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Background and aims: Madrid regional immunization plan (RIP) included PCV7 in 2006 in children <24 months, subsequently switched to PCV13 in May-2010, later on excluded from the RIP for children born after May 1st 2012, resulting in a reduction of vaccination rates down to 67% in the target population. We evaluated the impact of PCV13 exlusion from the RIP in observed vs. expected cases of PCV13-type IPDs.

Methods: A prospective, laboratory-confirmed surveillance of all hospitalized IPDs in children <15 years (observed cases) was performed as previously presented. Expected cases (had PCV-13 not been excluded from RIP) were estimated using the evolution of observed cases since the introduction of PCV7/13 in a Triple Exponential Smoothing 'Holt-Winters" (TES-HW) time-series model.

Results: The evolution of PCV13-type IPD cases by period is shown in Table1. The evolution of observed vs. expected cases of PCV13-type IPD before and after PCV13 inclusion and exclusion from the RIP is presented in Graph1. The number of observed PCV13-type IPD cases in 2013-14 was 22, whereas 2 cases were expected according to TES-HW.

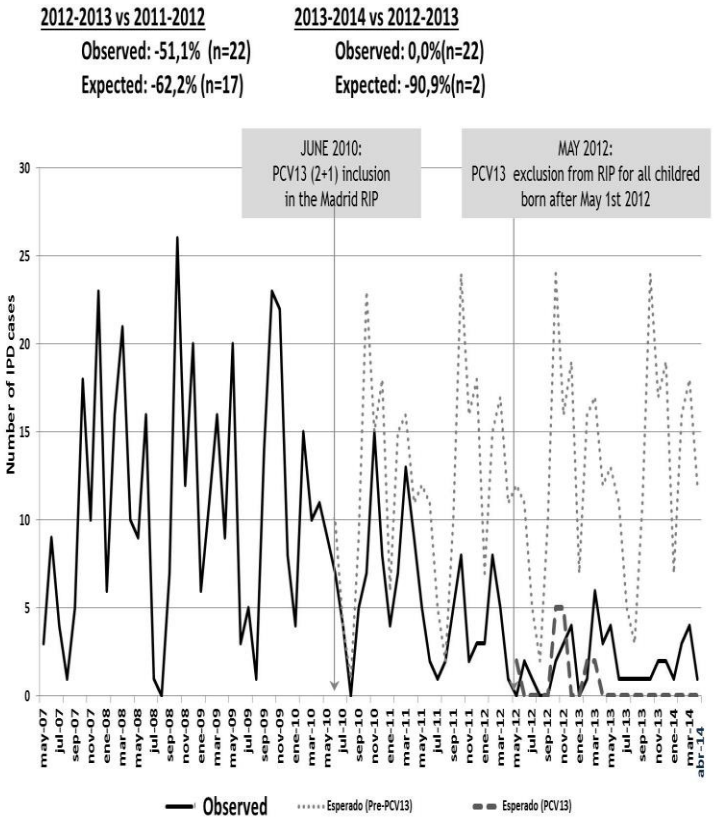
Conclusions: The drop of PCV13 vaccination rates down to 67% in the population target for vaccination in the period 2013/14 was accompanied by no further decrease of PCV13-type IPD cases compared to the previous period. A total of 20 avoidable cases of PCV13-type IPD in 2013/14 was estimated, had the

vaccine remained in the RIP.

TABLE 1: Evolution of PCV13-type IPD cases and vaccination rates by period

	PCV7 RIP			PCV13 RIP		PCV13 non-RIP	
	Period I (2007-'08)	Period II ('08-'09)	Period III ('09-'10)	Period IV ('10-'11)	Period V ('11-'12)	Period VI ('12-'13)	Period VII ('13-'14)
Vaccination rates	95%	95%	95%	95%	95%	82%	67%
PCV13-type IPD cases	125	134	135	89	45	22	22

GRAPH 1: Evolution of the observed vs. expected cases of PCV13-type IPD before and after PCV13 inclusion and exclusion from the RIP



ESPID-0614
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

TURICELLA OTITIDIS: A POTENTIAL PATHOGEN IN OTITIS MEDIA IN CHILDREN

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Background and aim: *Turicella otitidis* is a coryneform bacterium, member of the normal flora of the external ear canal. The aim of the study was to investigate the role of *T. otitidis* in the pathogenesis of otitis media, which is still unclear.

Methods: A total of 515 children (3 months to 14 years) with otitis media (acute otitis media - AOM: 402, otitis media with effusion – OME: 113) were included. Specimens for culture were obtained after tympanocentesis or from otorrhea fluid. The identification of *T.otitidis* was performed by colony morphology (whitish - creamy) on blood agar, Gram stain, resistance to erythromycin and clindamycin, DNAase production and APICoryne (numerical code 2100004). Susceptibility testing was performed by disk diffusion method in Muller Hinton agar with 5% sheep blood, using CLSI breakpoints for streptococci.

Results: Of the 515 specimens tested, 425 were positive for common pathogens (82.5%). *T.otitidis* was isolated from 64/425 specimens (15%). The isolation rates of *T.otitidis* in children with AOM was 19.5% (61/312), with exclusive growth 73.8% (45/61), and in OME was 2.7% (3/113), all in mixed culture. All isolates were resistant to erythromycin and clindamycin and susceptible to beta-lactams, gentamicin, rifampicin, vancomycin and teicoplanin. There was a variant resistance to cotrimoxazole and quinolones.

Conclusions: The high rates of *T.otitidis* isolation in the cultures of middle ear fluid indicate that this microorganism may play a causative role in the pathogenesis of otitis media. The identification of corynebacteria to the level of species, may elucidate its pathogenetic role in otitis media.

ESPID-0714
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RESPIRATORY SYNCYTIAL VIRUS ACTIVITY AND CLIMATE PARAMETERS: A 25-YEARS RETROSPECTIVE STUDY IN GREECE.

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Background and aims: The epidemic pattern of respiratory syncytial virus (RSV) infection during long periods and the factors that determine seasonality are not well studied. The aim of the study was to correlate the RSV epidemic activity with climate parameters in Athens, Greece, during 25 years.

Methods: This is a retrospective study of all hospitalized children in the major tertiary pediatric hospital in Greece who had an RSV test performed because of respiratory tract infection from 1/1989-12/2013. Data regarding temperature and humidity were obtained from the Hellenic National Meteorological Service.

Results: The annual RSV infection positivity rate during the study period varied between 5% and 40.72%. A peak of RSV activity was measured in years 2000-2003 and 2006 (>35% positive). RSV infection rate was higher during 2001-2013 (27.19%) than the previous decade 1989-2000 (19.57%) ($p < 0.005$). The time period from December to April was found as the RSV infection season in our area with higher incidence during January through March. Regarding climate conditions, a statistically significant positive association was found between monthly RSV activity and mean monthly relative humidity (rho=0.66, p-value=0.02), whereas it was found a negative correlation with mean monthly temperature (rho=-0.81, p-value=0.002).

Conclusions: Mean temperature and relative humidity are main climatic factors that strongly correlate with annual and intra-annual patterns of RSV activity. The model presented is a step toward predicting annual RSV epidemics using weather forecast data.

ESPID-0766
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ATYPICAL PRESENTATION OF HUMAN BOCAVIRUS: SEVERE RESPIRATORY TRACT INFECTION COMPLICATED WITH ENCEPHALOPATHY

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Background: Human bocavirus (HBOV) has been reported as a worldwide distributed respiratory pathogen since 2005. It has also been associated with encephalitis recently. This retrospective study aimed to present clinical features of HBOV infections in children with respiratory symptoms and describe unexplained encephalopathy in a subgroup of these patients.

Methods: Results of 1143 pediatric nasal samples from mid-December 2013 to July 2014 were reviewed for detection of HBOV. A real time reverse transcriptase polymerase chain reaction based multiplex kit was used for detection of 21 respiratory pathogens. Medical records of HBOV detected patients were retrospectively analyzed.

Results: HBOV was detected in 30 specimens from 30 patients (2,6%). Co-infection was present in 23,3% of samples. Median age was 14 months (5-80 months). Clinical diagnoses were upper respiratory tract infection (n=10), bronchopneumonia (n=9), acute bronchiolitis (n=5), pneumonia (n=4), acute bronchitis (n=1) and asthma execarbation (n=1). Hospitalization was required in 16 (53,3%) patients and 10 (62,5%) of them admitted to pediatric intensive care unit (PICU). Intractable seizures developed in 4 patients while mechanically ventilated on the 2nd to 3rd days of PICU admission. No spesific reason for encephalopathy was found after a thorough investigation. No mortality was observed but 2 patients were discharged with neurological sequela.

Conclusion: HBOV may lead to respiratory infections in a wide spectrum of severity. This report indicates its potential to cause severe respiratory infections requiring PICU admission and highlights possible clinical association of HBOV and encephalopathy, which developed during severe respiratory infection.

ESPID-0844
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

VIRAL PATHOGENS OF ACUTE RESPIRATORY INFECTIONS (ARI) IN HOSPITALIZED GERMAN CHILDREN, 2013-2014

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Background
In Germany, the viral aetiology of ARI is mostly unknown. We investigated viral pathogens in children hospitalized with ARI at the University of Würzburg from July 2013 to June 2014.

Methods
Respiratory specimens of children < 17 years of age, hospitalized with ARI symptoms, were tested by multiplex PCR for 19 viral pathogens (FTD® Respiratory pathogens 21, Fast Track Diagnostics, Luxembourg).

Results
A total of 457 ARI patients (49.7% upper ARI; 50.3% lower ARI) with a median age of 2.0 years (IQR 1.1-4.5) were enrolled. In 310 (68%) ARI patients, at least one virus could be detected: rhinovirus (RhV) 41.6%; adenovirus (AdV) 18.7%; human bocavirus (hBoV) 15.8%; parainfluenzavirus (PIV) 1-4 13.2%; coronavirus (CoV) NL63/ OC43/ HKU1/ 229E 12.9%; human metapneumovirus (hMPV) 12.6%; RSV A/B 10.3%; rhino-/enterovirus 6.1%; influenzavirus (IV) A(H1)/A(H3)/B 4.8%; enterovirus (EV) 2.6%; parechovirus (PeV) 0.6%. There were 69.7% viral mono-infections and 30.3% viral co-infections (2 viruses: 23.9%, 3 viruses: 4.2%, 4 viruses: 1.6%, 5 viruses: 0.6%). The highest proportion of mono-infections was found for IV (93% of 15 patients), hMPV (67% of 39 patients) and RhV (58% of 129 patients). The highest proportion of viral co-infections showed hBoV (73% of 49 patients) followed by CoV (73% of 40 patients).

Conclusions
Viral pathogens could be detected in a large part of children hospitalized with ARI, with RhV and AdV accounting for most cases. Simultaneous detection of two or more viruses occurred in one third of these patients, suggesting a high frequency of viral co-infections.

ESPID-0873
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

STREPTOCOCCUS PYOGENES EMM TYPES AND CLUSTERS DURING A 7-YEAR PERIOD (2007-2013) IN PHARYNGEAL AND NON-PHARYNGEAL PEDIATRIC ISOLATES

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Background and aims: *Group A streptococcus* (GAS) is an important cause of morbidity and mortality worldwide. Surveillance of *emm* types has important implications as they can serve as baseline information for possible implementation of vaccination.

Methods: A total of 1282 pharyngeal (84%) and non-pharyngeal (16%) isolates, collected during a 7-year period (2007-2013) were *emm* typed, according to CDC protocol.

Results: Thirty five different GAS *emm* types including 14 sub-types were identified. The most prevalent *emm* types identified were 1(16.7%), 12(13.6%), 77(10.9%), 4(10.8%), 28(10.4%), 6(6.8%) 3(6.6%), 89(6.6%) and accounting for 82.3% of total isolates. Rheumatogenic *emm* types comprised 16.3% of total isolates. *emm* types 12,4 and 77 were more prevalent among pharyngeal isolates and *emm* types 1,89,6,75 and 11 among non-pharyngeal. The *emm* types identified belong to 13 *emm*-clusters and the 8 most prevalent clusters comprise 97% of all isolates. Prevalence of *emm*1 declined from 19.8% to 11.9%($p=0.01$), *emm*4 from 14.4% to 8.6%($p=0.04$) and *emm*77 from 15.5% to 2.7%($p<0.001$). In contrast prevalence of *emm*89 increased from 1.3% to 16.2%($p<0.001$). Proposed 30-valent GAS vaccine, currently in preclinical studies, encompasses 97.2% of *emm* types detected in our study and 97.4% of erythromycin resistant strains. In addition, it includes 93.3% of *emm* types involved in bacteremia.

Conclusions: A much greater diversity of GAS *emm* types was identified in our area than previously described. Seasonal fluctuations and introduction of new *emm* types was observed. However, the majority of the circulating *emm* types are included in the 30-valent vaccine, currently in preclinical studies.

ESPID-1046
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ENTEROVIRUS D68 (EVD-68) PNEUMONIA IN CHILDREN IN ITALY

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Background and aims: Recently, a number of children infected by EV-D68 with severe respiratory illness and associated neuromuscular problems have been described in USA and Canada. It was suggested that EV-D68 might be more virulent than expected. Here, 4 cases of community-acquired pneumonia (CAP) due to EV-D68 identified in Milan, Italy, are described.

Methods: All the nasopharyngeal samples collected in children hospitalized for radiographically-confirmed CAP between July, 1st, and December 31st, , 2014,were tested for EV-D68 by a specifically developed PCR method. All the data concerning clinical course and outcome of the disease were recorded.

Results: A total of 176 nasopharyngeal swabs collected in children admitted to the hospital were evaluated. Among them, four (2.3%), all obtained in females seen during October, were positive for EV-D68. Three of the children, aged 5 months, 9.5 and 11.2 years, had a moderate disease, requiring hospitalization with discharge in 7 days. The fourth child, aged 5 years and who had a mitochondrial disease, showed a very severe disease, with progressive reduction of oxygen saturation below 90% requiring admission to PICU and mechanical ventilation: she died because of respiratory failure in 18 days.

Conclusions: The 4 cases of CAP due to EV-D68 identified in Milan, Italy, indicate that EV-D68 had spread outside North America. The severity of respiratory involvement in one child seems to confirm the unexpected virulence of this virus. Surveillance of its circulation and information about changes in antigenicity are essential to understand its role and guarantee efficient responses in the future.

ESPID-1081
MODERATED E-POSTER WALK 8 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

Pneumococcal strains from children with otitis media and pneumonia in Brasov, Romania: a five-year prospective surveillance

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Background: Streptococcus pneumoniae (Pnc) remains a leading cause of mortality in children. In Romania, Pnc is commonly antibiotic resistant, restricting treatment options. We conducted five-year surveillance between 2009-2014, on antibiotic resistance pattern of Pnc strains isolated from mucosal and sterile sites, in children.

Patients and methods: This was a prospective study looking at Pnc isolates from nasopharynx, sputum, middle ear fluid, pleural fluid, conjunctiva and blood. Antibiotic susceptibility and serotyping were performed as previously described.

Results: Of 250 strains sent for serotyping, tests on 130 were so far completed. The isolates were obtained from laryngo-tracheal secretions (32%), nasal swabs (28%), middle ear fluid (21%), blood (3%) and pleural fluid (

Conclusion: In Brasov, Romania clinical Pnc isolate are frequently antibiotic resistant. However, most of resistance is covered by PCVs, especially PCV13.

ESPID-0258
MODERATED E-POSTER WALK 9 - EPIDEMIOLOGY AND RESPIRATORY DISEASE

ECONOMIC EVALUATION OF THE PAEDIATRIC INFLUENZA IMMUNISATION PROGRAMME COMPARED TO OTHER PAEDIATRIC IMMUNISATION PROGRAMMES: A SYSTEMATIC REVIEW

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Background: Similar to otherinterventions, assessments of vaccination programmes in the form ofcost-effective (CE) evaluations are based on value to society. Althoughchallenges and limitations in disease assessment exist, this review discussesliterature comparisons across immunisation programmes with focus onpaediatric influenza.

Methods: This review followed the Drummondcriteria to compare economic value of paediatric influenzavaccinations (PIV) to other interventions. A preselected contextualcomparison to other paediatric vaccines (PV) (rotavirus, varicellazoster, pneumococcus, meningococcal disease [MD], hepatitis B and humanpapillomavirus [HPV]) of economic impact was conducted.

Results: The review provided 45 economic evaluations (EE) – 9 for PIV and 36 PV forassessment. Studies demonstrated a CE/cost-saving strategy with PIVfrom a EU5 and US perspective; point estimates for cost/quality adjusted lifeyears from dominance (cost saving with more effect) to £50,000 have been reported.Herd immunity (HI) contributes significantly to influenza infectionsand mortality averted. EE forselected PV are comparable to influenza programs.

Indication	Minimum cost/QALY (£)	Maximum cost/QALY (£)
Influenza	Cost-saving	50,000
Rotavirus	13,000	120,000
Pneumococcus	Cost-saving	86,000
Meningococcal disease (MD)	23,000	170,000
Hepatitis B	Cost-saving	100,000
Human papillomavirus (HPV)	3,000	30,000
Varicella zoster	5,000	110,000

Conclusions: Independentof perspective and type of analysis, the economic impact of paediatricinfluenza immunisation is influenced by vaccine efficacy, vaccinationcoverage, costs, and largely by HI – many EE include the indirect effects.Influenza vaccination offers protection against infections with cost-effectivenesscomparable to other PV: particularly HPV and pneumococcus.

ESPID-0469
MODERATED E-POSTER WALK 9 - EPIDEMIOLOGY AND RESPIRATORY DISEASE

ACUTE FLACCID PARALYSIS IN THE COURSE OF ENTEROVIRUS D68 ASSOCIATED PNEUMONIA

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Background and aims. Human Enterovirus D68 (EV-D68) is known to be associated with mild to severe respiratory infections. Recent reports in the USA and Canada of acute flaccid paralysis (AFP) in children with detection of EV-D68 in respiratory samples have raised concerns about the etiological role of this EV type in severe neurological disease. We report the first European AFP case occurring in the course of EV-D68 infection.

Patient. The patient was a previously healthy 4 years old boy with up to date immunization against poliomyelitis.

Results. The clinical course was marked by meningitis, a severe respiratory infection requiring mechanical ventilation, and a transient acute myocarditis. AFP occurred 7 days after. Spinal MRI showed enhancement of the ventral nerve roots of the cauda equina. Only the motor pathway was stricken.Cerebrospinal fluid showed pleiocytosis with a majority of lymphocytes. Screening for neurotropic viruses, including EV and bacteria was negative. EV-D68 was detected in nasopharyngeal aspirates, broncho-alveolar fluid and a stool specimen collected in the first 7 days of the onset of AFP. Plasmapheresis and intravenous immunoglobulin were implemented. After 4 months, the recovery is still incomplete with deficit of the right upper limb and of the axial tone. Ventilatory support remains partially necessary.

Conclusion. There are increasingly numerous reportsof polio-like illness in the US(as of January 5, 103 cases; only one child has recovered).AFP surveillance is important to detect similar cases and alert public health instances but etiological diagnosis still remain challenging.

ESPID-0471
MODERATED E-POSTER WALK 9 - EPIDEMIOLOGY AND RESPIRATORY DISEASE

IMPACT OF UNIVERSAL VERSUS TARGETED VACCINATION POLICY ON CHILDHOOD INFLUENZA VACCINATION RATES IN CHILDREN WITH ASTHMA IN THE UNITED KINGDOM

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Background: The 2013/2014 extension of the UK's influenza immunisation programme to all 2–3 year-olds provides an opportunity to examine the effect of universal versus targeted vaccination policy on vaccination rates in children with high-risk prevalent conditions, particularly asthma.

Methods: All children aged 2–17 years on September 1, 2012 (season 2012/13) or September 1, 2013 (season 2013/14) with ≥12 months' medical history in the UK Clinical Practice Research Datalink (CPRD) were included in this analysis.

Information on administration of influenza vaccine was retrieved from immunisation, clinical, and therapy records between September 1 and February 28 of each season. High-risk conditions were defined using definitions adapted from PRIMIS specifications (University of Nottingham). Presence of asthma was based on asthma diagnosis with either inhaled steroid prescription or oral steroid prescription/record of Accident & Emergency (A&E) visit for asthma in the 12 months prior to September 1.

Results: In total, 807,277 and 747,597 children were included for the 2012/2013 and 2013/2014 seasons, respectively. During 2013/2014, 6.5% (n=48,719) children presented with ≥1 high-risk condition; 4.7% (n=35,089) had asthma. These proportions were similar in 2012/2013: 6.7% (n=54,251) and 4.9% (n=39,820), respectively.

Table 1: Vaccination rate by age category in children with any high-risk condition and asthma

	Any high-risk condition		Asthma	
Age (years)	Season 12/13, %	Season 13/14, %	Season 12/13, %	Season 13/14, %
2 to 3	41.0	60.8	43.2	62.2
4 to 8	41.6	45.0	43.3	47.2
9 to 17	41.0	42.4	42.4	44.1

Conclusions: The increase in the vaccination rate for all children with high-risk conditions including asthma – in 2–3 year olds but also, to a lesser extent, in 4–17 year olds – suggests that universal influenza vaccination policy can increase uptake for children with asthma who are most at risk from influenza.

This study was sponsored by MedImmune, the biological division of AstraZeneca.

ESPID-0529
MODERATED E-POSTER WALK 9 - EPIDEMIOLOGY AND RESPIRATORY DISEASE

INFLUENZA VACCINATION OF CHRONICALLY ILL CHILDREN THROUGH A TERTIARY-BASED VACCINATION CLINIC: WHAT ABOUT USING A LIVE-ATTENUATED INFLUENZA VACCINE?

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Background:
Children with underlying chronic conditions should be vaccinated yearly against influenza yet vaccination coverage remains low. For the last 3 influenza seasons, we set-up an influenza vaccination clinic for this at-risk population and their household members located in a tertiary care hospital and will describe vaccine preference.

Methods:
The clinic offered both trivalent inactivated (TIV) and live-attenuated vaccines (LAIV). A pre-piloted questionnaire was used to understand vaccine type preference.

Results:
In 2014, 2769 people were vaccinated at the clinic – a 2.6-fold increase compared to previous years – 1379 (49.8%) were children with an underlying chronic condition. Of the 1208 children for whom we have detailed information, 582 received LAIV as recommended by the Quebec Immunization Committee: 67.4% of children in whom LAIV was not contra-indicated. Of interest, 10% (35/350) of children who had received LAIV last year chose against LAIV this year; mean age 11.2 years. The prolonged feeling of runny nose (4/19) was the main stated reason for not choosing LAIV. Of all children without contra-indication for LAIV, the main reason for not choosing LAIV was an active choice to receive an injection (25/61= 41%), as the route of vaccination.

Conclusions:
A designated influenza clinic located in a tertiary care hospital can facilitate yearly

influenza vaccination of children with a chronic illness and their household members. LAIV is still preferred when not contraindicated. However, surprisingly, a significant proportion of patients and parents made an active choice for the injection route of administration.

ESPID-0679
MODERATED E-POSTER WALK 9 - EPIDEMIOLOGY AND RESPIRATORY DISEASE

PRACTICE-LEVEL DESCRIPTION OF PRIMARY CARE OUTCOMES FOR THE ASSESSMENT OF INFLUENZA DISEASE BURDEN IN CHILDREN IN ENGLAND

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Aims: Influenzais associated with increased incidence of respiratory illnesses. This studydescribes the distribution of practice-level incidence-rates (IRs) of seveninfluenza-related disorders in children ascertained through to generalpractitioner (GP) practices in England, where childhood influenza vaccinationimplementation is currently being rolled out in increasing age groups.

Methods: Demographicand diagnoses data on 4,341,884 subjects (including 821,227 children) across323 practices was retrospectively obtained for four consecutive influenzaseasons (2010-2014) from the Clinical Research Practitioners Datalink. A seasonwas defined from September-April, and diagnoses by Disease Read codes. The distributionof crude practice-level IRs was summarized by means, medians, interquartileranges [IQR], and coefficient of variation [CV]) across practices for eachdiagnosis and each season. IRs for the total population were also described.

Results: Table 1describes key characteristics of the study population. Table 2 and Table 3describe the distributions of IRs of influenza-related diagnoses for childrenand the total population respectively. Across seasons, similar variationpatterns are observed for all diagnoses in both population groups, with areduced incidence observed during the 2013-2014 season.

Conclusions: Trends in IRs for all diagnoses areconsistent with Public Health England annual influenza reports, and support theuse of such retrospective study designs to assess/inform childhood vaccinationimpact in coming years. Future studies will require careful handling ofinter-practice diagnosing variations.

Table 1: Patient characteristics

Practice Mean % (SD) Practice median % (IQR: Q1-Q3)	**2010-2011** **(n=1,155,030)**	**2011-2012** **(n=1,144,394)**	**2012-2013** **(n=1,099,475)**	**2013-2014** **(n=942,985)**	**All seasons** **(n=1,355,350)**
% male	**44.12 (1.62)** 43.97 (1.8)	**44.12 (1.52)** 44.07 (1.72)	**44.25 (1.45)** 44.16 (1.6)	**44.36 (1.39)** 44.26 (1.6)	**44.29 (1.51)** 44.11 (1.6)
Age 0-<6 months	**0.01 (0.02)** 0.00 (0)	**0.01 (0.02)** 0.00 (0.02)	**0.01 (0.01)** 0.00 (0)	**0.01 (0.02)** 0.00 (0)	**0.01 (0.02)** 0.00 (0.01)
Age 6 months - <2 years	**1.47 (0.49)** 1.43 (0.6)	**1.80 (0.61)** 1.74 (0.73)	**1.85 (0.60)** 1.80 (0.68)	**1.55 (0.51)** 1.51 (0.59)	**3.69 (1.37)** 3.72 (1.63)
Age 2 years - <4 years	**2.91 (0.91)** 2.79 (1.02)	**3.25 (0.95)** 3.13 (1.12)	**3.73 (1.13)** 3.67 (1.2)	**4.11 (1.21)** 4.04 (1.3)	**3.53 (1.08)** 3.42 (1.25)
Age 4 years - <5 years	**1.24 (0.40)** 1.20 (0.46)	**1.42 (0.48)** 1.35 (0.53)	**1.59 (0.49)** 1.56 (0.58)	**1.67 (0.52)** 1.65 (0.57)	**1.43 (0.48)** 1.38 (0.56)
Age 5 years - <11 years	**5.57 (1.54)** 5.36 (1.73)	**6.04 (1.65)** 5.81 (1.87)	**6.64 (1.85)** 6.39 (2.02)	**7.34 (2.04)** 7.14 (2.26)	**5.87 (1.67)** 5.67 (1.94)
11 years - <18 years	**5.70 (1.26)** 5.70 (1.6)	**5.74 (1.25)** 5.67 (1.51)	**5.75 (1.25)** 5.71 (1.37)	**5.76 (1.25)** 5.71 (1.48)	**5.18 (1.22)** 5.09 (1.49)
% patients classified as high risk of developing influenza related complications (including adults)	**47.77 (7.60)** 47.22 (9.18)	**46.85 (7.01)** 46.52 (9.15)	**47.33 (7.21)** 47.00 (9.02)	**47.81 (7.12)** 47.79 (9.2)	**55.66 (6.94)** 55.38 (9.65)

Table 2: IR and inter-practice CV of Influenza related GP diagnoses for children (<18 year old)

Mean IR[1](SD) *Median (IQR: Q1-Q3)* CV	2010-2011 (n=197,189)	2011-2012 (n=210,950)	2012-2013 (n=217,728)	2013-2014 (n=195,860)	All seasons (n=821,227)
Total	**42079 (10388)** *41870 (11352)* 0.247	**34193 (6784)** *34701 (8285)* 0.198	**33329 (7708)** *33125 (8066)* 0.231	**27583 (5955)** *27436 (8047)* 0.216	**34775 (9521)** *34088 (11210)* 0.274
Influenza like illness	**250.4 (510.6)** *0.0 (298.5)* 2.039	**67.2 (198.3)** *0.0 (0)* 2.951	**108.1 (532.1)** *0.0 (86)* 4.922	**74.1 (460.8)** *0.0 (0)* 6.219	**129.8 (450.9)** *0.0 (113.6)* 3.474
Upper respiratory tract infection	**20488 (8773)** *19886 (10727)* 0.428	**16553 (6446)** *16207 (8235)* 0.389	**16945 (7058)** *16136 (8245)* 0.417	**13233 (5485)** *12605 (6975)* 0.415	**17043 (7574)** *16235 (9399)* 0.444
Lower respiratory tract infection	**5720 (3723)** *5071 (4750)* 0.651	**4617 (2866)** *4071 (3679)* 0.621	**4200 (2923)** *3638 (3356)* 0.696	**3437 (2551)** *2767 (2715)* 0.742	**4571 (3187)** *3880 (3829)* 0.697
Other acute respiratory tract infection	**12199 (4642)** *11301 (6100)* 0.381	**10259 (3753)** *9823 (4898)* 0.366	**9529 (3481)** *9333 (4257)* 0.365	**8891 (3276)** *8385 (4261)* 0.369	**10329 (4062)** *9843 (4924)* 0.393
Pneumonia	**141.0 (214.9)** *0.0 (237)* 1.524	**106.8 (191.7)** *0.0 (164.2)* 1.795	**65.6 (161.0)** *0.0 (91.7)* 2.454	**50.5 (90.9)** *0.0 (83.8)* 1.8	**94.2 (178.5)** *0.0 (144.1)* 1.895
Otitis media	**8282 (3719)** *7869.6 (4693)* 0.449	**6366 (2884)** *6140 (4340)* 0.453	**6218 (2819)** *6166 (3635)* 0.453	**4872 (2174)** *4935 (3059)* 0.446	**6546 (3232)** *6276 (4144)* 0.494
Asthma exacerbation	**2281 (1502)** *1996 (1636)* 0.659	**2016 (1387)** *1706 (1529)* 0.688	**1709 (1147)** *1451 (1297)* 0.671	**1548 (1117)** *1277 (1207)* 0.722	**1915 (1341)** *1626 (1439)* 0.7

[1]Incidence rates calculated as per 100,000 population

Table 3: IR and inter-practice CV of Influenza related GP diagnoses – Total population

Mean IR (SD)[1] *Median (IQR: Q1-Q3)* CV	**2010-2011 (n=1,155,030)**	**2011-2012 (n=1,144,394)**	**2012-2013 (n=942,985)**	**2013-2014 (n=1,355,350)**	**All seasons (n=4,341,884)**
Total	**23181 (6473)** *23510 (7812)* 0.279	**20148 (5096)** *20495 (6268)* 0.253	**20840 (5759)** *20980 (6043)* 0.276	**17881 (4492)** *17633 (5653)* 0.251	**20683 (5862)** *20609 (7173)* 0.283
Influenza like illness	**284.9 (515.8)** *144.1 (238.6)* 1.81	**98.1 (198.2)** *41.0 (111.3)* 2.02	**155.0 (402.5)** *57.1 (146)* 2.597	**87.4 (173.4)** *39.1 (91.7)* 1.984	**162.0 (370.1)** *64.3 (168.1)* 2.285
Upper respiratory tract infection	**8258 (4269)** *7909 (4967)* 0.517	**7118 (3561)** *6580 (4098)* 0.5	**7606 (4057)** *6916 (4593)* 0.533	**6283 (3119)** *5804 (3883)* 0.496	**7379 (3873)** *6720 (4549)* 0.525
Lower respiratory tract infection	**7114 (3586)** *6733 (4951)* 0.504	**6062 (2851)** *5989 (3929)* 0.47	**6228 (3177)** *5929.5 (4305)* 0.51	**5227 (2723)** *4891 (3517)* 0.521	**6219 (3193)** *5900 (4288)* 0.513
Other acute respiratory tract infection	**6623 (2290)** *6368 (2928)* 0.346	**5963 (2027)** *5846 (2902)* 0.34	**5930 (2061)** *5724 (2721.2)* 0.348	**5413 (1805)** *5261 (2473)* 0.333	**6022 (2109)** *5757 (2831)* 0.35
Pneumonia	**195.5 (161.7)** *169.9 (178.7)* 0.827	**183.1 (170.7)** *159.5 (166)* 0.932	**165.0 (164.7)** *149.7 (152.1)* 0.998	**139.7 (156.4)** *112.3 (133.5)* 1.12	**172.9 (164.8)** *147.8 (162.3)* 0.953
Otitis media	**2101 (997.6)** *2006 (1137)* 0.475	**1765 (849.8)** *1681.6 (984.3)* 0.481	**1804 (851.7)** *1774 (1008)* 0.472	**1515 (710.4)** *1492.7 (893.7)* 0.469	**1815 (890.9)** *1735 (1061)* 0.491
Asthma exacerbation	**1467 (1061)** *1238 (885.6)* 0.723	**1371 (1069)** *1065 (910.8)* 0.78	**1362 (1019)** *1063 (979.3)* 0.748	**1193 (852.1)** *975.7 (770.8)* 0.714	**1358 (1015)** *1092 (894)* 0.748

[1]Incidence rates calculated as per 100,000 population

ESPID-0814
MODERATED E-POSTER WALK 9 - EPIDEMIOLOGY AND RESPIRATORY DISEASE

REVIEW OF INFLUENZA B BURDEN IN LATIN AMERICAN (LATAM) REGION DURING THE PERIOD POST PANDEMIC, 2010-2014.

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Background and aims: New quadrivalent influenza vaccines (QIV) were recently licensed in LatAm countries, where there is limited information about influenza B burden. The aim of this study is to review information about influenza B in LatAm countries during the last 5 years.

Material and methods: An extensive search for published information in PUBMED, SCIELO, WHO, PAHO and Latin American Ministry of Health sites from January/2010 to December/2014 was performed. We analyzed data on influenza virus type/subtypes and lineage B by country and age groups.

Results: There was a large variation of influenza A and B strains circulation in Latin American countries. On average, influenza B was confirmed in about 20% of ILI cases, with a disproportional impact in children older than 5, adolescents and young adults. Limited information about mismatch in the LatAm region is available, but data from Brazil, Mexico, and Argentina were similar to those observed in US and Europe. Recently, 10 LatAm countries introduced information about B lineages in the PAHO website. In 2014, both lineages B were detected in at least 4 LatAm countries.

Conclusion: Influenza B imposes a heavy burden in Latin America. As influenza B mismatch with TIV cannot be anticipated, it is expected that the introduction of QIV

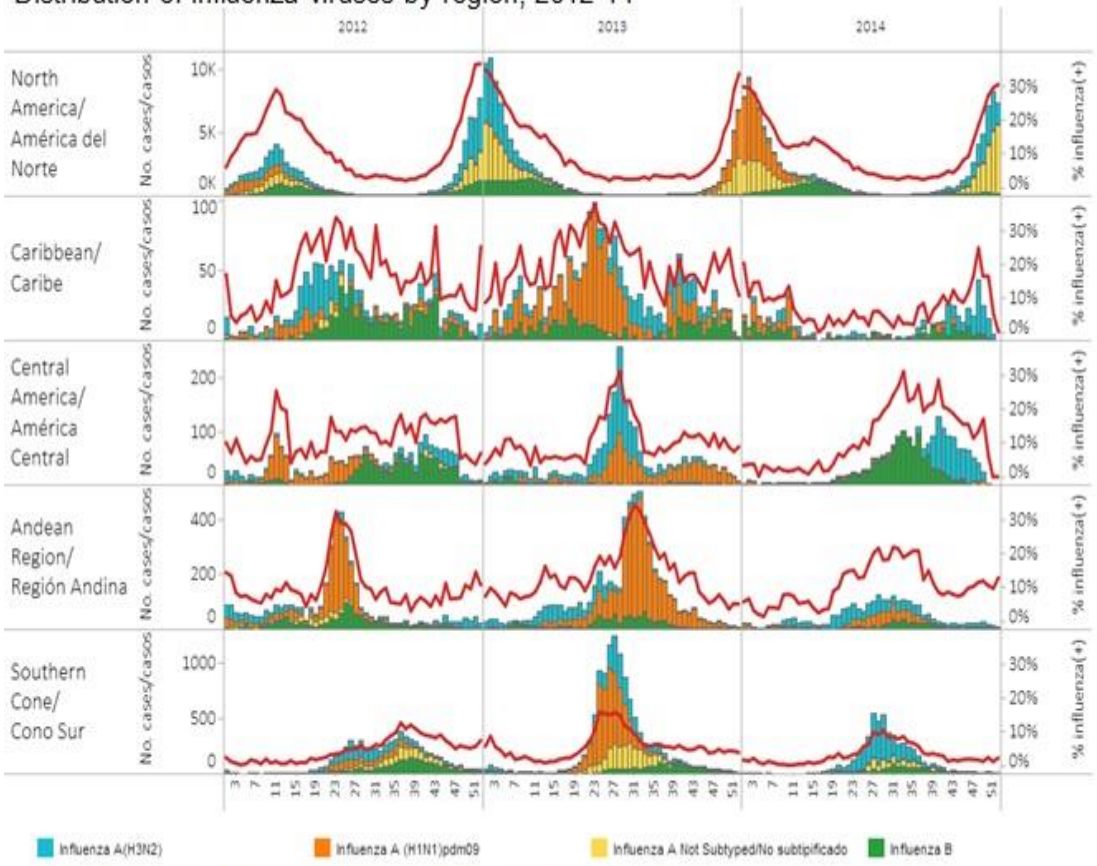
should be more effective as compared to trivalent influenza vaccines.

Figure 1 - Distribution of influenza virus by types and subtypes in selected Latin American countries from 2010 to 2014. *

Country	A (?)	%	A(H1N1)	%	A(H3N2)	%	B	%	Total
Argentina	**6,015**	**37.3**	3,796	23.5	3,273	20.3	3,058	18.9	16,142
Brazil	135	1.3	**4,726**	**47.2**	2,942	29.2	2,254	22.3	10,092
Chile	593	5.9	2,832	28.1	**5,274**	**52.3**	1,961	19.4	10,032
Colômbia	323	5.2	1874	30.0	1,149	18.5	**2,871**	**46.2**	6,217
Costa Rica	**1,141**	**50.0**	1,516	46.1	1,118	34.0	604	18.4	3,288
Cuba	48	1.5	**1,543**	**47.2**	1,060	32.5	613	18.8	3,264
Ecuador	181	5.8	**1,724**	**55.5**	804	25.9	399	12.8	3,108
El Salvador	39	3.1	323	25.2	427	33.8	**424**	**37.5**	1,263
Guatemala	**13,980**	**48.8**	8,444	35.5	453	1.9	908	3.8	23,785
Jamaica	8	2.5	67	21.1	108	34.1	**134**	**42.3**	317
Honduras	14	1.2	**453**	**37.7**	401	33.4	333	27.7	1,201
Martinica	5	3.1	38	23.9	**73**	**45.5**	43	27.0	159
México	1,821	7.4	**13,238**	**53.8**	6,663	27.1	2,860	11.6	24,582
Nicarágua	-	-	1,075	27.7	**1,578**	**40.8**	1,219	31.5	3,872
Panamá	12	1.3	174	19.1	**420**	**46.2**	303	33.8	909
Paraguay	164	4.4	684	18.3	**2,229**	**54.4**	851	22.8	3,728
Peru	361	7.8	**2,116**	**46,9**	1,201	26.6	838	18,6	4,516
Dominicana	1	0.2	**329**	**50.8**	193	29.9	125	19.3	648
Uruguay	8	0.8	320	33.6	**378**	**39.7**	245	25.8	951

Note: average numbers and percentages. Included only countries with information on PAHO website for all the period. Data on http://ais.paho.org/phip/viz/ed_flu.asp . Access 22 Dec/2014

Distribution of influenza viruses by region, 2012-14



PAHO. Distribution of influenza viruses by region, 2012-14 [updated 2014 Jan 14; cited 2014 Jan 14]. Available from: http://ais.paho.org/phip/viz/ed_flu.asp

ESPID-0140
MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

REACTOGENICITY OF A FIFTH DOSE OF 4CMENB ADMINISTERED TO 4-YEAR-OLD CHILDREN.

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Background: The licensed 4CMenB vaccine has demonstrable immunogenicity against a range of serogroup B meningococcal strains. However, high rates of systemic reactions, especially fever have been observed when administered concomitantly with routine infant vaccines. We assessed reactogenicity of 4CMenB following a fifth dose boost at 4 years of age.
Methods: Participants who received a variety of 3 dose infant priming schedules (2,3,4 or 2,4,6 months with routine vaccines; or 2,4,6 separate from routine vaccines) followed by a booster at 12, 18 or 24 months were enrolled and randomised to a vaccination or non-vaccination group. Solicited reactions were collected for 7 days after vaccination.
Results: Three hundred and fifty-four participants received a booster dose of the vaccine. The majority of participants (90 - 100%) experienced at least one solicited reaction. The most commonly reported solicited local and systemic symptoms were transient injection site pain, which was experienced by 84 - 100% (severe in 11 - 32%), and irritability (experienced by 47 - 74%, severe in 0 - 12%). Fever was seen in 4 - 21% of participants and was severe (≥40) in 2%. No serious adverse events were attributed to the vaccine.
Conclusion: Reactogenicity to a booster dose at 4 years is comparable, irrespective of priming and initial boosting schedules. Majority of children experience injection site

pain. Fever rates in this age group are lower than has been reported for infants. Expected symptoms should be discussed with parents at the time of vaccination.

ESPID-0141
MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

ANTIBODY PERSISTENCE TO FOUR YEARS OF AGE FOLLOWING A FOURTH DOSE OF 4CMENB ADMINISTERED TO TODDLERS.

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Background: A serogroup B meningococcal vaccine (4CMenB) is licensed for infant immunisation. We assessed (i) antibody persistence to 4 years of age following a variety of 3 dose infant priming schedules (2,3,4 or 2,4,6 months with routine vaccines or 2,4,6 separate from routine vaccines) followed by a booster at 12, 18 or 24 months and (ii) immunogenicity of a fifth dose of 4CMenB administered at 4 years.

Methods: Follow-on and age matched 4CMenB–naive participants had blood samples at four years for determining human complement serum bactericidal activity (hSBA) against four reference strains: H44/76 (for vaccine component fHbp), NZ98/254 (PorA), 5/99 (NadA) and M10713 (NHBA). A repeat blood sample was taken following a dose of 4CMenB administered to all vaccine-naïve participants and a subset of follow-on participants.

Results: A total of 805 children were enrolled: 354 (vaccination group), 242 (non-vaccination group) and 209 (controls). At baseline, the proportion of follow-on participants with hSBA titers ≥1: 5 was: 12 - 35% (H44/76); 8 - 12% (NZ98/254); 90 - 100% (5/99); and 52 - 81% (M10713). For vaccine naïve participants these were 0%, 0%, 5% and 60% respectively. Following a dose of 4CMenB this increased to 97-100% (H44/76), 80 - 95% (NZ98/54), 100% (5/99) and 84 – 100% (M10713) compared to 71%, 24%, 90% and 77% respectively.

Conclusion: A similar pattern of hSBA waning and response to a booster dose at 4 years is seen regardless of the infant priming schedule and toddler boosting time point.

MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

IMMUNOGENICITY AND SAFETY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE FORMULATED IN MULTI-DOSE VIALS (MDV) GIVEN WITH ROUTINE VACCINATION IN HEALTHY INFANTS

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Background
In developing countries, vaccine provision in MDV would optimize vaccine delivery and sustainable coverage. An MDV formulation of PCV13 containing the preservative 2-phenoxyethanol (2-PE) was developed. This trial compared the immunogenicity, safety, and tolerability of MDV to the current PCV13 without 2-PE in single-dose syringes (SDS).
Methods
500 healthy Gambian infants were randomized (1:1) to receive either 3 doses of PCV13 as MDV or SDS at 2, 3 and 4 months of age. Serotype-specific antipneumococcal antibody responses and opsonophagocytic activity ([OPA]; subset) were measured at 5 months of age. Noninferiority was declared if the lower bound of the 97.5%CI for the difference (MDV-SDS) in proportions of subjects achieving IgG concentrations ≥0.35µg/mL (primary endpoint) was greater than -10%. Reactogenicity and adverse events were assessed.
Results
489 subjects (MDV: n=245; SDS: n=244) were evaluable for immunogenicity. 1 month after last dose, non-inferiority of the MDV was determined for all serotypes as measured by percent response above the defined threshold. IgG geometric mean concentration (GMC; coprimary endpoint) also demonstrated non-inferiority of MDV; OPA supported these findings. Safety and tolerability were comparable in both groups.

Difference in proportion (MDV – SDS) of participants achieving pneumococcal IgG antibody concentration ≥ 0.35 µg/mL at age 5 months							
Serotype	1	3	4	5	6A	6B	7F
*Difference	- 0.8	- 0.8	0.0	- 1.2	- 1.2	0.0	- 0.4
97.5% CI	- 3.4, 1.2	- 3.7, 1.6	- 2.3, 2.4	- 5.4, 2.8	- 5.3, 2.6	- 4.7, 4.7	- 2.7, 1.6
Serotype	9V	14	18C	19A	19F	23F	
*Difference	- 0.4	- 0.8	1.2	0.8	- 0.4	0.0	
97.5% CI	- 3.8, 2.8	- 4.3, 2.5	- 1.6, 4.5	- 1.6, 3.6	- 4.4, 3.5	- 4.3, 4.4	
*Difference in proportion (MDV – SDS) expressed in percentage, CI = confidence interval							

Conclusions

PCV13 in MDV administered per routine schedule in Gambian infants was safe and immunogenic. MDV was non-inferior to SDS for all 13 serotypes. Once licensed, MDV would help ensure vaccine sustainability for infants in resource limited settings.

ESPID-0858
MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

USE OF A SEROGROUP C MENINGOCOCCAL CONJUGATE VACCINE AS A PROBE OF IMMUNE MEMORY IN PRIMED AND UNPRIMED 12-MONTH-OLD CHILDREN

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Background and Aims

Induction of immunologic memory with a serogroup C *Neisseria meningitidis* (MenC) conjugate vaccine in primed and naïve 12-month-old children was investigated in a randomised-controlled trial in the UK and Malta.

Methods

In the initial phase, 509 infants received either a dose of MenC-CRM_{197}, or MenC-TT at 3 months of age, or MenC-CRM_{197} at 3 and 4 months, or no MenC doses. At age 12 months all participants received a Hib-MenC-TT vaccine. Blood samples were taken prior to Hib-MenC-TT vaccination and 6 days later in 182 participants, including all MenC naïve participants and a random subset of those primed in infancy. A rabbit complement serum bactericidal antibody (rSBA) assay against MenC was used and

responses from pre to post Hib-MenC-TT vaccination, were expressed as geometric mean fold rises (GMFRs).

Results

Six days following Hib-MenC-TT vaccination, MenC rSBA GMFRs were significantly greater in those primed with one MenC-TT dose (606.7; 95%CI:347.8-1058.5) than in those who received one MenC-CRM dose (178.2; 95%CI: 94.2-336.9), two MenC-CRM_{197} doses (171.1; 95%CI: 93.0-314.6) or no MenC doses (124.1; 95%CI: 58.6-263.0). No significant differences were noted in the GMFRs following one or two MenC-CRM infant priming doses compared with unprimed participants.

Conclusion

Meningococcal plain polysaccharide vaccines have been classically used to demonstrate immune memory following conjugate MenC vaccine priming in infancy, but have recently been shown to impair subsequent memory responses. Conjugate MenC vaccines can distinguish primed from unprimed children and may be used as probes of immune memory in clinical trials.

ESPID-0936
MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

INVESTIGATIONAL HEXAVALENT VACCINE ADMINISTERED CONCOMITANTLY WITH MENINGOCOCCAL SEROGROUP C CONJUGATE VACCINES DURING PRIMARY SERIES

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BACKGROUND Concomitant administration of vaccines simplifies delivery. DTaP-HB-IPV-Hib/(Hexavalent) is an investigational, fully-liquid, combination vaccine against 6 diseases. This study evaluated the compatibility of Hexavalent with two MenC conjugate vaccines(MCC) in an infant schedule.

METHODS In a phase III, open-label study 284 healthy infants from 11 UK centres were enrolled to receive Hexavalent at 2,3 & 4m, Prevenar13 at 2 & 4m, Menitorix (Hib-MCC) and M-M-RVAXPRO at 12m, & randomised 1:1 to receive either NeisVac-C (MCC-TT)(n=141) or Menjugate (MCC-CRM)(n=143) at 3 & 4m. 266 completed the study per protocol(PP).

RESULTS By PP analysis, one-month MenC seroprotection rates (SPR)(% ≥1:8 serum bactericidal titre) were 100 and 96.4 after 1st, 100 and 99.1 after 2nd and 100 and 97.3 after 3rd (booster) dose of MCC in TT and CRM groups, respectively. One month after 3 doses of Hexavalent in both groups, IgG anti-PRP (Hib) SPR (% ≥0.15 µg/mL) were 97.8 and 100, anti-HBsAg (% ≥10 mIU/mL) 96.8 and 96.3 while all

subjects were seroprotected against diphtheria and tetanus (% ≥0.01 IU/mL), and poliovirus types 1, 2 and 3 (% ≥1:8 dil) and seroresponse rates to all pertussis antigens were ≥90.4%. Two vaccine-related-SAEs (transient severe abdominal pain and crying) occurred concomitantly in one subject in CRM group. Adverse event rates were similar to other studies of Hexavalent with pyrexia ≥38°C recorded in 10.9% of subjects following any doses.

CONCLUSIONS Study results suggest that Hexavalent given with MCC would be effective used in a 2-3-4 month infant priming schedule modified to add HepB protection.

ESPID-0962
MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

OROPHARYNGEAL CARRIAGE OF NEISSERIA MENINGITIDIS IN PORTUGUESE STUDENTS - NOT ALL CARRIERS ARE EQUAL

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BACKGROUND: Following high uptake catch up in 2006, Portugal currently immunises only 1 year olds with *Neisseria meningitidis* (Nm) group C conjugate vaccine. We used culture and PCR to study colonisation with Nm in young adults.

METHODS: In May 2012, oropharyngeal swabs were collected from 601 students at University of Coimbra into STGG broth, and stored at -80ºC. Neisseria spp. were identified by culture and genogrouped using PCR. DNA was extracted from broth samples and subjected to RTqPCR for sodC. Samples were "positive" if <36 cycles. A standard curve was constructed using a log phase broth culture of a standard Nm strain to convert CT values to colony forming units (CFU).

RESULTS: 80/601 (13.3%) throat swabs yielded Nm by culture - genogroups A=0, B=32, C=2, W=1, X=1, Y=10. 87/601(14.5%) samples were positive by PCR. 59 samples were positive by both techniques, 21 by culture only and 28 by PCR only. The distribution of bacterial density measured by PCR showed that 12/59 carried the organism at densities >104 CFU/mL (all culture positive). There were no significant differences in density noted between subjects carrying different genogroups.

CONCLUSIONS: Nm carriage in Portugal is mostly B and Y. C is circulating at a low level. Studying meningococcal carriage by both culture and PCR yields overlapping but distinct information. Both techniques reliably detect high density carriage which may reflect a higher degree of infectiousness and thus be important for studies evaluating the impact of vaccines on transmission.

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MODERATED E-POSTER WALK 10 - PNEUMOCOCCAL AND MENINGOCOCCAL VACCINATION

VARIATIONS IN MENINGOCOCCAL CARRIAGE DENSITY AND IMPLICATIONS FOR VACCINATION POLICY

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Background and aims: Invasive meningococcal disease primarily affects young children whereas asymptomatic nasopharyngeal carriage of meningococci peaks in teenagers. Vaccination strategies are usually chosen to maximise direct protection to the recipient, however if vaccination reduces transmission the herd effects generated can substantially reduce cases. While previous studies have assessed the presence/absence of meningococci in the nasopharynx, we aimed to measure the distribution of carriage density to allow the effect of vaccines on density, and thus potentially transmission, to be evaluated.

Methods: Pharyngeal swabs were taken from 15-19 year old school children in Bristol, UK, in a longitudinal cohort study. Swabs were placed into 1.5ml STGG broth on site, transferred to the laboratory within 2-6 hours, then processed and frozen at -80°C. Presence and density of meningococci were subsequently determined by qRT-PCR for sodC.

Results: As of January 2015 1,286 students had been recruited; laboratory results were available for 1,284 students and 2 had withdrawn. 7.8% (n=100) students were positive (PCR CT≤36) for *N.meningitidis*, of these there was wide variation in the density of meningococci detected. Most students carried at low density, but some had much higher densities of carriage (61.2% 0 to <10CFU/ml, 22.5% 10 to <100CFU/ml, 13.3% 100 to <1000CFU/ml, 1.0% 1000 to <10000CFU/ml, 2.0% 10000 to <100000CFU/ml).

Conclusion: Meningococcal carriage density in teenagers varies substantially. If vaccines affect carriage density this could substantially impact on transmission, but such potential indirect effects may not be captured by studies recording carriage prevalence only.

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MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

MUCORMYCOSIS IN CHILDREN: A PROSPECTIVE, EPIDEMIOLOGIC STUDY IN EUROPEAN AND NON-EUROPEAN COUNTRIES

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Background and aims: Mucormycosis has emerged as an important mould infection in patients of all ages with a high mortality. The aim of this study was to analyse its epidemiology, management and outcome in children.

Methods: In each country, a national co-ordinator prospectively collected mucormycosis cases recorded on specially provided case report forms that were centrally evaluated by the study co-ordinator. Paediatric (<19yrs) cases enrolled from January 2005 to December 2014 were analysed. Statistical analysis was performed with SPSS v.12.

Results: Twelve countries enrolled 46 cases (39 in European and 7 in non-European countries). Mean age was 11.9yrs (range 1mo-18.6yrs) and female gender 59.1%. Most common underlying conditions were haematological malignancies (50%), trauma/surgery (6.5%), diabetes mellitus (6.5%) and solid organ transplantation (6.5%); whereas, in 10.9% no underlying condition was found. The main sites of infection were lungs (23.9%), soft tissue/skin (21.7%), sinus/sino-orbital (17.4%) and rhino-cerebral region (10.9%); in 26.1% infection was disseminated. The isolated fungi included *Rhizopus* spp. (28.2%), *Lichtheimia* spp. (19.5%), *Mucor* spp. (10.9%), *Cunninghamella bertholletiae* (8.7%) and not specified (32.6%). 47.8% received amphotericin B alone, 2.2% received posaconazole only and 28.2% received both. Combined surgical plus antifungal therapy was reported in 43.5%. Mortality rate was 36.1%. The combination of antifungal therapy and surgery was most strongly associated with survival (p=0.003).

Conclusions: Mucormycosis in children mainly presents as disseminated or pulmonary infection. Outcome is dismal in 1/3 of children with mucormycosis; however, improved survival is found when active antifungal therapy and surgery are combined.

ESPID-0599
MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

VORICONAZOLE ANTIFUNGAL PROPHYLAXIS IN CHILDREN WITH MALIGNANCIES

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Background and aims: Optimal antifungal prophylaxis (AFP) in paediatric haemato-oncology patients has not been established yet. We evaluated efficacy and safety of voriconazole as primary AFP in paediatric high-risk cancer patients in two haemato-oncology centers.

Methods: Children ≤18 yrs with malignancies receiving primary AFP with voriconazole (either 5 or 7mg/kg q12h) during 5yrs (2008-2012) were enrolled. Statistical analysis was performed with SPSS v.13.

Results: Thee hundred and eleven cases (187 patients) were included. Mean age was 6.7yrs (0.4-18yrs) and female gender 46.2%. Most common underlying diseases were acute leukaemias (56.6%), lymphomas (8%), CNS tumours (11.2%) and other malignancies (24.2%). Median number of voriconazole AFP cases during chemotherapy per patient was 1.7 (range 1-4). During the last two weeks before AFP, the patients had severe neutropenia (62.5% of cases), mucositis (18.9%) and received steroids (36.2%) and induction chemotherapy (78.8% of cases). Mean duration of neutropenia was 9.8 days (range 1-45). Previous surgical operation and ICU admission was reported in 15.4% and 4.8%, respectively. During AFP only one breakthrough *Candida glabrata* blood stream infection occurred. Voriconazole-related adverse effects (as reported locally) were elevated liver enzymes (10.9%), hypopotassaemia (5.4%), nausea/headache/dizziness (0.9%), keratitis (0.3%), photophobia and colour perception disorders (1.5%). Mean time of onset of adverse events after voriconazole initiation was 5.4 days (range 0-20). Severity of adverse effects was grade I (4.2%), II (10.9%) and III (2.9%).

Conclusions: In this preliminary report, AFP with voriconazole was demonstrated to have an acceptable safety and useful efficacy in the management of paediatric high-risk cancer patients.

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MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

INVASIVE FUNGAL INFECTIONS (IFI) IN EUROPEAN NICUS – DATA FROM THE NEONIN SURVEILLANCE NETWORK

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Background and aims: IFI is an important cause of morbidity and mortality among premature hospitalised infants. The incidence of IFI varies significantly between centres and countries. We aimed to describe the epidemiology of IFI in countries participating in a neonatal infection surveillance network (neonIN).

Methods: Data for fungal infections between January 2005 to October 2014 were extracted; data for Greece and Estonia were available from January 2012. An episode of IFI was defined as a positive culture from blood and/or cerebrospinal fluid.

Results: 113 patients with IFI from the UK and Greece were included; no positive fungal cultures were reported from Estonia (5 neonatal-units). IFI were responsible for 3% (95% CI 3-4%) and 17% (95% CI 10-24%) of all infections in the UK and Greece, respectively. Incidence of IFI in the UK was similar between 2005-2011 and 2012-2014. Compared to Greece, neonates with IFI in the UK had lower gestational age and birth weight, however there was no difference in postnatal age. (Table 1).

Table 1. Incidence of IFI and demographic characteristics. Number of patients with IFI is shown in brackets

	UK 2005-2011 (n=59)	UK 2012-2014 (n=34)	Greece 2012-2014 (n=20)
Incidence of IFI (/1000 NICU admissions)	1.2*	0.8*	7.3*
Number of neonatal units	16	15	7
Gestational age (weeks) (mean, SD)	26.0 (±3.3)*	26,5 (±4.2)*	32.0 (±5.1)*
Birth weight (g) (mean, SD)	873.1 (±393.4)*	1037.1 (±730.7)*	1700.0 (±1068.8)*
Postnatal age (days) (median, IQR)	13.6 (8.5 – 20.0)	11.1 (7.9 – 19.5)	16.5 (8.0 – 37.0)
Maternal antibiotic therapy (n, %)	12/45(26.7%)	9/31 (29.0%)	5/18 (27.8)
Antibiotic use within 48h of culture (n, %)	43/58 (74.1%)	24/33 (72.7%)	16/19 (84.2)
Total parenteral nutrition within 24h of culture (n, %)	50/59 (84.8%)	29/33 (87.9%)	17/20 (85.0)
Central venous catheter within 48h of culture (n, %)	8/8 (100%)	28/32 (87.5%)	3/4 (75.0)

*p-value <0.001 (comparing three groups by chi-square or ANOVA).

The most common pathogen in the UK was *C. albicans* while *C. parapsilosis* was encountered most frequently in Greece (Table 2).

Table 2. Pathogen distribution and resistance to fluconazole. No of isolates identified to genus is sho brackets

	UK (n=90)	Greece (n=23)
Candida albicans (n, %)	62 (68.9) *	3 (13.0) *
Resistant to fluconazole	1/35	0/3
Candida parapsilosis (n, %)	13 (14.4)*	17 (73.9) *
Resistant to fluconazole	0/3	0/17
Other *Candida* (n, %)	15 (16.7) ¥	2 (8.7)
Of them not-typed	11 (12.2)	2 (8.7)
Resistant to fluconazole	1/10	0/1
Malassezia furfur	0	1 (4.3)

* p-value <0.001 (Chi-square)

¥ Among these were one case of *C. tropicalis* and *C. dubliniensis* each and two cases of *C. glabrata*.

Conclusions: The demographics and pathogen distribution in neonatal IFI vary across countries suggesting involvement of different risk factors. Further studies are needed to identify these in order to plan effective prevention strategies to decrease disease burden.

ESPID-0648
MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

EPIDEMIOLOGICAL AND MICROBIOLOGICAL EVALUATION OF NOSOCOMIAL INFECTIONS ASSOCIATED WITH CANDIDA SPECIES IN CHILDREN: A MULTICENTER STUDY FROM İSTANBUL, TURKEY

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Objective: To establish the species distribution of candida isolates from pediatric patients in Istanbul, and to determine risk factors associated with nosocomial candida infections.

Material/Method: This study was conducted between June 2013-June 2014 by participation of 8 medical centers in Istanbul. Candida spp strains isolated from the clinical specimens of pediatric patients aged 0-18 years were included. Clinical features of the patiens were recorded on a standardized data collection sheet.

Results: A total of 134 systemic candida infections were identified in 134 patients. The patients were hospitalized in pediatric and neonatal intensive care units (41.8%, 9.7% respectively) and in other pediatric wards (48,5%). C.albicans was the most prevalant species (47%), followed by C. parapsilosis (13.4%), C.tropicalis (8.2%), C.glabrata (4.5%) C.lusitanei (3.7%), C.keyfr (2.2%), C.guillermondi (1,5%), C.dublinensis (0.7%) and C.krusei (0.7%). Types of candida infections were determined as candidemia (50.8%), urinary tract infection (33.6%), surgical site infection (4.5%), central nervous system infection (3.7%), catheter infection (3.7%), intraabdominal infection (3,0%) and empyema (0,7%). In multivariate analysis, smaller age (1-24 months) and detection of non-albicans species was found to be risk factors associated with candidemia (Sig:0.040, OR:4.116, 95%CI:1,068-15,862; and Sig:0.02, OR:2.475, 95%CI:1,108-5,530 respectively) On the other hand, empirical

antifungal treatment was determined as protective against candidemia (sig:0.022, OR:0.356; 95%CI:0,147-0,863). Nonalbicans species was more strongly associated with candidemia in comparison to albicans species (Sig:0.004, OR:2.867, 95%CI: 1,400-5,875).

Conclusion: This study provides an update for the epidemiology of nosocomial candida infections in Istanbul, which is important for the management of patients and implementation of appropriate infection-control measures.

ESPID-0987
MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

EPIDEMIOLOGY OF FUNGEMIAS IN A TERTIARY PEDIATRIC HOSPITAL DURING A 7-YEARS PERIOD

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BACKGROUND AND AIMS

Fungemias mainly affect children who are immunocompromised because of underlying medical conditions or use of medications, such as haematology-oncology and bone marrow transplantation patients or preterm neonates.

METHODS

The setting of the study were the NICU, PICU, haematology-onclology and BMT departments of a tertiary Pediatric hospital. Medical records of children (0-14 years) diagnosed with fungemia from 2007-2013 were retrospectively analysed and epidemiological and microbiological date were retrieved. Identification of isolates was done conventionally and by PCR-sequencing.

RESULTS

Fungemias were diagnosed in 138 patients (males 47.5%) accounting for 1.8 cases (range:0.58-2.7)/1000 hospital admissions. Neonates comprised 52% of the total episodes, oncology-BMT patients 21%, PICU patients 13%. A predominance of *Candida species* (90%) was detected, while *Sacharomyces cereviciae* accounted for 5 children (4.3%). *Candida albicans* was isolated in 65 children (46.8%), *Candida parapsilosis* in 41 (29.5%), *Candida glabrata* in 8(5.8%) and *Candida crusei* in 3(2.2%) children. There was not increasing incidence of *non-albicans spp* during the study period (p-value: 0.36). *C.albicans spp.* were 100% sensitive to amphotericin, fluconazole, caspofungin and voriconazole while there has been 78% sensitivity to itraconazole. *C.parapsilosis* strains were 97% sensitive to amphotericin, caspofungin and voriconazole, 91% to fluconazole and 78% to itraconazole. *C.glabrata* strains were 100% sensitive to amphotericin, caspofungin, voriconazole and itraconazole, while 37.5% were intermediate susceptible to fluconazole.

CONCLUSIONS

In our study population the incidence of fungemias varied during the study period. *Candida albicans* strains remained sensitive to fluconazole, but *non-candida spp*. were detected to have variable resistance to antifungals.

ESPID-1035
MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

MENINGOENCEPHALITIS DUE TO CANDIDA ALBICANS IN A CONTEXT OF CHRONIC MUCOCUTANEOUS CANDIDIASIS REVEALING RARE PRIMARY IMMUNODEFICIENCY

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BACKGROUND

Central nervous system (CNS) infection caused by *Candida* is a rare condition most often seen in neonates. In addition to meningeal involvement, intracerebral lesions can be found and are associated with disseminated infection in immunocompromised hosts.

CASE REPORT

A 7-years-old child of Turkish origin presented with headache and vomiting in a context of prolonged fever of unknown source. At examination, oral candidiasis and chronic onychomycosis were noted.

Culture of the cerebrospinal fluid grew for multisensitive *Candida albicans*. Brain magnetic resonance (MRI) showed the presence of focal lesions in the left caudate nucleus and in the right cerebellar hemisphere. Medullar MRI showed diffuse meningeal nodular lesions.

Treatment with intravenous Amphotericin B liposomal was given during 6 months relayed by oral Fluconazole after regression of CNS lesions was observed on MRI.

A complete immune evaluation was performed and genetic analysis detected homozygous CARD9 mutation.

CONCLUSION

Fungal invasive infection highly suggests underlying immune deficiency, primary or acquired, which is necessary to rule out in order to properly guide the curative treatment. CARD9 deficiency have been associated with deep dermatophytosis. Curative treatment of this condition is not yet well established and fluconazole should be given lifelong.

ESPID-1044
MODERATED E-POSTER WALK 11 - FUNGAL INFECTIONS

MULTIFOCAL OSTEOMYELITIS IN A CHILD WITH INTERLEUKIN-12 RECEPTOR B1 (IL12RB1) DEFICIENCY MIMETIZING CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO)

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Introduction: The IL-12p40/IL-12Rb1 and INF-GR1/INF-GR2/STAT1 signaling pathways are important for clearing intracellular bacteria. IL-12RB1 deficiency is the most commom genetic defect and predisposes to disseminated disease caused by Mycobaterium bovis, the most frequent in child, environmental *Mycobacteria*, non-typhoidal Salmonella and *Fungi*.
Case report: We report a 14-months child with an insidious history of intermittent fever, pustular lesions in limbs and swelling of right ankle, refusing to walk. Laboratory studies revealed nonspecific elevated inflammatory indices. Radiological studies showed symmetrical osteolytic lesions in ribs, jaw and all long bones. Serological, biology molecular and cultural tests of blood and skin and bone biopsies were negative to infectious agents. QuantiFeron-TB Gold® test was indeterminate. Bone biopsy revealed a fibro-osteosclerotic lesion process, compatible with CRMO; however genetic tests were negative. She did broad-spectrum antibiotic empirically, without improvement. Defects of innate immunity, as INF-G/IL-12 axis, were investigated and IL12RB1 deficiency was confirmed. She initiated interferon and antituberculosis empirically and she needed corticoid and pamidronate, with clinical and analytic improvement. During follow-up, there was clinical worsening and, after an extended investigation, it was isolated *Malassezia furfur* at the blood culture. Her mother had pityriasis versicolor. She started antifungal with favorable outcome.
Conclusion: In cases of IL12RB1 deficiency bone infections can mimic the clinical picture of CRMO, the clinical presentation can be insidious and the etiological agents are rare, so the diagnosis is a challenge. In this case, the authors hypothesize that Malassezia furfur could be the initial etiological agent of osteomyelitis.

ESPID-0032
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PNEUMOCOCCAL COLONIZATION DURING HOSPITALIZATION FOR THE FIRST WHEEZING EPISODE IN INFANCY: NO ASSOCIATION WITH ASTHMA OR ATOPY IN CHILDHOOD OR ADULTHOOD

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Background: Bacterial colonization during the first wheezing episode has been associated with short-term relapse of wheezing and neonatal *Streptococcus pneumoniae* colonization has been associated with later asthma in childhood. However, no study has yet addressed the effects of *S.pneumoniae* colonization on long-term outcome of wheezing in infancy.

Aim: The aim of the present study was to evaluate how *S. pneumoniae* colonization during the first wheezing episode in infancy is associated with atopy, wheezing, asthma or lung function in later childhood, adolescence and adulthood.

Methods: In 1981-82 83 infants were hospitalized for the first wheezing episode at less than 24 months of age. On hospital admission *S. pneumoniae* was studied with culture and antigen detection in nasopharyngeal aspirates. A positive sample in one of these tests was regarded as *S. pneumoniae colonization*. We have performed repeated clinical follow-up studies for this group from infancy until the age of 28-30 years. Doctor-diagnosed atopy and repeated wheezing or asthma were diagnosed on all visits. Spirometry was conducted at the ages of 8-10, 18-20 and 28-30 years.

Results: *S. pneumoniae* colonization was found in 25/83 (30%) infants during hospitalization for wheezing in infancy. *S. pneumoniae* colonization was not associated with later atopy, repeated wheezing or asthma at any time during the 28-30-years prospective follow-up. In addition colonization had no effect on lung function indices during the follow-up.

Conclusions: *S. pneumoniae* colonization in infancy does not increase the risk for atopy, recurrent wheezing in childhood or the risk for asthma in later childhood or adulthood.

ESPID-0095
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RESPIRATORY VIRUSES ASSOCIATED WITH COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN – MATCHED CASE-CONTROL STUDY

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Background: Community-acquired pneumonia (CAP) is the leading cause of death in children and a substantial proportion of childhood CAP is caused by viruses. A better understanding of the role of specific respiratory viruses in childhood CAP is needed to improve clinical management and preventive measures. The aim of the study was to assess the association between specific viruses and childhood CAP.

Methods: A case-control study was conducted during three respiratory seasons in Stockholm, Sweden. Cases were children ≤5 years with radiological CAP. Healthy controls were consecutively enrolled at child welfare centers during routine visits and matched to cases on age and calendar time. Nasopharyngeal aspirates were obtained from all study subjects and analyzed by real-time polymerase chain reaction for 15 viruses. Odds ratios (OR) with 95% confidence intervals (CI) were calculated with multivariate conditional logistic regression that accounted for concomitant presence of other viruses.

Results: Viruses were detected in 81.0% of the cases and 55.8% of the controls. Significant associations with CAP with high odds ratios were seen for influenza virus (OR=12.1, CI: 2.8-51.7), metapneumovirus (OR=15.8, CI: 6.3-39.7) and respiratory syncytial virus (OR=21.6, CI: 9.2-51.1). A tendency of association was seen between

adenovirus and CAP (OR=2.9, CI: 1.1-.7.3). Coronavirus (OR=0.2, CI: 0.1-0.8) and bocavirus (OR=0.3, CI: 0.1-0.7) were inversely associated with CAP.

Conclusions: Respiratory viruses are commonly detected in children with radiological CAP. Influenza virus, metapneumovirus and respiratory syncytial virus are significantly associated with radiological CAP, which needs to be considered when managing these patients.

ESPID-0257
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

WHEEZING: A PREDICTOR OF VIRAL INFECTION AMONG CHILDREN UNDER-5 YEARS WITH COMMUNITY-ACQUIRED PNEUMONIA

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Aims: We assessed whether there is difference on the frequency of symptoms and signs among children with community-acquired pneumonia(CAP) with viral or bacterial infection.

Methods: Children <5-years-old hospitalized with CAP in a 21-month period were investigated in this prospective study in Salvador, Brazil. On admission, clinical data were registered in pre-defined forms and biological samples were collected to investigate 19 etiological agents (11 viruses, 8 bacteria). For this analysis, viral infection comprised the subgroups with sole viral or mixed viral-bacterial infection.

Results: Out of 277 enrolled patients, 225 (81%) had a probable etiology established and then comprised the study group. Overall, median (IQR) age was 17(9; 28) months and there were 130 (58%) males. Cough (96%), fever (94%), difficulty breathing (85%), vomiting (56%), and wheezing (45%) were reported and tachypnea (82%), crackles (71%), chest indrawing (61%), fever (58%), chest recession (57%), wheezing (45%) and rhonchi (35%) were found. Asthma was registered for 22%. Sole viral (53%), mixed viral-bacterial (29%) and sole bacterial infection (18%) were established. Report of wheezing (49.5% *vs.* 25.0%; P=0.005), rhonchi (40.0% *vs.* 15.0%; P=0.003) and wheezing (51.9% *vs.* 15%; P < 0.001) detected on physical examination were the only differences found. The positive predictive value of detected wheezing for viral infection was 94.1% (95%CI: 88-98%). Among the wheezing cases, 50% of the cases with sole bacterial infection and 47% of those with viral infection had presented difficulty breathing in the previous 12 months.

Conclusions: Wheezing detected on physical examination is highly predictive of viral infection.

ESPID-0369
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RISK FACTORS FOR COMPLICATIONS IN CHILDREN WITH BACTEREMIC, COMMUNITY ACQUIRED PNEUMONIA.

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Background: Children with bacteremic, community-acquired pneumonia (BCAP) can develop complications.

Aim: To investigate risk factors associated with complications in children with BCAP.

Methods: Cohort study, from 2009 onwards. We recruited all BCAP

Results: We recruited 91 patients. *S. pneumoniae* caused 71 BCAP (78%). Serotypes included in PCV13 (but not in PCV7) accounted for 80% of *S. pneumoniae* cultures. *S. aureus* was isolated in 6 patients (6,6%), and *H. influenzae* in 5 patients (5,5%). Patients were immunized as follows: no PCV, 13%; PCV7 (3 doses), 53%; PCV13 (2 doses), 16%; and PCV13 (3 doses), 13%. No patient >2 years had >2 doses of PCV13. Complications occurred in 23 patients (25%), 22 of them were pulmonary. Risk factors for complications were: age >2 years [p=0.026, RR 2.3 (CI95%: 1.0-5.1), and CRP >150 mg/L [p=0.029, RR 2.8 (CI95%: 1.0-7.0)]. Two doses of PCV13 protected against complications [p=0.063, RR 0.7 (0.6-0.9)], and specifically against empyema [p=0.061, RR 0.8 (CI95%: 0.7-0.9)]. CRP >200 mg/L was a risk factor for empyema [RR 5.5 (CI95%: 1.3-23)], surgery [RR 4.2 (CI95%: 0.9-18)] and pleural effusion [RR 3.2 (CI95%: 1.1-8.8)] (p<0.03).

Conclusions: In patients with BCAP, immunization with 2 doses of PCV13 is a protection factor for empyema and pulmonary complications. High C-reactive protein levels are a risk factor for complications.

ESPID-0370
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DEXAMETHASONE FOR PARAPNEUMONIC PLEURAL EFFUSION: PRELIMINARY RESULTS OF A PILOT, DOUBLE BLIND CLINICAL TRIAL (CORTEEC).

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Background and aims:

Pleural effusion and empyema are complications of pneumonia. Our objective was to investigate whether dexamethasone (DXM) decreases the time to cure . Secondary aim was to evaluate the occurrence of adverse events.

Methods

CORTEEC is a phase II, multi-centre, stratified (uncomplicated / complicated pleural effusion), randomized, double blind, placebo-controlled, parallel-group pilot study with 56 patients with parapneumonic pleural effusion or empyema. Nine centres (3 secondary and 6 tertiary centres) from Spain participated. Patients were stratified in uncomplicated or complicated effusion. Patients were assigned to one study drug (i.v. DXM 0,25 mg/kg/6 hours, or matching placebo) for 48 hours, plus cefotaxime 50 mg/kg/6 hours, and ranitidine 5 mg/kg/day. Patients received the first dose of the study drug

Results

Recruitment is currently ongoing (92% patients recruited as of January, 2015). An interim analysis was done in May 2013, with 66% patients recruited. Time to cure for uncomplicated patients on drug A was 81,6 ± 19,9 hours, vs. 172,6 ± 36,8 for drug B group (p=0.013). Time to cure for complicated patients on drug A was 303 ± 34,3 hours, vs. 355,1 ± 75 in B group (p=0.559). Adverse events attributable to medication were not different (group A: 86% vs. group B: 55%, p=0,077). Severe adverse events were not different (6% vs. 5%).

Conclusion

Interim analysis showed a better outcome for uncomplicated pleural effusion on drug A, and a non-significant increase in non severe adverse events.

ESPID-0385
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

TOLL-LIKE RECEPTORS 3, 4, 7 AND 8 ENCODING GENES IN INFANTS WITH BRONCHIOLITIS AND POST-BRONCHIOLITIS ASTHMA

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Background: Toll-like receptors (TLRs) recognize microbes involving with infection, inflammation and later consequences.
Aim: The aim of the study was to evaluate whether polymorphisms in TLR 3, 4, 7 and 8 encoding genes are associated with post-bronhiolitis asthma.
Methods: 126 children who were hospitalized for bronhiolitis at less than 6-months-of-age were examined in the follow-up study at the mean age of 6.4 years. The occurence of asthma, atopic dermatitis and allergic rhinitis currently, and asthma ever were evaluated. Blood samples were analyzed for *TLR3* rs3775291, *TLR4* rs4986790, *TLR7* rs179008 and *TLR8* rs2407992 polymorphisms. Since *TLR7* and *TLR8* genes are located in X chromosomes, polymorphisms were analyzed separately for boys and girls.
Results: In case of *TLR7*, current asthma was present in 4/10 (40.0%) of the boys with minor allele T compared to 12.2% of those with major allele A (p=0.06). In girls, current atopic dermatitis, but nor current asthma or allergic rhinitis, was more common in those with TT genotype or who were allele T carriers. There were no significant differences between polymorphisms in *TLR3*, *TLR4* or *TLR8* and occurence of asthma, atopic dermatitis or allergic rhinitis currently, or asthma ever.
Conclusion: Preliminary evidence was found that the minor allele T in the *TLR7* rs179008 gene is associated with an increased risk of asthma in boys and with an increased risk of atopic dermatitis in girls.

ESPID-0428
MODERATED E-POSTER WALK 12 - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PROGRESSIVE COMPLEXIFICATION OF THE UPPER RESPIRATORY TRACT MICROBIOTA IN HEALTHY INFANTS (6W-6M)

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Background and aims

In the hours after birth a neonate acquires spatially undifferentiated microbiota which evolve in site-specific fashion during infancy. The way that the oropharyngeal microbiota becomes established has implications for future health, in relation to developing immunity against localised or disseminated bacterial infection, and (it is speculated) risk of allergic disease. We are exploring the development of the oropharyngeal microbiota in a cohort of term infants, while closely monitoring their health and vaccination status.

Methods

204 infants were recruited, and oropharyngeal swabs and clinical data were collected at 6, 13, 18 and 26 weeks of age. 16S rRNA gene regions were PCR-amplified from total bacterial DNA extracted from swabs, and sequenced using the 454 GS FLX (Roche) platform. High quality sequences recovered after denoising and chimera removal were aligned using the SILVA reference database.

Results

1,464,190 sequences were obtained from two massively parallel sequencing runs. From this dataset, we defined the microbiota of paired 6 weeks and 6 months oropharyngeal samples from 155 infants. We observed an increase in microbiota diversity from 6 weeks to 6 months of life ($p<0.001$), with the initial predominance of Streptococcus declining as other genera such as Actinobacillus, Neisseria, Prevotella and Moraxella begin to comprise a larger proportion of the oropharyngeal microbiota (p values all <0.001).

Conclusions

The oropharyngeal microbiota diversifies with age, with a change in community composition potentially driven by mode of delivery, feeding choices, immunisation, viral infection and antibiotic use.

ESPID-0075
MODERATED E-POSTER WALK 13 - BACTERIAL INFECTIONS

EARLY TRENDS IN PEDIATRIC PNEUMOCOCCAL PLEURAL EMPYEMA FOLLOWING PNEUMOCOCCAL CONJUGATE 13-VALENT VACCINATION: 9 YEARS OF ACTIVE SURVEILLANCE IN A MEXICAN HOSPITAL

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BACKGROUND AND AIMS: We have previously published the first Mexican study showing a decrease in pneumococcal invasive disease following implementation of the 13-valent pneumococcal conjugate vaccine (PCV13) however, the impact of this vaccine on Pneumococcal Pleural Empyema (PPE) and serotypes distribution has not been reported.

METHODS: Since October-2005 until September-2014, active surveillance for pleural empyema (PE) in children < 16 years old was performed in the Tijuana, Mexico, General Hospital (TGH). Diagnosis of PE was established by Lyell criteria of a pleural effusion with a community acquired pneumonia +- bacterial isolation. For *Streptococcus pneumoniae* isolates serotype identification was performed using the Quellung reaction (Statens Serum Institute®, Copenhagen,Denmark). A descriptive analysis for all PPE was performed using Excel®.

RESULTS: A total of 42 PE were diagnosed. Bacterial identification was possible in 30 (71.4%) cases. Among these, 24 (80%) were caused by *S. pneumoniae.* Median age for PPE was of 3.9 years (4 months -15 years), pleural decortication was performed in 9 patients (37.5%), and one patient died. Before PCV13 implementation (a period of 59 months), the total number of PPE were of 14, with serotypes 3, 19A and 6A/C accounting for 64.3% of all cases. After PCV13 implementation (31 months period), PPE dropped to 3 cases (serotypes 6A/C, 7B and 15).

CONCLUSIONS: 1. Following PCV13 universal vaccination, all PPE cases have decreased, with an early trend on apparent absence of serotypes 3 and 19A. 2. This is the first Mexican study showing the impact of PCV13 on PPE.

ESPID-0169
MODERATED E-POSTER WALK 13 - BACTERIAL INFECTIONS

OCCULT BACTEREMIA (OB) IN FEBRILE CHILDREN AGED 3-36 MONTHS AT THE PEDIATRIC EMERGENCY ROOM (PER) IN SOUTHERN ISRAEL, BEFORE AND AFTER ROUTINE ANTI-PNEUMOCOCCAL IMMUNIZATION (2005-2012)

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Objectives: To characterize the epidemiological/microbiological picture of OB among infants/children aged 3-36 months, before and after the introduction of PCVs in the national immunization plan.

Patients and methods: A retrospective study enrolling all infants/young children diagnosed at PER with fever (>38^0C) without source, discharged and reported with a positive blood culture growing a true pathogen. PCV7 and PCV13 were introduced in the national immunization program in 7/2009 and 11/2010, respectively.

Results: Of 453 bacteremias at PER, 89 were defined as OB. Overall OB rate was 0.22%; a significant decrease was recorded in OB rates, with the highest rate during 2005 (0.34%) and the lowest during 2011 (0.15%). The OB cases decreased in the post-PCV vaccination (2010-2012) compared with the pre-vaccination period (2005-2009) from 66/22, 256 (0.3%) to 23/13,213 (0.17) cases (P=0.03). The most common OB pathogens were *S. pneumoniae* (SP), *Enterobacteriae* spp. *Streptococcus viridans* spp. and *Kingella kingae* (39.3, 11.2, 10.1 and 9 %, respectively). No changes were recorded in SP-OB cases; *K. kingae* isolates decreased (P=0.047). None of SP serotypes isolated during 2011-2012 belonged to PCV13. An increase in non-PCV13 serotypes was recorded during 2011-2012 (3/3, 100% *vs*. 7/32, 21.9% during 2005-2009, P=0.01). 60/89 (67.4%) patients had a F/U visit; a new infectious focus was detected in 9 patients.

***Conclusions*: 1.** OB rates decreased significantly following PCVs' introduction; **2.** SP was the main pathogen isolated in OB, but in lower percentages compared with the medical literature; **3.** PCV13 serotypes were eliminated as a cause of OB during 2011-2012.

ESPID-0271
MODERATED E-POSTER WALK 13 - BACTERIAL INFECTIONS

SYSTEMATIC REVIEW OF PAEDIATRIC ANTIBIOTIC CLINICAL TRIALS: WIDE VARIATION IN STUDY DESIGN AND OUTCOMES SUGGESTS AN URGENT NEED FOR HARMONISATION

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BACKGROUND
There is no consensus on the requirements for conducting clinical trials (CTs) in children with clinical infectious syndromes (CIS). So far, no formal guidance on the standardisation of CT design for antibiotics in neonates and children has been published. We aimed to review which standardised inclusion/exclusion criteria and endpoints identified by the FDA/EMA for adults have been used in paediatrics and describe how paediatric CTs have applied consistent definitions for enrolment and outcomes.

METHODS
A systematic review was conducted of CTs published/registered after 2000 reporting inclusion/exclusion criteria and primary/secondary endpoints of CIS *AND* antibiotics in children.

RESULTS
85 studies fulfilled inclusion criteria. 84% were conducted as randomized-controlled trials. 8 CTs are currently on-going and only 18 included neonates. The primary diagnosis was based on variable combinations of clinical signs and laboratory tests. Clinical findings were used as inclusion criteria in 88% of CTs, followed by haematological/biochemical (42%) and microbiological tests (27%). Chronic/underlying conditions and recent infection/antibiotic use were considered exclusion criteria in 62% and 53% of CTs, respectively. Clinical efficacy was the most commonly used outcome (66%) whereas microbiological efficacy and death were assessed in 16% and 18% of the studies. A wide variation was highlighted in terms of the time for evaluating the endpoints.

CONCLUSION
The lack of consensus for successfully conducting paediatric CTs on antibiotics is a major barrier to their effective introduction into clinical practice. Collaboration between all the stakeholders involved in new antibiotic development programmes leading to standardised case-definitions and outcome measures is urgently needed.

ESPID-0582
MODERATED E-POSTER WALK 13 - BACTERIAL INFECTIONS

BETA-LACTAMASE PRODUCING UROPATHOGENS IN CHILDREN

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Background/Aims: Resistance of Gram (-) *Enterobacteriaceae* against β-lactams through extended-spectrum β-lactamases (ESBL), cephamycinases and carbapenemases poses significant treatment difficulties. We investigated the prevalence trends and characteristics of children with urinary tract infection (UTI) caused by β-lactamase-producing uropathogens.

Methods: All *Enterobacteriaceae* uropathogens isolated from children <14 years hospitalized for UTI during 1997-2014 were included and broad-spectrum β-lactamase-producing organisms were phenotypically characterized. The affected patients' characteristics were reviewed.

Results: During the 18-year study-period,1040 *Enterobacteriaceae* were isolated from 887 children, of whom 83 (7.98%) isolated from 73 children, were identified as broad-spectrum β-lactamase-producing (36 *E. coli*,29 *Klebsiella* spp, 14 *Enterobacter* spp, 3 *Citrobacter* spp and 1 *Proteusmirabilis*) and exhibited high resistance rates to other antibiotic classes as well (cotrimoxazole 58%, aminoglycosides 41%, nitrofurantoin 68%, quinolones 21%). The β-lactamase types were 15 of ESBL, 54 of cephamycinase and 14 of carbapenemase phenotypes, the latter being almost exclusively *Klebsiella spp* strains. The prevalence of β-lactamase-producing strains increased during the study period, from 1.08% in 1997-1999 to 7.98% in 2012-1014 (p=0.003), mostly due to increasing rates of broad-spectrum β-lactamase-producing non-*E. coli* pathogens. More than half of UTIs by broad-spectrum β-lactamase-producing organisms were community acquired (47/83) and first UTI episodes (56/83). Affected children were of young age (median, 0.47 years,) and many had urinary tract abnormalities (35/73). Non-*E.coli* β-lactamase-producing pathogens were associated with antibiotic prophylaxis (p=0.035) and permanent scarring (p=0.034).

Conclusion. Uropathogens resistant to broad-spectrum β-lactams are mostly non-*E. coli*, steadily increasing and associated with antibiotic prophylaxis and permanent scarring.

ESPID-0978
MODERATED E-POSTER WALK 13 - BACTERIAL INFECTIONS

NECROTIZING PNEUMONIA AND LUNG ABCESS AS COMPLICATIONS OF PEDIATRIC BACTERIAL PNEUMONIA

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Background and aims: Necrotizing pneumonia and lung abscess are rare complications of pneumonia. Our objective was to analyze their clinical features, diagnosis, treatment and outcome.

Methods: Retrospective study of patients <14 years diagnosed with lung abscess or necrotizing pneumonia (2004-2014). Lung abscess was defined as a cavitated parenchymal lesion >2 cm, with thick wall and air-fluid level. The presence of multiple small (<2 cm) thin-walled lesions was considered necrotizing pneumonia.

Results: We diagnosed 39 cases of necrotizing pneumonia and 18 lung abscesses (median age 2.5 years). The most frequent symptoms were fever (100%), cough (64%), vomiting (32%) and costal/abdominal pain (29%). Forty-three patients (76%) associated pleural effusion, 58% of which required drainage. The most affected region was the right upper lobe (41%). X-rays were supplemented with ultrasound (74%) and chest CT (30%). Nineteen isolations (13 pleural fluid, 5 blood culture, 1 both) were obtained: 16 *S. pneumoniae* (85%), 1 *S. aureus* (5%), 1 *F. necrophorum* and 1 *S.pyogenes*. Thirteen pneumococcal strains were serotyped being 1(6 cases), 5(3), 19A(2), 7F(2). One case was resistant to penicillin, all were susceptible to cefotaxime. Cases with confirmed pneumococcal etiology decreased after the introduction of PCV-13: 14 cases in 2004-09 vs. 2 in 2010-14. All resolved with medical treatment (mean duration 4 weeks), none requiring open surgery.

Conclusions: Pneumonia with necrosis/abscesses is frequently associated with pleural effusion. Most cases are caused by serotypes included in PCV13, with low antibiotic resistance. Evolution is favorable with exclusive medical treatment alone or combined with pleural effusion drainage.

ESPID-0029
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

EVALUATING THE FEASIBILITY OF INTEGRATING SALIVARY TESTING FOR CONGENITAL CMV INTO THE NEWBORN HEARING SCREENING PROGRAMME IN THE UK

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Background and Aims

Congenital CMV (cCMV) accounts for 20% of all childhood sensorineural hearing loss (SNHL) but is not routinely tested for at birth. Valganciclovir has been shown to prevent hearing deterioration and improve neurocognitive outcomes if started in the first month of life. This study aimed to assess the feasibility of integrating testing for cCMV using salivary swabs into the Newborn Hearing Screening Programme (NHSP).

Methods

Parents of newborns <22 days old in south west London, who were referred after their initial newborn hearing for further audiological testing, were approached by hearing screeners to obtain a saliva sample for CMV DNA PCR. Hearing screeners completed a five point Likert psychometric questionnaire to assess their opinions on the feasibility of cCMV testing through the NHSP.

Results

80% (203/255) newborns who were eligible had a saliva swab taken by the hearing screener. >99% results were delivered within the first month of life. Two newborns were identified with cCMV and both seen on day 10 of life by the paediatric specialist. All saliva samples tested delivered a result using real time PCR. All hearing screeners (20/20) stated that integrating testing for cCMV into the NHSP was a good idea and felt confident to perform this.

Discussion

It is feasible for hearing screeners to obtain saliva swabs to test for CMV DNA using real time PCR in newborns referred after their initial hearing screen. Rapid diagnostic testing for cCMV needs a more detailed clinical and cost effectiveness analysis.

ESPID-0124
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

GROUP B STREPTOCOCCUS IN THE GAMBIA – 20 YEARS ON

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Background: 20 years ago GBS genital colonization in Gambian mothers was reportedly predominantly due to serotype-V. The trivalent capsular polysaccharide conjugate vaccine currently in phase III trials includes only serotypes Ia, Ib & III. Here we define the current epidemiology of GBS in Gambian mothers and babies.

Methods: Rectovaginal swabs from Gambian mothers and nasopharyngeal and rectal swabs from their infants were collected in a prospective cohort study. Swabs were pre-cultured in Todd Hewitt Broth (THB), followed by culture on selective agar. Negative samples were analysed for the presence of DNA via real-time PCR. Positive isolates were serotyped using multiplex PCR and gel-agarose electrophoresis.

Results: 750 women/infant pairs were recruited to the study. 270 women (36%) were GBS-colonized (260 by culture alone, 10 by culture and PCR). 134 infants were colonized (25%) at birth and all but one remained colonized at six days. By three months, 44 infants remained colonized (6%) and 12 infants were newly colonized (2%). The predominant serotypes were: serotypes V (40%), II (28%), Ib (20%), Ia (10%) and III (2%). 12 colonized infants were treated for presumed neonatal sepsis and 4 for presumed meningitis. Blood cultures were positive for GBS(serotype-V) in one case, equivalent to 1.4/1000 live-births.

Conclusions: The serotype distribution among colonizing GBS strains in the Gambia remains unchanged over the last twenty years with serotype V predominating. Knowledge of the current serotype prevalence in regions such as the Gambia is vital to ensure vaccine development matches regional requirements to maximize its impact in these settings.

ESPID-0417
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

COMPARISON OF EARLY ONSET SEPSIS AND COMMUNITY-ACQUIRED LATE ONSET SEPSIS IN INFANTS LESS THAN 3 MONTHS OF AGE

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Aim: To compare demographic and clinical characteristics of early onset sepsis (EOS) and community-acquired late onset sepsis (CA-LOS) in infants.

Methods: Our medical center is the sole hospital in southern Israel, enabling incidence calculations. EOS (<7 days) and CA-LOS (7-90 days) episodes recorded between 2007 and 2013 were reviewed retrospectively. Univariate and multivariate analyses were performed.

Results: 70 EOS and 114 CA-LOS episodes were recorded. The respective mean±SD annual rates per 1,000 live-births were 0.66±0.16 and 1.03±0.23. Prematurity (42.9% *vs*. 17.0%), premature rupture of membranes (PROM; 22.9% *vs*. 1.9%), leukopenia (29.0% *vs.* 11.6%), thrombocytopenia (44.9% *vs*. 14.3%) and *Streptococcus agalactiae* infections (22.7% *vs*. 8.1%) were significantly more common in EOS. In contrast, fever (79.1% *vs*. 25.4%) and *Streptococcus pneumoniae* infections (12.9% *vs*. 1.3%) were significantly more common in CA-LOS. In both groups, Gram-negative bacteria predominated (~60%). Longer hospitalization duration (23.3±25.1 *vs*. 10.3±8.6 days) and higher case fatality rate (20.0% *vs*. 5.3%) were noted in EOS. Antibiotic resistance rates to empiric EOS and CA-LOS treatments were 0.0% and 1.2%, respectively.

In multivariate analyses, prematurity, low birth-weight and PROM were risk factors for EOS. Thrombocytopenia, absence of fever and poor outcome characterized EOS.

Conclusions: EOS and CA-LOS rates were lower in southern Israel than in other developed countries. EOS episodes were characterized by higher rates of perinatal risk factors. Inflammatory response differed between EOS and CA-LOS. Gram-negative bacteria were common in both groups, but *Streptococcus agalactiae* predominated in EOS. Current empiric treatments seem adequate, considering isolated pathogens susceptibility patterns.

ESPID-0436
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

BACTERIAL SEPSIS AND PERTURBED MATURATION OF THE GASTROINTESTINAL MICROBIOTA IN PREMATURE INFANTS

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Background:

We sought to identify clinical characteristics and microbial signatures in the gastrointestinal microbiota preceding diagnosis of late onset bloodstream infection (LO-BSI) in premature infants.

Methods:

Daily fecal samples and clinical data were collected over two years from 369 premature neonates (<32 weeks gestation). Next-generation sequencing of 16S rRNA gene regions amplified by PCR from total fecal DNA was used to characterize the microbiota of fecal samples collected from 22 neonates in the period preceding LO-BSI diagnosis, and from 44 controls. Culture of selected samples was undertaken, and bacterial isolates identified using MALDI-TOF. Antibiograms from bloodstream and fecal isolates were compared to explore strain similarity.

Results:

A Staphylococcus operational taxonomic unit (OTU) was over-abundant in fecal samples collected before LO-BSI diagnosis. Infants with LO-BSI had higher proportions of fecal aerobes/facultative anaerobes compared to controls from the week prior to diagnosis. Risk factors for LO-BSI were identified by multivariate analysis; fecal Staphylococcus OTU over-abundance, and the number of days prior to diagnosis of mechanical ventilation and of the presence of centrally-placed lines. Staphylococcal sepsis was associated with higher gestational age; enterobacteriaceal sepsis, with antecedent multiple lines and low diversity of fecal microbiota with prominent Enterobacteriaceae. Antibiograms of 12 species isolated from LO-BSI fecal samples collected closest to diagnosis matched the infant's bloodstream isolate.

Conclusions:

The gastrointestinal tract is an important reservoir for LO-BSI organisms, pathogens potentially translocating across the epithelial barrier. LO-BSI is associated with an aberrant microbiota, with abundant staphylococci and a failure to mature towards predominance of obligate anaerobes.

ESPID-0573
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

ASYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS - CLINICAL ASPECTS AND HEARING LOSS, THE CONCERT STUDY

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Backgroundand aims

CongenitalCytomegalovirus (cCMV) infections often proceed unnoticed in the neonatalperiod. However, all cCMV infected neonates are at risk for developing sensorineuralhearing loss, visual impairment, cognitive deficits and delayed motordevelopment. Insight into the clinical aspects and course of hearing lossin cCMV infected infants withoutclinically evident disease in the neonatal period (asymptomatic cCMV infection)is essential as most children with permanent sequelae are born without manifestsigns.

Methods

Parents of infantswho failed neonatal hearing screening (NHS) in The Netherlands are invited toparticipate in the CONCERT study. Dried blood spots obtained within 5 days ofbirth, are tested for CMV. The outcome of audiological investigations, brainultrasound and MRI, and developmental assessments are recorded and analysed.

Results

745 infantswho failed NHS were tested for cCMV, and 32 (4,3%) tested positive. Atinclusion bilateral hearing loss was confirmed in 15, unilateral hearing lossin 14 and normal hearing in 3 infants. At audiological follow-up late-onsethearing loss, fluctuating, progressive and improved hearing were all observedin at least one infant. No ophthalmological abnormalities were found. On brainultrasound and MRI more than half of the infants showed abnormalities, rangingfrom a single calcification, lenticulastriate vasculopathy or cyst to severepolymicrogyria.

Conclusions

These data emphasize the serious risk fordeveloping permanent sequelae faced by all infants with cCMV and hearing losswithout apparent clinical disease. The course of the hearing loss isunpredictable, and can make hearing rehabilitation extremely challenging.

ESPID-0600
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

DEVELOPMENTAL DISORDERS AND SENSORY DYSFUNCTIONS OF CHILDREN WITH CONGENITAL RUBELLA SYNDROME IN CENTRAL VIETNAM: A TWO-YEAR FOLLOW-UP REPORT.

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Background and aims: Congenital rubellasyndrome (CRS) cases emerged in Khanh Hoa Province, Vietnam, following alarge-scale rubella outbreak in 2011. The aim of this study was to investigatethe features of developmental problems combined with sensory defects inchildren with CRS.

Methods: From October 2011 to September 2012, a prospective surveillance forCRS was conducted among infants with any manifestations suspected of CRS at areferral hospital in the region. Study subjects underwent standard physicalexaminations, echocardiography, automated auditory brainstem responses (AABR)and blood sampling for blood counts and rubella-specific antibodies atenrollment. An ophthalmologist and an otolaryngologist examined thoseavailable in October 2013, including the second AABR. Ages and Stages Questionnaire (ASQ), DenverII, and Modified Checklist for Autism in Toddlers (M-CHAT) were used fordevelopmental assessments in December 2013.

Results: A total of 38 childrenwith CRS were enrolled. Of those enrolled, 14 were dead and two were lost tofollow up at median age of 23.8 months; the remaining 22 were analyzed. Eighteen (83%) were suspected of having somedevelopmental problem(s), 16 having hearing defect and six having ophthhalmologicalproblem(s). Among 14 children examined, 13 (93%) and 11 (79%) failed on atleast one domain of ASQ and Denver-II, respectively, particularly in the communicationdomain in ASQ (n=12) and the language area in Denver II (n=10). Six (43%) weresuspected of having autistic spectrum disorder by M-CHAT.

Conclusions: Manychildren with CRS were suspected of having some developmental problem(s), largelycombined with some sensory dysfunction(s).

ESPID-1057
MODERATED E-POSTER WALK 14 - CONGENITAL AND PERINATAL INFECTIONS

LONG-TERM NEURODEVELOPMENTAL OUTCOME OF VERY PRETERM AND/OR VERY LOW-BIRTH-WEIGHT INFANTS WITH LATE ONSET SEPSIS

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Background: Late-onset sepsis (LOS) represents a risk for inflammatory-mediated white matter injury to the immature brain, with possible neurobehavioral impairments.
Aim: To evaluate the effect of LOS on mortality and neurodevelopmental outcome.
Methods: Cohort of very low-birth-weight (VLBW:<1500gr) and/or very preterm (<32wk) infants, born between 2006-2012, admitted to our neonatal intensive care unit. Exclusion criteria: death ≤72h of life, early-onset sepsis, congenital malformations/genetic syndromes. LOS definition: clinical and laboratory signs of infection >72h of life with/without positive blood culture. Neurodevelopment assessment: Schedule of Growing Skills II at 24 months' corrected age. Neurodevelopmental impairment (NDI) definition: global developmental coefficient <70, cerebral palsy, blindness or deafness.
Results: Among 406 preterm infants (mean gestational age: 29,5±2,2wk, mean birth weight: 1222±323gr), 73 (18%) developed LOS with germen isolation in 68% (50/73).The overall mortality rate was 4% (17/405) and lethality 12% (9/73); pathogen lethality rates: Gram-negative bacteria and fungi 45% (5/11), Gram-positive bacteria 33% (3/9), coagulase-negative *Staphylococcus* 0% (0/30). Among LOS survivors, neurodevelopmental outcome was accessed in 97% (60/62). LOS group had higher NDI rate [22% (13/60) vs 8% (22/286); OR adjusted for gestational age (ORa) (95%CI) 2,8(1,2-6,5)], slightly higher cerebral palsy rate (8% [5/60] vs 4% [12/296]) and higher deafness rate [5% (3/60) vs 0,3% (1/296)], albeit not statistically significant. Only one in LOS group had blindness. LOS was associated with significant increase in mortality and NDI [34% (24/71) vs 9% (27/291); ORa (95%CI) 3,2(1,6-6,4)].
Conclusions: Mortality and NDI were significantly higher in infants with LOS compared with very preterm/VLBW infants without infections.

ESPID-0080
MODERATED E-POSTER WALK 15 - DIAGNOSTIC TOOLS

DISCRIMINATORY POWER OF MALTDI-TOF DIAGNOSTICS FOR PAEDIATRIC CYSTIC FIBROSIS

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Background

Acquisition of *Pseudomonas aeruginosa* and members of the *Burkholderia cepacia* complex (Bcc) can have a life changing impact on lung health in Cystic Fibrosis (CF) sufferers. Due in part to the introduction of rigorous infection control measures and aggressive antibiotic treatment regimes, survival rates have dramatically improved over the decades but rapid, accurate bacterial identification methods are crucial to the success of such strategies. This study aimed to assess the discriminatory power of Maldi-TOF technology applied to CF pathogens from paediatric patients.

Methods

CF isolates cultured from patients attending a Paediatric CF Centre and a stock collection of 100 Bcc were tested in parallel on BioMerieux and Bruker Maldi-TOFs. Results were compared to those generated by molecular methodology in-house and on referral of isolates to a Reference Laboratory.

Results

Five isolates catergorised as *P.aeruginosa* on the BioMerieux system were identified by in-house 16s ribosomal DNA sequencing or Reference Laboratory testing as *P.nitroreducens.* On retesting on the Bruker Maldi-TOF all 5 strains were identified as *P.nitroreducens.* Ninety four PCR-confirmed Bcc strains were tested in parallel and both Maldi-TOF machines categorised them within the cepacia complex. At Genomovar level, *B.multivorans* and *B.vietnamiensis* gave concordant results on the 2 systems. All of 28 *B.cepacia* identified on the BioMerieux maldi-TOF were *B.cenocepacia* according to Bruker.

Conclusions

Refinement of Maldi-TOF databases to overcome the anomalies identified in this study is essential before this technology can replace current DNA based identification methods. Misidentification of isolates can have significant clinical impact on treatment options for patients.

ESPID-0488
MODERATED E-POSTER WALK 15 - DIAGNOSTIC TOOLS

A PNEUMOCOCCAL PROTEIN ARRAY AS A PLATFORM TO DISCOVER SERODIAGNOSTIC ANTIGENS AGAINST INFECTION

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BACKGROUND AND AIMS: *Streptococcus pneumoniae* is one of the major causes of pneumonia worldwide. Etiological diagnosis of pneumococcal pneumonia in pediatric patients is challenging due to limited sensitivity of blood cultures and interference of colonization in the interpretation of PCR results, antigen testing and serological studies.

METHODS: The detection of serological markers by immunoassay is widely used for establishing the infectious etiology of many diseases. To this regard, we have developed a protein array of 95 recombinant proteins to test in a fast and reliable way patient sera in order to assess their serological response, and to establish an antibody pattern that can be clearly related to pneumococcal infection in children.

RESULTS: Applying a proteomics-based approach to identify surface-exposed proteins, we selected a *bona fide* set of proteins to be produced recombinantly and printed on chips. Hybridization with children sera revealed the most serodominant protein antigens, including many known immunogenic antigens, but also others whose immunogenic capacity had not been previously shown, as the cell-wall protein PrtA and the prophage-encoded PblB, which has been demonstrated to be highly surface-exposed in other streptococcal species.

CONCLUSIONS: This is the first time in which a protein array has been used for detection of serological markers. The technique clearly discriminates groups of proteins that can be associated with pneumococcal infection. A new protein, PblB, has been found as a good diagnostic marker. Both the platform and the protein markers could be also used to improve vaccine discovery.

ESPID-0490
MODERATED E-POSTER WALK 15 - DIAGNOSTIC TOOLS

A MULTIPLEX LUMINEX-BASED ASSAY TO DISCOVER DIAGNOSTIC MARKERS OF PNEUMOCOCCAL INFECTION AND FOR USE IN PROGRAMS OF EPIDEMIOLOGICAL SURVEILLANCE

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Background and aims: Pneumococcal surface proteins are potential candidates for the development of protein-based vaccines and serological assays. The objective of the study was to develop a multiple bead-based immunoassay using Luminex xMAP® technology for the quantitation of natural antibodies against *Streptococcus pneumoniae* proteins and the characterization of the acute serum response following pneumococcal pneumonia in children.

Methods: 64 recombinantly produced pneumococcal proteins were coupled to fluorescent SeroMAP® beads and anti-pneumococcal specific IgG levels were determined in sera. These samples were collected from children with microbiologically proven pneumococcal pneumonia (n=54) and from a control group of healthy children (n= 31) and pediatric patients with non-pneumococcal infectious diseases (n=21).

Results: Multiplex assay was validated through comparison of IgG levels to 14 randomly chosen pneumococcal antigens by using multiplex and singleplex assays (R^2=0.97). There were marked variations among the individual proteins. Median fluorescence intensity values (MFI) ranged from 37 for SpxB to 17889 for PspC. The seroresponses for the children with pneumococcal pneumonia compared to controls showed higher antibody titers in pneumonia patients against 40 (63%) proteins and lower IgG titers for the remaining 24 antigens. Acute anti-Sp0464, anti-PrsA and anti-RrgB IgG titers were significantly lower in pneumonia patients than in control children.

Conclusions: A multiplex Luminex assay to measure the seroresponses to 64 pneumococcal proteins was developed. This methodology could be useful in vaccine studies and for investigating etiological diagnosis of pneumococcal pneumonia in children because some proteins showed differential acute phase IgG responses compared to controls.

ESPID-0495
MODERATED E-POSTER WALK 15 - DIAGNOSTIC TOOLS

PEDIATRIC POPULATION: MALDITOF IDENTIFICATION IN BLOOD CULTURES REDUCES TIME TO APPROPRIATE ANTIBIOTIC THERAPY.

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Background: Approximately 30000 Canadians develop sepsis each year with an associated mortality rate of 30%. Early institution of appropriate antibiotics is associated with improved outcomes.

Aim: Compare the time to initiation of appropriate antibiotic therapy in patients with blood stream infections during corresponding periods in 2012, 2013 and 2014 to assess the impact of short incubation culture and MALDI-TOF identification (SMI) methods.

Methods: Charts of patients at London Health Sciences with positive blood cultures were reviewed for a 6 week period in 2012 (standard incubation and ID using Vitek), 2013 (MALDI-TOF identification after standard incubation) and a comparable 6 week period in 2014 (short term incubation and ID using Maldi TOF) The time to initiation of appropriate antibiotic, as directed by pathogen identification was compared.

Results: We identified 8/38 patients in 2012, 13/35 patients in 2013 and 11/25 patients in 2014 where empirical antibiotics needed to be changed. The average time to final identification of the pathogen was respectively 87, 75.7 and 70.5 for the respective periods. In 2014 we adapted a process whereby the interim identification obtained from the SMI was reported, this resulted in a reduction in time to initiation of more appropriate antibiotics from 68.76 hours (2012 and 2013) to 58 hours in 2014.

Conclusions: We concluded that a rapid detection method for pathogens from positive blood cultures reduces time to initiation of appropriate antibiotics in a patient population with blood stream infections. Further studies are required to see whether this impacts patient outcomes.

ESPID-0833
MODERATED E-POSTER WALK 15 - DIAGNOSTIC TOOLS

QUANTITATIVE NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY DISTINGUISHES METABOLITE SIGNATURES IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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Background: CAP is caused by a wide array of pathogens. Available tests for etiological differentiation are insensitive, invasive, or impractical in children. Our objective was to identify metabolite signature candidates of pneumonia-causing pathogens in urine samples from children diagnosed with CAP.

Methods: We conducted a case control study of children, 3 months-18 years old. Cases were diagnosed with chest x-ray confirmed CAP in the emergency department and age- and sex-matched to controls who were healthy children with no known infection. Patients with chronic medical conditions or who were hospitalized 14 days prior were excluded. Influenza and respiratory syncytial virus (RSV) were confirmed by PCR from nasopharyngeal swabs. Urine samples were collected at time of presentation. One-dimensional ^{1}H-NMR spectra of urine samples were obtained on a 500 MHz NMR spectrometer. Raw spectra were processed using Chenomx software. Quantified metabolite data were standardized for urine creatinine and a partial least squares-discriminant analysis (PLS-DA) was performed.

Results: Three distinct profiles were found for healthy children (n=14), children with influenza pneumonia (n=4) and children with RSV pneumonia (n=3) (Figure 1A). We identified six metabolites which differentiated these groups: acetoacetate, acetone, 3-hydroxybutyrate, hypoxanthine, phenylalanine, and taurine (Figure 1B).

Conclusions: We found unique urine metabolite signatures using quantitative ^{1}H-NMR from children with no infection, with RSV and with influenza. These findings show the potential of urine metabolomics to provide a sensitive, efficient, and noninvasive approach for etiological differentiation in children with pneumonia.

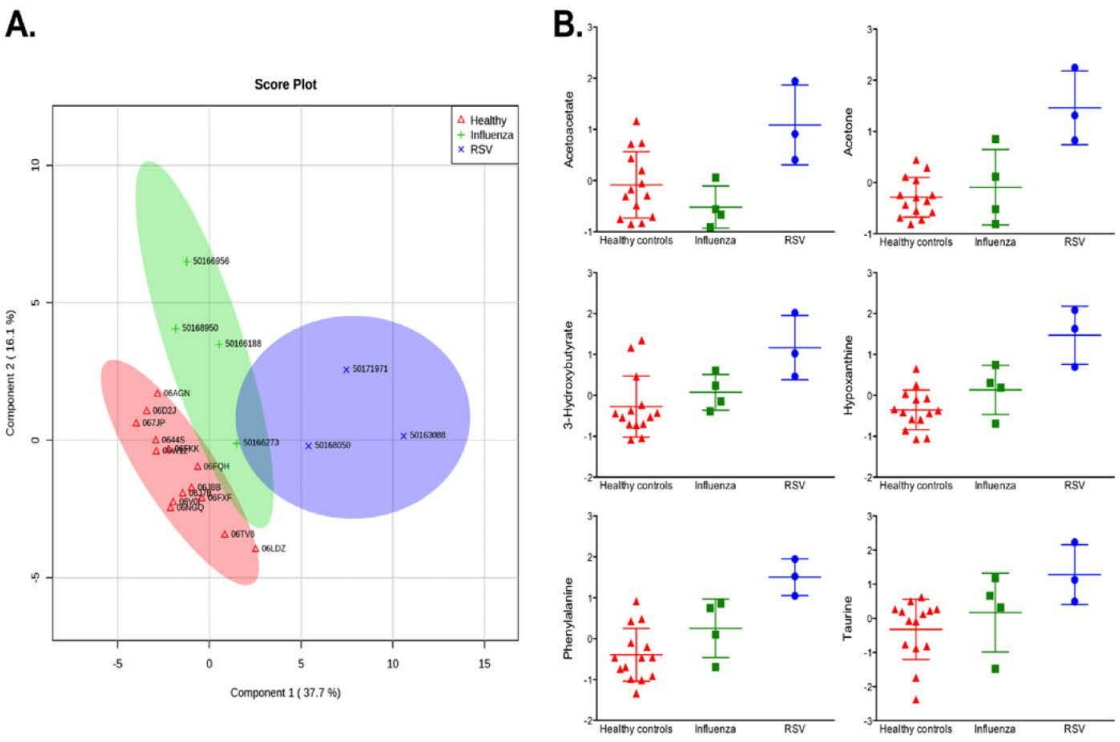

Figure 1: Quantitative ^{1}H-NMR metabolomics of urine from pediatric healthy controls (n=14; red) and patients with either influenza (n=4; green) or respiratory syncytial virus (RSV;n=3; blue). **A**) PLS-DA of the three data sets that support the concept that the three groups are metabolically distinct. **B**) Normalized concentration data of metabolites that contribute to differences between the groups, these include, from left to right: acetoacetate, acetone, 3-hydroxybutyrate, hypoxanthine, phenylalanine, and taurine. Cross-bars are the mean normalized concentration data (±S.D).

ESPID-0982
MODERATED E-POSTER WALK 15 - DIAGNOSTIC TOOLS

EVALUATION OF BLOOD CULTURE BOTTLE VOLUMES IN CHILDREN WITH SUSPECTED BACTERIAL INFECTIONS

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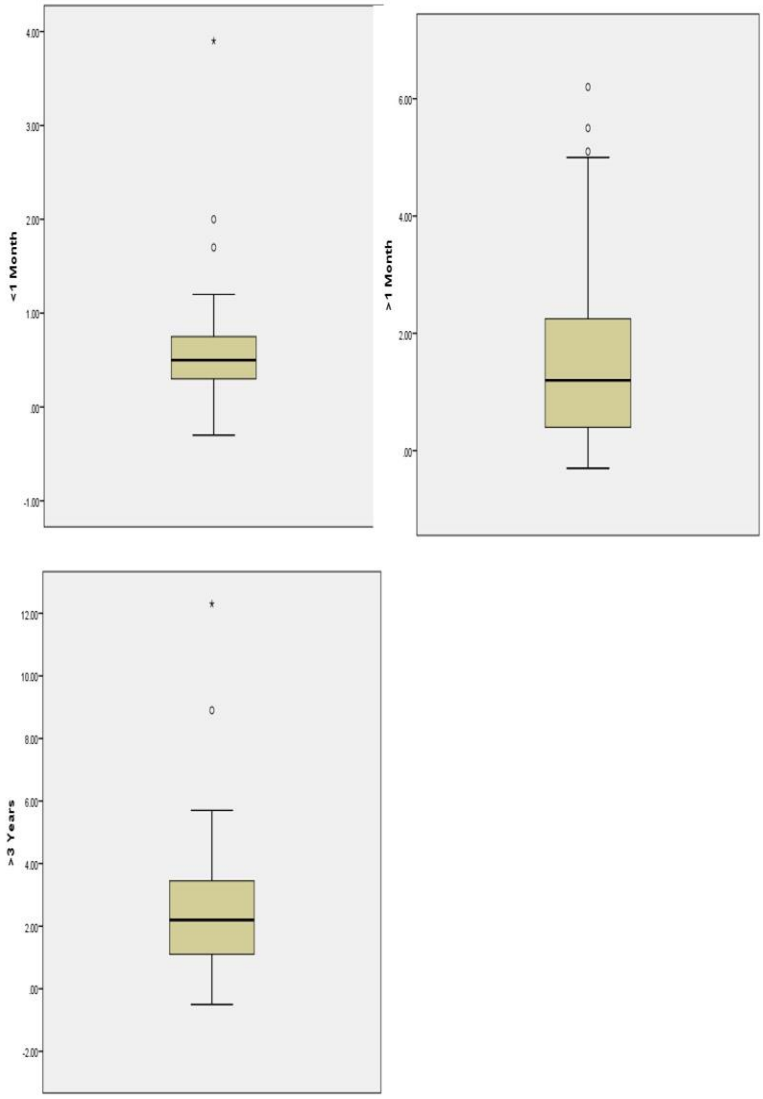
Previous studies have shown there is a correlation between the volume of blood used in blood cultures and the sensitivity of the test. This has implications for the validity of the test as low fill rates may lead to a high number of false negative results. This is relevant as other studies have shown that low fill rates are a problem in hospitals. In light of this an audit was undertaken in a regional children's hospital to assess whether this was occurring.

The audit was over a 3 month period and total of 358 blood cultures were assessed. The data was split into 3 age categories each with a different acceptable volume requirement; under 1 month (0.5ml), 1 to 36 months (1ml), greater than 36 months (4ml). In the <1 month group 21/39 (54%) were adequately filled with a median of 0.5ml, 1-36 month 104/184 (56.5%) with a median of 1.2ml, >36 months 20/135 (14.8%) with a median of 2.2ml.



The lowest rates were seen in frontline units, Accident & Emergency and the Paediatric Assessment Unit, however no unit had 100% adequacy.

The results show this is a vital area requiring addressing. This was has been addressed but an education intervention involving presentations, posters, and teaching sessions. To assess the effectiveness of this intervention a re-audit is currently in progress.

ESPID-0263
MODERATED E-POSTER WALK 16 - TUBERCULOSIS AND TROPICAL DISEASES

ENVIRONMENTAL TEMPERATURE IMPACTS ON THE PERFORMANCE OF QUANTIFERON-TB GOLD IN-TUBE ASSAYS USED FOR THE DIAGNOSIS OF TUBERCULOSIS

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Background and aims:

QuantiFERON-TB Gold-In-Tube (QFT) assays are interferon-gamma release assays used for the diagnosis of TB in routine clinical practice. Indeterminate QFT results are not uncommon and pose a considerable management dilemma. The majority of indeterminate results are due to insufficient interferon-gamma responses in the positive control sample. This study investigated the impact of environmental temperatures on QFT assay performance.

Methods:

Seventeen healthy adult volunteers (10 male, 7 female) were recruited into the study. From each participant 5 duplicate sets of samples [comprising QFT positive (PHA-stimulated) control and nil (unstimulated) control samples] were obtained and maintained for 16 hours at the following temperatures: 4°C, 15°C, 22°C (as per manufacturer's instructions), 30°C, and 37°C. All samples were then incubated at 37°C for another 24 hours after which the supernatants were harvested, as per manufacturer's instructions. Interferon-gamma concentrations in supernatants were determined by Luminex xMAP assays (ProcartaPlex, eBioscience).

Results:

The PHA-induced interferon-gamma concentrations in the positive control samples were significantly lower in samples initially maintained at 4°C, 15°C, or 22°C (median concentrations 62.8, 53.5, and 54.8 IU/mL, respectively) compared with samples maintained at 30°C or 37°C (median concentrations 214.3 and 189.5 IU/mL, respectively; repeated measures ANOVA $p<0.0001$). In contrast, there was no

significant difference between interferon-gamma concentrations in the nil control samples across different temperatures (repeated measures ANOVA p=0.2045).

Conclusions:

The results show that environmental temperatures during the pre-incubation period have a significant impact on PHA-induced interferon-gamma responses. Therefore, optimisation of temperatures during transport and processing may reduce indeterminate QFT results.

ESPID-0395
MODERATED E-POSTER WALK 16 - TUBERCULOSIS AND TROPICAL DISEASES

PROFILE OF DENGUE AMONG CHILDREN TREATED IN A COMMUNITY HOSPITAL AND COMPARISON OF EFFICACY OF NS1 ANTIGEN ASSAY WITH MAC-ELISA FOR DIAGNOSIS OF DENGUE

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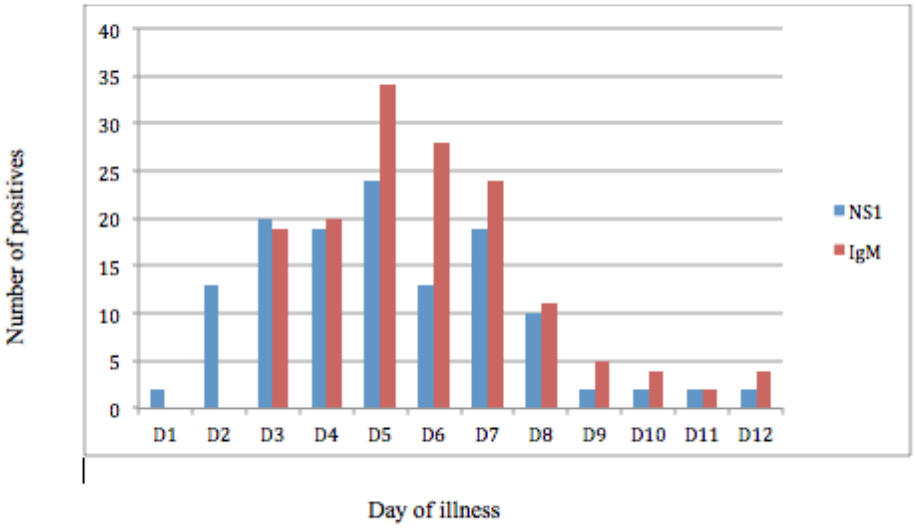
Aims: 1. To study profile of Dengue infection, 2. To compare efficacy of NS1 antigen assay with MAC-ELISA for diagnosis of dengue, during acute and convalescent phases, 3. To assess time frames for test positivity
Methods: This prospective cohort study was done in the pediatric department of an Indian community hospital between July 2011 and July 2012 after IRB approval and informed written parental consent. Clinical features and diagnostic test results (dengue NS1 antigen, IgM and IgG ELISA done on the day of hospitalisation) of 178 children with Dengue infection were studied.
Results: Majority of children (37.7%) were 11 to 15 years of age. 59.4% were males. Proportion of males was higher in extremes of age groups. Clinical manifestations were fever (91.6%), rash (35.8%), hepatomegaly (33%), ascites (11.3%), bleeding manifestations (17%) and pleural effusion (3.7%). 21.7% had DHF; 7.5% had DSS. Laboratory findings included thrombocytopenia (77%), leucopenia (24.5%) and raised SGPT (63.2%).
33% presented in acute phase and 67% in convalescent phase (5-7 days: 53.8%, >7 days: 13.2%).
94.3% tested positive for NS1Ag or IgM or both. NS1 and IgM ELISA positivity were 88.6% and 51.4% respectively in acute phase and 63.38% and 92.8% respectively in convalescent phase (p
Conclusions: Typical clinical features and laboratory investigations aid early and accurate diagnosis of dengue. NS1Ag and IgM ELISA are good diagnostic tools in acute and convalescent phases respectively.

Graph 1: Time Frame for Positivity of NS1 antigen and IgM ELISA



ESPID-0596
MODERATED E-POSTER WALK 16 - TUBERCULOSIS AND TROPICAL DISEASES

BCG ADENITIS – A 6 YEAR REVIEW

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Background and aims: The most common complication of BCG vaccine is axillary adenitis. The aim of this study was to characterise patients with adenitis associated with BCG.

Methods: Retrospective review of all cases of children with BCG adenitis in a paediatric centre from 2009 to 2014.

Results: During the 6 years of the study, 79 children were diagnosed with BCG adenitis. Median age of appearance was 5M (0.5-18M). Location was: 83.5% axillary, 6.3% supraclavicular, 6.3% axillary and supraclavicular, 1.3% infraclavicular and 1.3% cervical. After the initial assessment, 57/79 (72.2%) continued follow-up in hospital. Investigation was done in 54.4%: 49.4% (39) complete blood count, 19% (15) ultrasound and 13.9% (11) had immunological testing, which was altered only in one child, diagnosed later with chronic granulomatous disease (CGD). This patient presented with exuberant axillary adenitis since 3M of age, hepatosplenic lesions and a family history of a brother's death during the first year of life.

In 44 (55.7%) patients spontaneous drainage occurred and in 3 (3.8%) surgical drainage was done. Suppuration occurred on average 4.9M after the appearance of adenitis. Lymph node excision was not performed in any case. Antituberculosis drugs were started in the patient with CGD. The average time for clinical resolution was 8.7M (1-33M).

Conclusions: Most cases of BCG adenitis are axillary, benign and self-limited, although duration may be prolonged, and suppuration frequent. Usually investigation is unnecessary. Only one case, with serious clinical manifestations and risk factors, was diagnosed with a primary immunodeficiency.

ESPID-0828
MODERATED E-POSTER WALK 16 - TUBERCULOSIS AND TROPICAL DISEASES

PARADOXICAL REACTION TO ANTITUBERCULOSIS THERAPY IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND DISEMINATED TB INFECTION.

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INTRODUCTION

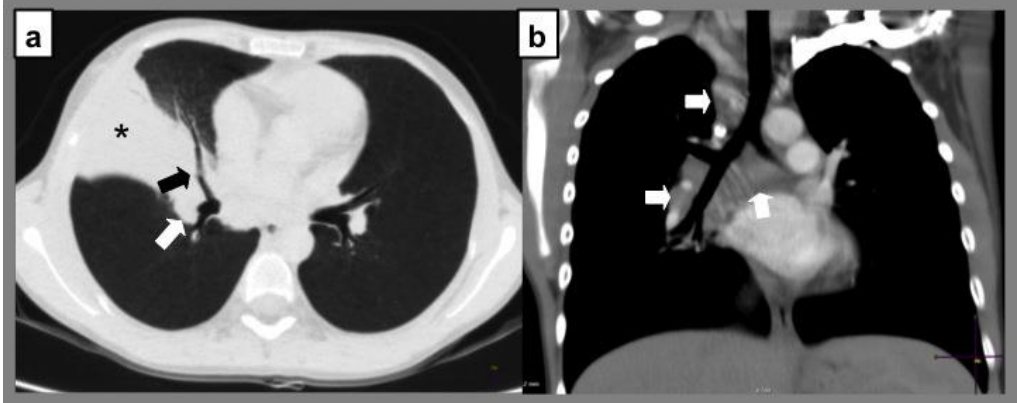
Tuberculosis in children continues to be an important health problem worldwide. Diagnosis and treatment is especially challenging in inmunocompromised patients and complications are more frequent.

CLINICAL CASE

A 13-year-old Moroccan girl who lived in Spain, with a history of systemic lupus erythematosus in treatment with corticosteroids and mycophenolate mofetil, presented to the emergency department a month after a holiday in Morocco with fever and cough. She was diagnosed of pneumonia and admitted for IV antibiotics despite which the fever persisted. Pulmonary tuberculosis was suspected and confirmed by real time PCR (GeneXpert MTB/RIF) in auramine-positive sputum. After initiating treatment with 4 active anti-TB drugs (HRZE) she continued to spike high daily fevers, symptoms worsened and ocular tuberculosis and splenic dissemination were found in further investigations. A chest CT showed enlarged lymphadenopathies causing amputation of the bronchus for the lateral segment of the middle lobe (figure) that did not exist prior to treatment. Paradoxical reaction to the anti-TB treatment was suspected and high-dose corticosteroids were started and tapered after 6 weeks, once symptoms were under control. Her recovery is slow but satisfactory after tapering the steroids.

CONCLUSIONS

Although tuberculosis is a disease with curative treatment, the control of the disease is difficult in inmunocompromissed patients in whom dissemination is frequent. If patients respond inadequately or symptoms worsen while on anti-TB therapy, it is very important to consider a paradoxical response.



a. Axial MinIP CT reconstruction. Amputation of the bronchus for the lateral segment of the middle lobe due to right hilar adenopathies and segmental atelectasis.

b. Coronal MPR CT reconstruction after iodinated intravenous contrast injection. Right paratracheal, right hilar and subcarinal adenopathies are depicted.

ESPID-0842
MODERATED E-POSTER WALK 16 - TUBERCULOSIS AND TROPICAL DISEASES

MANAGEMENT OF CHILDREN WITH NONTUBERCULOUS MYCOBACTERIAL (NTM) NECK LYMPHADENOPATHY

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Background

The optimal treatment of nontuberculous mycobacterial (NTM) lymphadenitis in childhood is discussed controversially. Therefore, this study compares the complication rates of different therapy options (surgical therapy vs. Wait&See) among children.

Methods

All children who were treated for NTM lymphadenitis colli in our hospital between March 2000 and August 2013 were included in the retrospective study and invited to the prospective follow-up.

Results

Retrospective analysis identified 36 children (20 girls, 16 boys, mean age 3.6 years). 27 children were classified as verified NTM (PCR/culture), 6 children as probable NTM (typical histology) and 6 children as possible NTM (typical clinical picture). 28/36 children were treated surgically; 17 received additional drug therapy. 8/36 children were treated non-surgically (3 drug therapy, 5 Wait&See strategy).

Follow-up included 30/36 children (24 with surgical and 6 with conservative treatment). In 7/24 children with surgical treatment (29%) cranial nerve palsy was found: 1 permanent Horner`s syndrome, 1 permanent accessory nerve palsy, 5 permanent facial nerve palsy and 2 transient facial nerve palsy. All cases with permanent palsy were caused by extensive lymph node dissections. 5/6 non-operatively treated children did not show any cranial nerve palsy but developed relapsing purulent fistulas and showed wider scars with worse cosmetic outcome.

Conclusion

For the development of therapy recommendations a larger study population is needed. We conclude that in case of surgical therapy, dissections should be restricted to avoid nerve injury; non-operative treatment may result in a prolonged course of the disease with open wounds and unfavourable cosmetic outcome.

ESPID-1038
MODERATED E-POSTER WALK 16 - TUBERCULOSIS AND TROPICAL DISEASES

ONE YEAR OF CHILDHOOD TUBERCULOSIS IN SPAIN: FIRST DATA FROM THE SPANISH PAEDIATRIC TB RESEARCH NETWORK (PTBRED).

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Background and aims

A multidisciplinary network of paediatricians throughout the Spanish geography (pTBred) was launched in 2013 with the aim to register all new childhood tuberculosis (TB) cases. We present the 1st-year results of this cohort.

Methods

Children <18 years diagnosed with TB disease from 69 hospitals within 2014 were prospectively enrolled.

Results

In 2014, 37 out of 69 institutions enrolled 154 TB cases (50.3% males; median[IQR]

age 4.4[2.1-11.2]yr). Most of them were born in Spain (81.8%), one half to foreign parents (50.6%), and 83.3% were previously healthy. Extrapulmonary disease was diagnosed in 19% (15 lymphatic, 6 CNS, 3 osteoarticular, 9 other). Overall, 55/141(39%) were confirmed TB cases (32.6% by culture (46/141), 6.4% by PCR (9/141)) and 2/46 (4.34%) were drug resistant (DR): 1 isoniazid-resistant, 1 pyrazinamide-resistant. Two additional isoniazid-resistant cases were diagnosed among non-confirmed cases (DR index case). TB complications occurred in 14.6%: 11 at diagnosis (6 respiratory, 2 CNS, 2 osteoarticular, 1 renal), and 9 paradoxical reactions during treatment. Complications were more frequent in children born abroad (p=0.013) or to immigrant parents (p=0.022), TB exposure abroad (p=0.001), CNS TB (p=0.026) and osteoarticular TB (p=0.009). Adherence to therapy was optimal in 97.1% of cases.

Conclusions

One half of children diagnosed with TB in Spain in 2014 were born to foreign parents, showing higher rates of complications. Drug resistance rate was low This new research network will be an invaluable basis for future high quality studies in our country and within the European Paediatric TB Network.

Poster Presentations

ESPID-0954
CONGENITAL AND PERINATAL INFECTIONS

ANTIVIRAL THERAPY FOR SYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS INFECTION IN NEONATES AND INFANTS

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Background. Cytomegalovirus is the leading cause of congenital infection in developed countries and non-genetic cause of sensorineural hearing loss, optic nerve atrophy and neurodevelopment delay. The prevention of cognitive, developmental, motor, visual or audiological sequelae may reach using specific therapy.

Aim. To assess the efficacy of antiviral therapy in infants with symptomatic congenital cytomegalovirus infection in connection with the consequences in children at one year.

Methods. We examined 40 patients with symptomatic congenital cytomegalovirus infection. They were divided into 2 groups, of which 26 (65%) patients received a specific treatment with ganciclovir (subgroup 1) and 14 (35%) infants - not received therapy (subgroup 2). Patients in subgroup 1 and subgroup 2 had the same clinical features and were comparable ($p>0.05$). Ganciclovir was used ntravenous in a single dose of 6 mg/kg two times a day, Median of course was 21 (18-21) days. The efficacy of antiviral therapy established in connection with consequences of the disease. The side effects: neutropenia, thrombocytopenia, anemia did not registered

Results. Analysis of results of ganciclovir showed that in patients aged 1 year in the subgroup 2 without treatment compared with the subgroup 1 registered neurological outcomes significantly more often ($\chi2=6,5$, $p<0.05$) in the form of hydrocephalus ($\chi2 =5,1$; $p <0.05$) and psychomotor development delay ($\chi2 = 5,0$; $p<0.05$).

Conclusions. The treatment with ganciclovir in newborns and infants reduces neurological sequelaes in children in the first year of life.

ESPID-0907
CONGENITAL AND PERINATAL INFECTIONS

PREGNANCY-RELATED LISTERIA MONOCYTOGENES INFECTIONS IN NOTHERN SPAIN: CLINICAL FEATURES AND OUTCOME

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Background and aims:
Listeria monocytogenes, having a great affinity for placental tissue, can cause miscarriages, preterm births and severe neonatal infections. The aim of this study is to analyze pregnancy-related Listeria infections in Nothern Spain.

Methods:
Descriptive retrospective study of cases of pregnant women and infants up to 3 months old, with a positive culture for *L. monocytogenes* registered in public hospitals in Asturias (Spain) from 2003 to 2014 (population: 1,058,976).

Results:
Ten cases of neonatal listeriosis were diagnosed: 8 early-onset infections (6 sepsis and 2 bacteriemia with meningitis; mean gestational age 33 weeks, all with infection risk factors; 3 newborns needed advanced resuscitation measures) and 2 late-onset meningitis (term infants from uncomplicated pregnancies, 13 and 36 days old). C-reactive protein was elevated in 9 cases (median 69.5 mg/l, 3.9-188 mg/l). All cases received adequate empirical antibiotherapy. One newborn died and another developed severe neurological impairment. *L. monocytogenes* was isolated in placental culture in 3/3 cases and pathology showed acute chorioamnionitis in 4/5 cases.
L. monocytogenes was detected in different biological samples from other 10 pregnant women; all of them developed fever before delivery. Three pregnancies finished in spontaneous abortions (gestacional age: 12, 21 and 32 weeks). Blood cultures in the other 7 newborns were negative and they all had a favorable outcome.

Conclusions:
Pregnancy-related listeriosis is a disease with a high morbimortality. Early-onset infections often occur in preterm births with infection risk factors. Late-onset Listeria infection is less common and affects term infants with no risk factors.

ESPID-0892
CONGENITAL AND PERINATAL INFECTIONS

DIFFERENT ONSETS OF GROUP B STREPTOCOCCAL INFECTION IN NEONATES

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Background:

Maternal colonization is the primary risk factor for group B streptococcal (GBS) infection in neonates and young infants. This disease is classified by age at onset, and it may present with a wide spectrum of clinical manifestations.

Methods:

We describe 3 cases of different neonatal GBS infection onsets. The etiology was confirmed by isolation of GBS in blood culture in all of them, but presented with distinct clinical pictures. Two of them were late-onset GBS infections, one associated with cellulitis-adenitis which presented at 28 days of age (mother colonized at delivery, complete prophylaxis administrated), the other one with meningeal involvement presented at 2 months of age (mother not colonized at delivery). The third case presented as an early-onset GBS infection (mother colonized at delivery, incomplete prophylaxis provided). All of them had favorable evolution with endovenous treatment (up to 21 days of ampicillin in the case with meningitis).

Discussion:

Intrapartum antibiotic prophylaxis, provided to mothers colonized by GBS, make their infants less likely to have sepsis/documented GBS bacteremia, as presentation of early-onset GBS disease.

However, application of these preventive strategies has had no impact on the incidence of late-onset disease. GBS exposures of these infants are thought to occur from colonized parents or siblings at home.

Conclusions:

Despite the decline in its incidence after implementation of strategies for detection and prophylaxis of colonized mothers, early-onset neonatal GBS infection continues

to occur. Moreover, neonatal GBS disease may occur even in the absence of maternal colonization, so it must always be considered.

ESPID-0773
CONGENITAL AND PERINATAL INFECTIONS

COAGULASE-NEGATIVE STAPHYLOCOCCUS SEPSIS IN VERY-LOW-BIRTH-WEIGHT AND/ OR VERY PRETERM INFANTS - OUTCOMES

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Background and aims: Late-onset sepsis caused by coagulase-negative staphylococcus (CoNS) is a significant problem in neonatal intensive care units. The aim was to evaluate the impact of CoNS sepsis in very-low-birth-weight (VLBW) and/or very preterm (PT) infants on the neurodevelopment outcomes at 24-30 months of age.

Methods: Retrospective study, including all very PT [<32 weeks gestational age (WGA)] and/or VLBW] admitted to MBB in 2006-2012, with Schedule of Growing Skills' follow-up. Congenital malformations, genetic syndromes, infections/sepsis by other agents or with negative blood culture were excluded. Two groups, with or without CoNS sepsis (CoNS-positive and CoNS-negative, respectively), were compared. Statistical analysis by SPSS-17.0.

Results: The study included 355 infants, 30 CoNS-positive (8,4%). Risk of sepsis was higher in PT <28 WGA (OR 4,7; CI 95%: 2,1-10,9; p<0,001) or <1000g (OR 4,6; CI 95%: 2,1-9,9; p<0,05). CoNS-positive needed more invasive procedures (CPR, ventilation, transfusions, parenteral nutrition, central catheters, p<0,05) and had more associated comorbilities (necrotizing enterocolitis and patent ductus arterious, p<0,05). The GA-adjusted risk of cerebral damage (intraventricular hemorrhage grade ≥III and/or cystic leukomalacia) was 3,6 times higher on CoNS-positive (CI 95%: 1,2-11,3, p<0,05). That group also showed more cerebral palsy (10% versus 4%) and a lower average of the development quotient (91,8±16 versus 95,9±11), albeit with no significant meaning.

Conclusions: Altough the two groups were very different (CoNS sepsis occurred more in younger and lighter infants), cerebral damage were more common in the CoNS-positive one, but no difference between them was found in neurodevelopment outcomes at 24-30 months of age.

ESPID-0897
CONGENITAL AND PERINATAL INFECTIONS

STAY HUNGRY, STAY ALIVE – MONOCYTES ARE CAPABLE TO FIGHT TWICE

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Background: Recently, bystander apoptosis ofnon-phagocyting monocytes was described.This phenomenon was found reduced in cordblood. Hypothesis: Phagocytosis is the drivingforce of bystander apoptosis. We addressed the question whether a second infectionwith bacteria leads to different peri-phagocytic reactions and consequences amodified bystander apoptosis. Experimental setup: *E.coli* infection model with as described before. Infections weremade in 24 h intervals (d0: first infefction, d1: second infection) at a multiplicityof infection (MOI) of 10. ROS production, phagocytic indices and apoptosis weremeasured 30 h post infectionem (p.i.). Cytokine secretion was assessed byELISA. Results: As determined 24 hours after the 2nd infection , pre-challenge of PBMO and CBMO didnot result in a decrease of total phagocytic properties. More PBMO were double-phagocytingcompared to CBMO (p> 0.05 vs. PBMO). We did not find any reduced ROS productionafter re-challenge of PBMO and CBMO. Re-challenge resulted in a reduced IL-10secretion in CBMO compared to PBMO, the TNF-a secretion was not affected. Bystanderapoptosis (7.3 ± 4.2%; p=0.026 vs. control) wasdetectable 24 hours p.i.for PBMO. Previously we did not observe bystanderapoptosis CBMO ap to 4 h p.i.. However, 24 h p.i. CBMO became apoptotic in thesame range Conclusion: Both, PBMO and CBMO were capable to phagocyte *E. coli* twice, at an interval of 24hours and to intracellularly degrade bacteria. The finding, that bystander kill can beinduced in CBMO points to a delayed or less effective signalling in neonatalmonocytes.

ESPID-0616
CONGENITAL AND PERINATAL INFECTIONS

ASSOCIATION BETWEEN PSYCHOSOCIAL DISORDER DURING PREGNANCY AND CHILDHOOD AUTISM SPECTRUM DISORDER BY GESTATIONAL AGE OF EXPOSURE AND RACE/ETHNICITY.

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Background: Psychosocial stressors (PSD) during fetal development upregulates pro-inflammatory cytokines and chemokines at the maternal-fetal interface and in the fetal brain. This risk is most pronounced when the exposure occurs early in the gestation. We examined the association between PSD and autism spectrum disorders (ASD) based on child race/ethnicity, gestational age, and length of exposure.

Methods: A retrospective cohort study of singleton born children age 3-17 years (n=406,465) delivered in Kaiser Permanente Southern California hospitals (1991-2009) was performed using the electronic medical records (EMRs). ICD-9 codes and medication-specific for PSD from EMRs were used to ascertain the exposure and outcomes of interest. Cox proportional hazard regression was used to estimate hazard ratios (HR).

Results: The incidence rate of ASD among children with and without prenatal exposure to PSD were 3.27 and 1.46/1000 persons-year, respectively (HR=1.82, 95%CI 1.65-2.01). Children of White (HR=2.51, 95%CI 2.11-2.99), Black (HR=2.40, 95%CI 1.79-3.23), Hispanic (HR=1.53, 95% CI 1.28-1.83), and multiple (HR=1.53, 95%CI 1.27-1.86) race/ethnicity who were exposed to PSD *in utero* were at increased risk of ASD, but not Asian/Pacific-Islanders (HR=0.95, 95%CI 0.52-1.72). Risk of ASD among those exposed to PSD *in utero* is increased regardless of the timing or length of exposure.

Conclusion: PSD during pregnancy is associated with risk of ASD for White, Black, Hispanic, and multiple race/ethnicity. Although exposure to stressor early in the gestation is known to increase risk, children exposed to PSD during late gestation may be also at increased risk. Identification of at-risk children for ASD may help early diagnosis.

ESPID-1045
CONGENITAL AND PERINATAL INFECTIONS

POSITIVE CYTOMEGALOVIRUS PCR IN CEREBROSPINAL FLUID OF PATIENTS WITH CONGENITAL CYTOMEGALOVIRUS INFECTION: DOES IT HAVE A PROGNOSIS VALUE?

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Background and aims

In neonates with congenital cytomegalovirus (CMV) infection, a positive cerebrospinal fluid (CSF) PCR correlates with poor neurodevelopmental outcome. To further analyze its prognosis value, we compared patients with congenital CMV infection and positive CSF-PCR with those with negative results.

Methods

An observational and descriptive study was performed using Spanish Congenital Cytomegalovirus Infection Database (REDICCMV; http://www.cmvcongenito.es). Patients in whom CMV PCR in CSF was performed were evaluated. Those with

immunodeficiency, maternal immunodeficiency, other congenital infections and blood-tinged CSF sample were excluded.

Results

Eighty-four patients (mean gestational age 37.1 weeks) met inclusion criteria: 16 (19%) with positive CMV PCR in CSF and 68 (81%) with negative results. All positive PCR patients were symptomatic at birth, compared with 67.6% of infants in the negative PCR group (p=0.04). Microcephaly (54.5% vs. 32.8%), cerebral magnetic resonance abnormalities (63.6% vs. 60%), cerebral ultrasound abnormalities (43.7% vs. 34.9%), hearing loss in any ear (55.5% vs. 38.8%) and neurodevelopmental delay at 6 months of age (28.5% vs. 13.16%) were more frequent in the positive CSF-PCR group, although differences with the negative group were not statistically significant.

Conclusions

Congenital infected infants with positive CSF-PCR for CMV are symptomatic at birth. A higher frequency of neurological symptoms and neuroimaging abnormalities are seen in this group, but differences with negative CSF-PCR infants did not reach statistical significance, possibly due to small sample size. Prospective studies in larger number of patients are needed to establish the prognosis value of this technique.

ESPID-0843
CONGENITAL AND PERINATAL INFECTIONS

NEONATAL INFECTION: TWO DIFFERENT PATIENTS WITH A SIMILAR ONSET AND THE SAME PATHOGEN

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Background and aims:

Listeria monocytogenes is an uncommon cause of neonatal infection. It usually affects to immunocompromised patients (pregnant women, newborn...), and the incidence is increasing. The aim of this report is to describe two infections which presented in neonatal period.

Methods:

We describe two cases of early-onset listeriosis detected in the Neonatal Intensive Care Unit (NICU) of our hospital, the differences and similarities between them.

Results:

The two cases were born by urgent caesarean section because of fetal suffering and maternal choriamnionitis suspicion, with mechonial amniotic liquid: 1st case, term infant, and 2nd case, preterm of 29+2 weeks of gestation; appropiate weight both. They responded to resuscitation with intubation, and required ventilation when admitted to NICU.

Blood analyses revealed a high Reactive C Protein (RCP) in both cases: 26.5 mg/dL at 30 minutes of life in the first one, and 9.5 mg/dL at 1 hour of life in the second. Besides, 1st case had a ratio I/T 0.28, and the 2nd a Procalcitonin of 21.64 ng/mL. Chest X-ray showed pulmonary infiltrates in the two patients.

Inicial empiric antibiotherapy included ampicilin and cefotaxime in the 1st case, and ampicilin plus gentamicin in the 2nd one. The term newborn developed pulmonary hypertension and neurological symptoms, and the preterm infant showed skin lesions and intracerebral lesions.

Conclusions:

We have to suspect listeriosis in neonatal infections with mechonial fluid delivery, specially if presented in preterm infants. Treatment is ampicilin and gentamicin, while cephalosporins are not active against Listeria.

ESPID-0260
CONGENITAL AND PERINATAL INFECTIONS

NEWBORN CONJUNCTIVITIS: THE NEWBORN AS LAST VICTIM OF SEXUALLY TRANSMITTED DISEASES.

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Background and aims – 'Ophtalmia neonatorum" or neonatal conjunctivitis (NC) has been a significant public health problem for centuries. If untreated, it leads to permanent ocular damage and blindness. In the recent years, an increased incidence of sexually transmitted infections (STI) has been demonstrated among young women in our country with the subsequent risk of NC.

A diagnostic-therapeutic protocol of NC was introduced in two Spanish hospitals in 2013 (figure 1). A study after protocol implementation was designed to describe the epidemiology and clinical features of NC and to assess the effectiveness of preventive measures in the newborn.

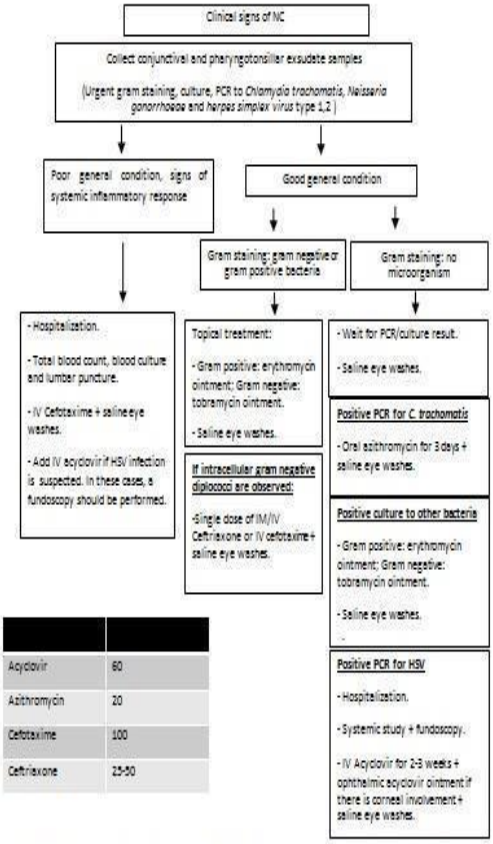
Methods - Retrospective study performed from January 2013 to August 2014 including all confirmed cases of NC. Demographic data, mode of delivery, age at onset of symptoms and microbiological studies were collected.

Results: Twenty-three patients out of 1615 newborn who attended both Emergency Departments were identified. All affected newborn had received prophylaxis with erythromycin ointment 0.5% at birth. *Chlamydia trachomatis* was identified in 8 cases (34.8%) and *herpes simplex virus* type 2 in 1 case (4.3%). No cases of *Neisseria gonorrhoeae NC* were demonstrated. All cases of NC caused by *C. trachomatis* were exclusively diagnosed by PCR techniques.

Conclusions: According to these findings, we suggest the need of an established protocol designed to improve the diagnosis and management of NC, particularly those NC caused by *Chlamydia trachomatis*, and to reconsider the appropriateness

of current preventive measures.

Figure 1. Local protocol in cases of suspicion of NC.



Acyclovir	60
Azithromycin	20
Cefotaxime	100
Ceftriaxone	25-50

* If skin lesions are suggestive of herpes infection: initiate treatment with acyclovir before obtaining PCR results.

HSV: *Herpes Simplex virus*; IV: intravenous; IM: intramuscular.

The current and extended version is available from http://www.uplip.com/files/20140623104856_3365_deca7d28-8e51-4d08-e3f2-eef937edf161.pdf

ESPID-0484
CONGENITAL AND PERINATAL INFECTIONS

BACTERIAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF NEONATAL SEPSIS IN DR KANUJOSO DJATIWIBOWO HOSPITAL BALIKPAPAN IN 2012-2013

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Background: Neonatal sepsis is the highest contributor to neonatal death. Antimicrobial therapy should be chosen based on maternal history, bacterial profile, and antimicrobial susceptibility pattern in each neonatal intensive care unit.

Objective: To determine bacterial profile and antimicrobial susceptibility pattern in neonatal intensive care unit of dr. Kanujoso Djatiwibowo Hospital, Balikpapan

Material and Methods: Descriptive observational study was carried out on neonates who are diagnosed with neonatal sepsis and have positive blood culture in the period January 1st 2012 to December 31st 2013. The data were obtained from medical records.

Results: There were 125 cases of neonatal sepsis with positive culture. Neonatal sepsis was dominant in male (56,8%). Late onset sepsis was present in 64,8% of cases. Gram-negative bacteria were the leading cause of neonatal sepsis in this study. Isolated bacterial pathogens were predominantly *Serratia sp*, *Staphylococcus sp* and *Acinetobacter baumannii*. Most of the gram-negative bacteria still have high susceptibility to Meropenem, except *Acinetobacter baumannii. Staphylococcus sp* has low susceptibility to first, second and third line antibiotics, but it has high susceptibility to Amikacin. In general, the bacterial pathogens have the highest susceptibility to Meropenem and the lowest susceptibility to Penicillins.

Conclusion: *Serratia sp*, *Staphylococcus sp* and *Acinetobacter baumannii* are the predominant bacterial pathogens. Most gram-negative bacteria, except *Acinetobacter baumannii,* have high susceptibility to Meropenem,.The bacterial pathogens have the highest susceptibility to Meropenem and the lowest susceptibility to Penicillins.

ESPID-0398
CONGENITAL AND PERINATAL INFECTIONS

MANIFESTATION OF CLINICAL CONFIRMED CONGENITAL RUBELLA SYNDROME CASES AT MOHAMMAD HOESIN HOSPITAL, INDONESIA: A NEED OF PREVENTION EFFORTS

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Background and Aims

Congenital Rubella Syndrome (CRS) is related with various birth defects which will lead to devastating health burden. The incidence of CRS in developed countries has dramatically decline by the introduction rubella vaccine. In Indonesia, Rubella vaccine has not been included into the national routine immunization program. World Health Organization has recommended the case definiton of clinical confirmed CRS which strongly suggest a definite CRS. The aim of this study is to report the manifestations of children with clincally confirmed CRS in our hospital that could reflect the burden of disease.

Methods

This descripitve study was conducted in Mohammad Hoesin Hospital Palembang. Pediatric patient with clinical confirmed Congenital Rubella Syndrome were retrospectively identified from hospital's medical records for 2012-2104. Data of patient's clinical manifesations were collected.

Results

There were ten cases of clinical confirmed CRS identified within 3 years. Consisted of 7 males and 3 females, with the youngest case came in the age of 4 months. Congenital cataracts were found in all cases. The second most commonly clinical manifestation was microcephaly (4 cases), followed by patent ductus arteriosus (3 cases), sensorinueral deafness and global developmental delay (2 cases each) and 1 case with arterial septal defect.

Conclusions

Clinical confirmed Congenital Rubella Syndrome cases are found in Mohammad Hoesin Hospital, Indonesia, with significant impairment. The most common clinical finding was congenital cataracts. Other clinical manifestation included defects on brain, ears, and cardiocvascular system. Prevention strategies are required to be implementated soon.

ESPID-0160
CONGENITAL AND PERINATAL INFECTIONS

A CASE OF PERINATAL CAMPYLOBACTER JEJUNI INFECTION

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Backgroud : Campylobacter spp. is a common pathogen in adult and usually associated with mild gastroenteritis. However, in case of neonates, the disease spectrum of Campylobacter spp. vary from mild gastroenteritis to severe condition such as Guillain-Barre syndrome, which could be fatal. Hereby, we report a rare case of perinatal Campylobacter jejuni infection.
Case report: A 3-day-old baby was admitted of fever for 1 day. He was born at full term by normal spontaneous vaginal delivery with birth weight of 3kg. No specific abnormality was found in the physical examination. Laboratory findings, including CSF study were normal except leukopenia(3,480/μL) and mildly elevated C-reactive protein(1.18mg/dL). Campylobacter species were isolated from stool culture. We discovered that the mother of the baby suffered from a gastroenteritis just before delivery, and the same pathogen was found in his mother's stool as well. After 7 days of treatment with azithromycin, fever was subsided, and the follow up stool culture revealed no growth of Campylobacter jejuni.
Discussion : Campylobacter spp. is commonly found in poultry products. According to the in-patient data of our medical center, as many as 23.6% of bacterial gastroenteritis involves Campylobacter spp. in young adult during the spring-summer season. As prevalence of Campylobacter spp, increases, it’s resistance to constitutional antibiotics is reported more frequently.
Conclusion : Perinatal infection is deeply associated with maternal medical status. Therefore, in case of a febrile newborn whose mother had gastroenteritis during perinatal period, Campylobater infection must be considered and full evaluation must take place.

ESPID-1013
CONGENITAL AND PERINATAL INFECTIONS

BACTEREMIA ASSOCIATED WITH THE URINARY TRACT INFECTIONS IN THE TERM NEWBORNS

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Backgraund and Aim *:* Urinary tract infection (UTI) in newborns frequently is associated with bacteremia and may result in long-term complications.The purpose in this study was to identifications the bacterial microorganisms caused UTI and associated with systemic infection in the newborns hospitalized during the period of 2002 ,2003 ,2004.

Method: We used clinical, microbiological and laboratory methods.

Results: 2086 infants were treated at the Center of Neonatology during the period of 2002-2004. Infants born at term (NT) were 1391, and infants born preterm (NPT) were 682.In the group of NT In 528 were proven infections (omphalitis 44,9%,sepsis and /or meningitis 10,9%,pneumonia 18,5%, cutaneus infections 8,7%, conjunctivitis 5,5%, otitis media 3,8%,mastitis 1,7 %,diarrhea 0,2%, UTI 5,5%.
UTI was obsrved in 27 NT.Overall rate in all hospitalisated infants was 1,3% ,and 4,6% of all proven infections .Of the total UIT, 96.5% occurs in NT, in period of 2-4 weeks of life (χ^2=18.721; p<0.01). The common cause UTI is *Escherichia coli (E.coli)*, and it is proven by urine culture in 19 children, or 67.8%, followed by *Enterococcus* in 7 children, or 25%, *Pseudomonas* and *Enterobacter* had proven in one newborn , or 3.5%. At the age of 4-7 days UTI had five children, aged between 8 days and more UTI had 23 children. In 3 NT *E. coli* was isolated in blood and urine culture, and in 2 NT was associated with meningitis.

Conclusions *:E coli* is dominant pathogen in our study.The sepsis was proven in 3 and meningitis in 2 newborns.

ESPID-1021
CONGENITAL AND PERINATAL INFECTIONS

NEONATAL SYSTEMIC CANDIDIASIS: INCIDENCE AND OUTCOME

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Background

The incidence of systemic candidiasis increased over the past two decades with the more aggressive approaches to the treatment of VLBW neonates.

Aim

The aim of our study was to evaluate the incidence and outcome of systemic candidiasis in the NICU of 1st Department of Neonatology in Cluj Napoca , Romania.

Methods

We conducted a retrospective study between 2012-2014 .In the study group were enrolled neonates with systemic candidiasis .

Results

During the study period were admitted 5751 neonates with 892 patient - NICU admission . Ten newborns presented systemic candidiasis . Three patient from the study group were term and 7 patient preterm neonates. At five cases was isolated candida parapsilosis (50%) , 4 cases presented candida albicans (40%) and one case candida spp (10%). All patient from the study received broad spectrum of antibiotics before there fungal infection. At one case(10%) we had early onset sepsis and at 9(90%) patient presented late onset sepsis. All patient of the study group had central venous catheter. In one case we had associated pericarditis and two patient had severe asphyxia . At 4 patient the antifungal treatment was fluconazole. Two patient received a special antifungal treatment , one patient was treated with Caspofungin and three of them were treated with Voriconazole. The outcome of the neonatal candidiasis was unfavorable at 4 cases .

Conclusion

The incidence of neonatal candidiasis was 1,1‰ at the patient admitted in NICU. In 60% of the cases the outcome was favorable.One patient with unfavorable outcome had congenital heart disease associated .

ESPID-0231
CONGENITAL AND PERINATAL INFECTIONS

DON'T FORGET THE CHILDREN: VIRAL HEPATITIS SCREENING OF CHILDREN OF INFECTED PARTENTS

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Background

The UK Department of Health recommends testing children of mothers withhepatitis B at one year of age. The UK does not routinely immuniseagainst hepatitis B.

Objective

To set a systematic screeningprocess to ensure all children of hepatitis B or C infected adults are screenedand vaccinated against hepatitis B.

Method

Laboratory resultsof hepatitis B surface antigen positive or hepatitis C antibody positive adultsin the last 18 months were requested at Pennine Acute Trust, UK. Through the patientadministration system children in those families were identified. Results oftesting for viral hepatitis were searched for those children. The infectiousdiseases clinicians responsible for the adults were informed of the childrenwithout results to request testing. Priority was given to children of positivemothers.

Results

The total number ofadults with HBsAg and anti-HCV antibody is 1284 of which 432 are females: hepatitisB adult females 217; and hepatitis C adult females 217; 2 females with both. Wehave identified 1169 children <16 years old matched to address of 1470 labpositive patients needing checking. We have screened 96 children so far. 15%did not attend for their appointment.

There are 24children with hepatitis B and 8 with hepatitis C in the clinic.

Conclusion

A prospective system for ensuring that the children of adults withhepatitis B or C are tested as soon as the parent is diagnosed will enable thechildren to be identified and not lost to follow up.

ESPID-0392
CONGENITAL AND PERINATAL INFECTIONS

GONOCOCCAL OPHTHALMIA IN A NEWBORN: A REPORT OF A CASE

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Goal: to present a clinical case of gonococcal ophthalmia in a 24 hours newborn .

Methods: it is about a newborn admitted in neonatology 24 hours after birth (vaginal delivery) because of suppuration of the right eye.
Samples are collected by swabbing. Two swabs are sent to the laboratory.

Microscopic examination after staining with methylene blue is realized and the cultivation is done on blood agar incubated in CO2-enriched atmosphere.
The identification of *Neisseria gonorrhoeae* is made by standard tests. The study of antibiotic sensitivity is performed according to the recommendations of the CLSI.
Results:
gonococcal Opthalmia is confirmed by the presence of Gram negative cocci coffee bean intra- and extracellular direct examination of the eye pus and positive culture *Neisseria gonorrhoeae* sensitive to all antibiotics.
family screening has revealed: gonorrhea in the father and cervicitis in the mother .
Genital samples were taken in parents and bacteriological diagnosis was positive for the same strain, *Neisseria gonorrhoeae* isolated in the newborn.
The couple was treated with ceftriaxone dose associated with a macrolide. Infectious serology (HIV, hepatitis B and syphilis) was negative.
The newborn had a good evolution without sequelae.
Conclusion: any eye discharge from a newborn should evoke a sexually transmitted infection. The examination is the key to diagnosis.

ESPID-0360
CONGENITAL AND PERINATAL INFECTIONS

NEONATAL BLOOD STREAM INFECTION AT LEVEL III NEONATAL UNIT NEW DELHI: CHANGING MICROBIOLOGICAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY

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Background and aim: Blood Stream Infection (BSI) contributes significantly to morbidity and mortality among newborns. Microbiological profile and their antimicrobial susceptibility are dynamic. Aim was to compare profile of microorganisms causing blood stream infection in the year 2012 and 2013 and to assess change if any in their antimicrobial susceptibility.

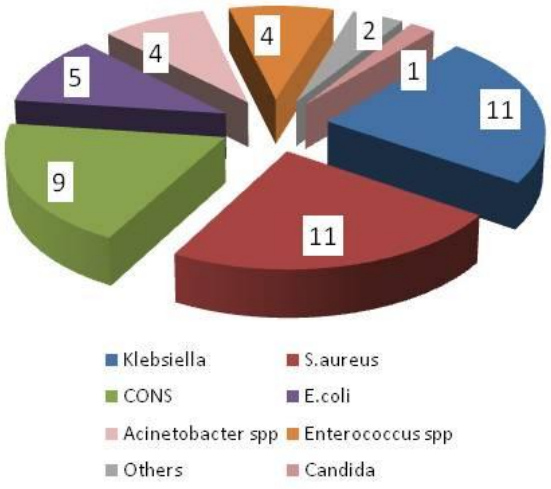
Methods: Medical records of newborns admitted in the Unit in the period between January 2012 and December 2013 were reviewed. Data on microorganisms identified and their antimicrobial susceptibility were retrieved.

Results: Forty seven (18.9%) out of total of 248 and sixty nine (6.8%) out of total of 1012 blood cultures sent in 2012 and 2013 respectively grew microorganisms. *Klebsiella* remained the commonest organism isolated followed by *S.aureus* and *E.coli.* There was increase in early onset sepsis caused by gram negative organisms from 56.6% to 77.8% in the year 2013. Among gram positive bacteria resistance to penicillins, gentamycin, amoxycillin-clavulinic acid, and erythromycin was very high. There was some improvement in sensitivity to quinolones in the year 2013. Gram negative organisms remained resistant to third generation cephalosporins, and quinolones. Carbapenem susceptibility improved to 82.3% from 57.1%. There was moderate to good susceptibility to piperacillin-tazobactum, colistin, and tigecycline with some improvement in susceptibility to aminoglycosides in the year 2013.

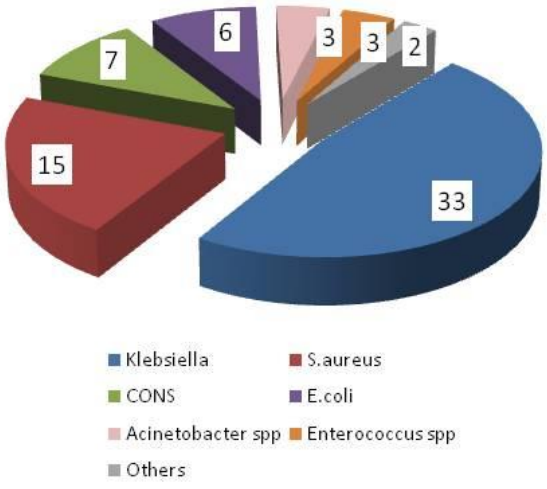
Conclusions: High incidence of resistance to commonly used antimicrobials remained a significant problem.

Microbiological Profile Year 2012 and Year 2013

Year 2012 (n=47)



Year 2013 (n=69)

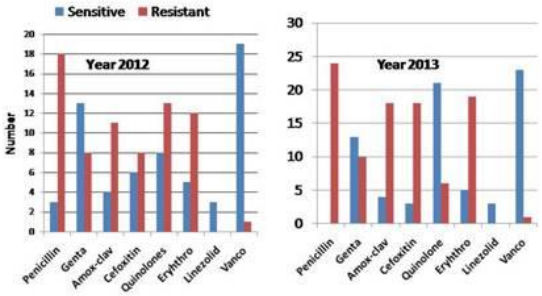


Microbiological Profile in relation to time of onset of Sepsis

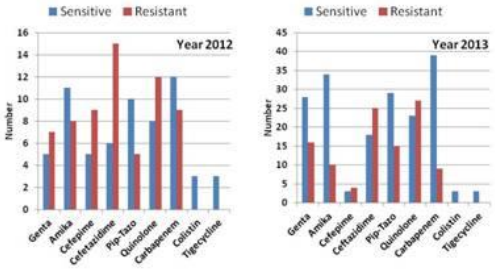
Organisms	EOS		LOS		Total Sepsis	
	2012 No (%)	2013 No (%)	2012 No (%)	2013 No (%)	2012 No (%)	2013 No (%)
Gram Positive	8 (44.4)	8 (22.2)	16 (55.2)	17(51.5)	24 (51.1)	25(36.2)
Gram Negative	10 (56.6)	28(77.8)	12 (41.4)	16(48.5)	22 (46.8)	44(63.8)
Candida spp.	0 (0)	0(0)	1 (3.4)	0(0)	1 (2.1)	0(0)

Changing Antimicrobial Resistance

Gram Positive



Gram Negative



ESPID-0835
CONGENITAL AND PERINATAL INFECTIONS

LATE DIAGNOSIS OF CONGENITAL CYTOMEGALOVIRUS INFECTION: MISSHAPENS AND PITFALLS

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Cytomegalovirus (CMV) infection occurs in about 1% of newborns and in 90% is clinically silent. We describe 2 cases with a late diagnosis.
Case 1: Six years old girl, born at full-term, after a normal pregnancy with antenatal care. Following an unremarkable neonatal period, she presented with slight psychomotor developmental delay (PSMD), mainly motor, attributed to developmental dysplasia of the hip. A favorable outcome with full resolution at 42 months of age was followed by progressive PSMD with cognitive impairment, especially of language and at 6 years of age, she developed sudden severe neurossensorial deafness requiring hearing aids. Cerebral magnetic resonance imaging (MRI) showed widespread lesions compatible with intrauterine infection. Polymerase Chain Reaction (PCR) on the *Guthrie* early metabolic test card revealed to be positive for CMV.
Case 2: She was a full term delivered after a pregnancy with the intrauterine diagnosis of microcephaly, confirmed post-natally. Sometime along the way there was an history of nonfebrile convulsions. At five and a half years old, she was referred to the developmental assessment outpatients due to moderate to severe PSMD. On examination, she presented with craniofacial dysmorphia, “bird like” features. Cerebral MRI suggested antenatal infection confirmed by positive CMV PCR on the *Guthrie* test card.
These were two examples of severe sequelae of congenital CMV infections diagnosed somewhat late in childhood. The first case, due to the paucity of symptoms, until the full blown neurossensorial deficit; the second case, the whole picture, should have evoked the possible diagnosis considerably earlier.

ESPID-0663
CONGENITAL AND PERINATAL INFECTIONS

CLINICAL AND EPIDEMIOLOGICAL PARAMETERS IN PERINATALLY HIV-INFECTED MOTHERS IN MADRID

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Background: The number of perinatally HIV-infected women becoming pregnant is increasing. There is little information on the outcome of their pregnancies and their newborns.

Methods: A prospective study analyzing gestational parameters in perinatally HIV-infected mothers from the Madrid Cohort of HIV-infected children and adolescents before and during pregnancy.

Results: Among the 159 HIV-1 perinatally infected women in the Madrid Cohort, 20 gestations from 17 (10.7%) mothers were analyzed. All women were Spanish, 70.6% carried B-subtype and the median age at the time of delivery was 20 years[IQR 18-22]. These women received HAART throughout their life and 40% where on triple-therapy before pregnancy presenting undetectable viral load (≤50 copies/ml) and the median CD4 count (cells/mm^3) was 525[IQR 402.25-761.5].
Before pregnancy, 12 *pol* sequences were available reporting a drug resistance rate of 25%, 33.3% and 58.3% to PI, NRTI and NNRTI, respectively. During the gestational period all women were on HAART and 95% received PI-based HAART. Intrapartum AZT was administered in 80% of women. At the time of delivery, 75% of women presented viral suppression. Vaginal delivery was performed in half (55%) of HIV-infected women and only two reported detectable viral load. The median gestational age was 38+5 weeks[IQR 37-40] and the median weight of the newborns was 2920g [IQR 2740-3017]. There was no perinatal transmission of HIV-1 to the offspring.

Conclusions: In our cohort of perinatally acquired HIV-infected women, effective therapeutic regimens during pregnancy were successful in the prevention of vertical HIV transmission without eventful events for the mother and newborns.

ESPID-0635
CONGENITAL AND PERINATAL INFECTIONS

COLONIZATION OF GASTROINTESTINAL TRACT (GIT) OF PRETERM NEONATES WITH STAPHYLOCOCCUS EPIDERMIDIS (SE) PRESENT IN MOTHER'S OWN UNPASTEURIZED BREAST MILK (BM)

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Background and aims

In preterm neonates GIT is potential reservoir of invasive strains, including SE, whereas BM is considered as source of beneficial bacteria. We aimed to study colonization of preterm neonates with SE present in their mother's BM.

Methods

Stool was collected from breast-fed very preterm (gestational age <32 weeks) and late-preterm (gestational age 32-36 weeks) neonates and BM from mothers once a week within the first month of life. Samples were cultured onto salt-mannitol agar; 5 colonies typical to coagulase-negative staphylococci were randomly picked and identified to species level by MALDI-TOF MS. Relatedness of SE strains was evaluated by multilocus variable-number tandem-repeats analysis (MLVA).

Results

SE colonization with median of 4 different MLVA-types (IQR 2.5…5) occurred in 19 of 21 very preterm and all 7 late-preterm neonates. BM of all mothers and all but two samples contained SE (median 7 MLVA-types; IQR 4.5…8), median count of coagulase-negative staphylococci was $3.1x10^4$cfu/mL (IQR $7.9x10^3$…$1.4x10^5$). SE genotypically similar to strains isolated from BM before or at the same sampling time as GIT colonized 60.7%(17/28) of neonates (12/21 very preterm, 5/7 late-preterm). By the age of 21 days, SE genotypically similar to or different from BM strains colonized 39%(11/28) and 86% (24/28) of neonates, respectively (Figure).

Conclusions

Delayed colonization of preterm neonates with SE genotypically similar to BM strains implies to alternative sources of SE for early GIT-colonization, thus rendering neonates vulnerable to colonization with hospital-adapted potentially invasive strains.

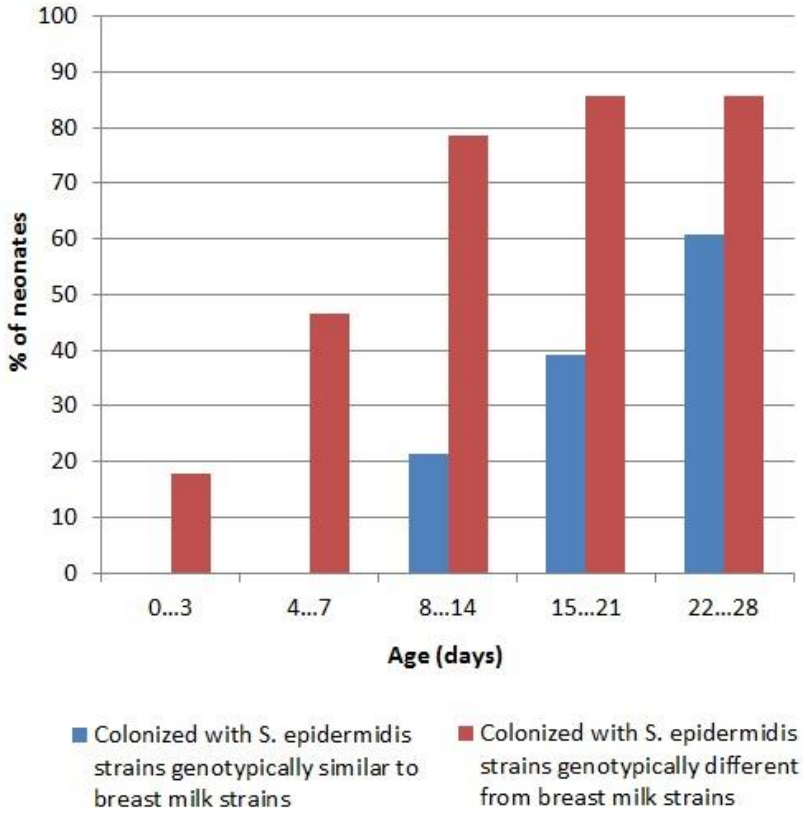

Figure. Cumulative proportion of preterm neonates colonized with *S. epidermidis* strains genotypically similar to strains in breast milk (blue bars) or genotypically different strains (red bars).

ESPID-0456
CONGENITAL AND PERINATAL INFECTIONS

INTRODUCING A NEONATAL SEPSIS PROTOCOL IN RURAL UGANDA

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Background and Aims

Infections account for 31% of neonatal deaths in Uganda, making it the largest cause. The aim of this audit was to rationalise antibiotic prescribing in our neonatal unit.

Methods

A retrospective case note review was performed on all admissions to the neonatal unit in August 2014. A neonatal sepsis protocol was introduced and re-audits were done in October and December 2014.

Results

Between 17 and 19 babies were included in each audit cycle.

Antibiotics were given to 100% of babies in August 2014 as per hospital policy. Following the introduction of a neonatal antibiotic protocol, antibiotics were commenced in 95% of babies in October 2014 and 100% of babies in December 2014.

The commonest danger signs for infection were abnormal temperatures and respiratory problems. During the audit period there has been a steady increase in the identification and documentation of danger signs.

Half of gentamicin doses given to preterm babies were incorrect in Aug 2014 but all were correct on both re-audits.

History of risk factors for sepsis was taken in 0% of admissions in August 2014. This increased to 16% in October 2014 and to 29% in December 2014.

Conclusions

Implementing the neonatal sepsis guideline has not reduced antibiotic prescribing in the neonatal unit. However there has been an increase in documentation of risk factors for sepsis, documentation of danger signs of infection and antibiotic doses have been more accurate.

ESPID-0259
CONGENITAL AND PERINATAL INFECTIONS

MANAGEMENT OF MATERNAL VARICELLA INFECTION IN THE NURSERY

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[1]neonatology, Life Memorial Hospital University Titu Maiorescu. Faculty of Medicine, Bucharest, Romania
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Background and aim:. We present the case of a mother developing varicella in the maternity hospital, the management of the neonate and contacts and the outcome of the cases.

Material and method: A mother developed varicella 48 hours after delivery in the maternity hospital. The mother and her neonate were isolated, history and VZV(varicella-zostervirus) antibody status were checked for all the mothers and VZV antibodes were determined for the neonates. The varicella status of the personel was also reviewed. Acyclovir prophylaxis was administered to the infected mother and her child and to the VZV negative mothers and neonates. All the patients were re-evaluated at regular time intervals.

Results: 17mothers and their neonates were present at that moment in the unit. The anti VZV antibodies tested in the neonates showed the following results: 10/10 with known maternal varicella infection inthe past were IgG positive (Mean532.9(±237)Units), 3/4 with unknown status were IgG positive, 1/4 with unknown status and 2/2 with no infection in the mother as well as the newborn of the infected mother were IgG,IgM, and IgA negative. Thus, 4/18(22.22%)neonates were at risk of infection and received acyclovir prophylaxis. No one in the 18 neonates developed neonatal varicella and no mother developed varicella during themonths after exposure.

Conclusions: Even if the risk for neonatal varicella was 22%, isolation of the index case and acyclovir transmission of the virus and an outbrake of varicella in the nursery. We recommend the determination of all mothers' VZV antibody status before delivery.

ESPID-0477
CONGENITAL AND PERINATAL INFECTIONS

REAL-TIME REVERSE TRANSCRIPTION POLYMERASE CHAIN REACTION DETECTION OF CONGENITAL RUBELLA INFECTION IN INFANT'S USING SALIVA

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Background and aims:

Congenital rubella virus infections cause malformations in infants, a condition known as congenital rubella syndrome. However, some infants develop asymptomatic congenital rubella infections (aCRIs). Therefore, we aimed to investigate the incidence of aCRI in infants by performing screening tests for the rubella virus on saliva samples.

Methods:

This prospective cross-sectional study conducted from February to December 2014 included infants younger than 2 months without acute illness. Saliva samples were collected in 2 hospitals and 4 clinics in Tokyo, where a rubella outbreak occurred in 2013. Clinical information for the infants and their mothers was obtained from self-reporting. Saliva samples (200 µL) were collected in Salimetric Swab® storage tubes and then used for real-time reverse transcription polymerase chain reaction (PCR) analysis for the rubella virus. Positive PCR results warranted repeating PCR analysis using throat swabs and rubella serology to confirm the diagnosis of aCRI.

Results:

Herein, 213 infants were enrolled, and the data for 167 infants (82 male) were available. Their median age was 6 days (interquartile range: 5–33 days). Clinical characteristics of the mothers are shown in Table 1. We collected sufficient volumes (>200 µL) for 110 samples, and 57 samples were small (100–200 µL, n = 33; 50–100 µL, n = 16;

Conclusions:

The incidence of aCRI 1 year after the rubella outbreak in Tokyo was

Acknowledgement:

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Table 1. Clinical characteristics of the infants' mothers

N = 167	n		
Age (years, median, IQR)	166	34 (30–37)	
Antibody titre (haemagglutination inhibition) (median, IQR)	83		
<×8		2	2.4%
×8		8	9.6%
×16		19	22.9%
×32		19	22.9%
×64		21	25.3%
×128		10	12.0%
×256		4	4.8%
History of rubella	165		
Yes		51	30.9%
Yes (during pregnancy)		0	0%
No		99	60.0%
Unknown		15	9.1%
Rubella vaccine	165		
Yes		82	49.7%
No		33	20.0%
Unknown		50	30.0%
Fever during pregnancy	164	31	18.9%
Rash during pregnancy	163	4	2.5%
Contact with rubella patient during pregnancy	165		
Yes		3	1.8%
No		158	95.8%
Unknown		4	2.4%

ESPID-0724
CONGENITAL AND PERINATAL INFECTIONS

ASSESSMENT OF NEONATAL INFECTION AND RISK FACTORS IN A III LEVEL UNIT

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· Background and aims

Bacterial infection is important cause of morbidity and mortality in newborn.

Aim: To assess early and late neonatal infections in NICU .

Methods

We performed a retrospective study on 2429 infants admitted in the Department of Neonatology I ,Cluj-Napoca, Romania ,between 01.05.2012-11.01.2013.

Inclusion criteria were : infectious circumstances, clinical signs .

In the study group were 120 newborns : 78 preterm and 42 term , with birth weight :1400. 8 ± 325.4g and 3186.9 ± 325.4g.The data were processed by SPSS.

· Results

Risk factors for early onset infections were : meconium amniotic fluid 37%, premature rupture of membranes 28%, placenta praevia 13%, urinary infection 6%, chorioamniotitis 1%.

Blood cultures were positive in 22 (18.3%) cases: *E.coli*, *S.aureus, Serratia, Enterobacter* in preterm and *Staphylococcus spp.* for term.

The etiology of late onset sepsis was: *K. pneumonia and E. coli* for preterm and *Staphylococcus spp., K. pneumonia* in term infants.

Etiology of catheter colonization was *Enterobacter cloacae* 5.3%, *K. pneumoniae* 31.6%, *Serratia* 5.3%, *E. coli* 5.3%, *Staphylococcus spp.* 42.3%, *K. terrigene* 10.5%

Conclusions

1. Overall incidence of neonatal sepsis in premature infants is 3,2‰ and 1,72 ‰ for term.

2. Etiology of early onset infections in premature infants is: *S. aureus, E. coli, Serratia, Enterobacter cloacae* and *Staphylococcus species* for term

3. The etiology of late onset infections in premature infants: *K. pneumoniae* and *E. coli and for term: Staphylococcus species and K. pneumoniae.*

4. The main risk factors for early infections were meconium amniotic fluid 37%, premature rupture of membranes 28%.

ESPID-0384
DIAGNOSTIC TOOLS

BLOOD CULTURES IN PAEDIATRIC PRACTICE. IS OUR CURRENT PRACTICE GOOD ENOUGH?

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Background: Blood cultures are routinely used to investigate children with possible sepsis. Decisions regarding length of antibiotic course are aided by microbiology results, and therefore sensitivity of cultures is vital. We were concerned about low positivity rates and possible reasons behind this. Delay in incubation of blood cultures can affect their yield, which potentially impacts on antibiotic duration and hospital stay, both of which incur costs.

Methods: Blood cultures taken during a 3 month period in a tertiary children's hospital were reviewed retrospectively. Samples taken in intensive care and the haematology/oncology wards were excluded.

Results: 699 blood cultures were taken from 563 patients (median age 2.2years, IQR 0.37-6.8). 52(7%) yielded organisms. 19(37% of positive cultures) grew significant organisms; 18(95%) were culture positive within 24 hours. 33(63%) grew organisms considered contaminants; only 4 were positive within 24 hours. Time to start of incubation varied considerably: median 3.5hours, IQR 1.7-6.55.

Conclusions: The percentage of positive cultures was higher than expected, despite concern regarding low blood volumes taken. Connell (2007) showed positive cultures in only 0.6%(1/169) with blood volumes <0.5ml. Overall, positive culture percentages were similar in this study but we remain concerned about falsely negative results and reasons why, including delayed incubation. Rates of contamination were also higher than desirable. Interventions to reduce contamination and delay in incubation of samples have occurred and a prospective study is ongoing investigating the association between blood volume and blood culture positivity to ensure that the positive and negative predictive value of blood cultures is maximised.

ESPID-0475
DIAGNOSTIC TOOLS

EVALUATION OF ADEQUACY OF VOLUMES OF BLOOD INOCULATED INTO PAEDIATRIC BLOOD CULTURE VIALS AND DELAYS IN TRANSIT TO THE LABORATORY AT A LONDON (U.K.) HOSPITAL

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Aims:
This study assessed the adequacy of volumes of inoculum comparing patient age, location of collection and grade of clinician collecting the sample as well as evaluating time the specimen spent in-transit to the laboratory.

Methods:
Paediatric blood culture vials (BD BACTEC PEDS+) were weighed before and after inoculation (pre-incubation). We attempted to correlate delays in specimen transit with the length of stay in hospital.

Results:
159 vials were assessed during a 3-month period. 74 (47%) were from neonates (<1 month of age), 80 (50%) were from children aged 1 month-12 years of age and 5 (3%) were from adolescents (12-16 years of age).

38 (24%) had an adequate volume of inoculum (1-3ml). 111 vials (70%) were under-filled, with 52 (33%) inoculated with less than 0.5ml and 59 (37%) inoculated with (0.5-1ml).
The volume of inoculum varied with patient age; the lowest volumes collected in neonates but similar volumes in children and adolescents.
The volume varied with location of collection; areas dealing with neonates had lower volumes of inoculation than others. Median volumes of inoculum were similar between grades of collectors.
The distribution of the time specimens spent in transit to the laboratory varied significantly between the clinical areas where they were collected with the ED performing worst. There was no association between length of time in transit and length of hospital stay.

Conclusions:
The study identified key areas for improvement in the technique of taking adequate blood cultures and the aspect of prompt delivery of specimens to the laboratory.

ESPID-0813
DIAGNOSTIC TOOLS

EVALUATION OF 4 COMMERCIALIZED KITS USED IN THE MOLECULAR DIAGNOSIS OF WHOOPING COUGH USING REAL TIME PCR

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Objectives: simultaneous detection of DNA from *Bordetella pertussis* and from *B. parapertussis* is recommended. Several commercialized tests are now available to amplify simultaneously the both target. The aim of our study was to evaluate the performance of four kits: *Bordetella pertussis*/*parapertussis* triplex – PCR temps réel (Bio-Evolution), SmartCycler *B. pertussis*/*B. parapertussis* Assay (Cepheid), Diagenode *Bordetella pertussis* and *parapertussis* Real-Time PCR kit (Diagenode) et EurobioPlex *Bordetella pertussis* & *parapertussis* (Eurobio).

Methodes: Kits were evaluated by comparison to a in-house method. The amplification was realized using a SmartCycler (Cepheid). The limit of detection of each kit was determined using a quantification standard of dilution of DNA extracted from suspensions. The different kits were tested using DNA extracted from 140 naso-pharyngeal, 58 positive and 82 negative.

Résults: The limit of detection of the four techniques was at least 50 copies by assay for IS481 and also for IS1001. All the negative samples were found negative and all the positives were also detected whatever the method. The *IS481* was detected in 55 samples (54 *B. pertussis* and 1 *B. holmesii)* and the *IS1001* in 3 samples. The difference observed between the kits concerned only minor variation of the threshold cycle without impact on the result.

Conclusion: the equivalent and efficient performance of the different kits allows their use in routine laboratories for the diagnostic of whooping cough. The choice of the kits will depend of the format and the contents of the box the time of the RT-PCR and of course of the price.

ESPID-0768
DIAGNOSTIC TOOLS

EVALUATION OF THE NOVEL ALERE I INFLUENZA A&B RAPID TEST FOR PRE-HOSPITALIZATION SCREENING IN CHILDREN WITH ACUTE RESPIRATORY TRACT INFECTION

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Background:
Early recognition of influenza infection is essential for optimized clinical management including infection control and specific therapy.
Rapid diagnosis of influenza in the point-of-care setting is hampered by low sensitivity of widely available rapid antigen detection tests.
The novel **Alere i Influenza A&B rapid test** is based on isothermal nucleic acid amplification and first reports suggest that this novel approach might offer a considerably improved test sensitivity.

Objective:
To evaluate the test performance of the Alere i influenza A&B isothermal nucleic acid amplification test in comparison to multiplex real-time PCR in children under 7 years of age with acute respiratory tract infection.

Methods and Study design:
Respiratory specimens (nasal swabs) were prospectively collected from children under the age of 7 that were admitted to the Center of Pediatric and Adolescent Medicine, University Hospital Heidelberg, Germany with clinical symptoms of acute respiratory tract infection with written informed consent by legal guardians. The specimens were stored at 4°C and tested at the Department of Infectious Diseases, Virology, within 24 h of sample collection. Clinical data of the patients was collected and analyzed.

Results:
As a preliminary result, the overall sensitivity and specificity of the Alere i influenza A&B assay for infuenza A is above 95% and above 98% respectively. First results fulfill a high sensitivity for influenza B detection.

Conclusion:
The novel Alere i influenza A&B test offers high test sensitivity and specificity combined with short sampling-to-test-result time and could thus improve influenza virus detection at the clinical point-of-care setting.

ESPID-0620
DIAGNOSTIC TOOLS

FEATURES IN SEPSIS DIFFER BETWEEN CHILDREN WITH- OR WITHOUT-SEVERE ACUTE MALNUTRITION, AND THE RISK FACTORS OF MORTALITY IN SEPSIS

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Background and aims: Knowledge of biochemical-derangements in sepsis among children with severe-acute-malnutrition (SAM) would be helpful. This study aimed to describe the features of sepsis in children with SAM and non-SAM, and the risk/associated factors of death in septic-children.

Methods: Children aged 6-59 months with SAM (WHZ <-3) or bi-pedal-edema, and non-SAM admitted with diarrhea and sepsis at the icddr,b's Dhaka-hospital from April2010 to December2011 were studied prospectively.

Results: Total 126 (48-SAM and 78-non-SAM) children were studied, all had diarrhea+sepsis. Their mean±SD age was 19.1±14.2 months; 52% were female; capillary-refill-time, neutrophil and band %, BUN, PH, Hb, platelet, serum-TCO_2, phosphate, calcium, CRP, creatinine, and creatinine-phosphokinase were similar between SAM and non-SAM children ($p>0.05$). But, serum-sodium and albumin were lower while, leukocyte count, hypoglycemia, septic-shock and mortality were higher in SAM than non-SAM children ($p<0.05$). Logistic-regression showed: septic-SAM children had 13 times more-often chance of fever or hypothermia than septic-non-SAM children.

Among these 126 children, 25 (19.8%) died. WHZ (-3.0±2.1 vs. -2.7±1.5), % band-cell(5.2±6.4 vs. 2.6±5.5), Na(154±29 vs. 142±21) and BUN(25.7±21.5 vs. 17.8±16.1), septic-shock(92% vs. 9%) were significantly higher, and Hb(9.2±1.6 vs. 10.3±2.0) and albumin(2.9±1.1 vs. 3.4±0.8) were significantly lower among who died than alive children respectively. Logistic-regression showed: children who died were 4 times more likely to be severely wasted and 3 times more likely to had moderate-anemia.

Conclusions: Case fatality rate is significantly high in sepsis particularly in septic-shock and SAM children. These features may help in the better management of septic-children with/without SAM and thus reduce fatality.

ESPID-0030
DIAGNOSTIC TOOLS

VALUABILITY OF YALE OBSERVATION SCALE (YOS) IN EVALUATION OF CHILDREN 3-36 MONTHS WITH FEVER WITHOUT LOCALIZING SIGN

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Background and aims:

Fever without localizing sign is one of the medical diagnostic challenge specially between children 3-36 months. Some clinical and laboratory tests such as general appearance, body temperature, white blood cell count, ESR and CRP are used for early evaluation of these children. YOS as an observatory value is also known for evaluating the persons with fever without origin. Although that accuracy is not exactly clear.

Methods:

87 children 3-36 months with fever without sign entered this study. Firstly, body temperature and general appearance were recorded and blood samples for evaluating white blood cell count and differentiation, blood culture, ESR and CRP were obtained .YOS for any individual was measured and recorded and after receiving lab data and finding the final diagnosis , all data were compared statistically.

Results:

Mean age and standard deviation of the participants in this study were 16.25+/-9.18 month. Out of 87 patients,25 (28.7%) had a serious disease. Sensitivity, specificity,positive predictive value and negative predictive value for achieving score 11and more of YOS in differentiation between serious and non serious diseases were 64%, 75.8%, 51.6% and 83.9%respectively. These items for achieving score 15 and more were 52%, 83.9%,56.5% and 81.3% respectively.

Conclusion:

While YOS , specially when the measured score is 15 and more,can be used as a helpful tool in differentiation of serious and non serious diseases in children with fever without localizing sign by physicians, in lower scores, it is not accurate and can't rule out possibility of serious infection.

ESPID-0550
DIAGNOSTIC TOOLS

THE EFFECTIVENESS OF USING BACTERIAL MENINGITIS SCORE

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In Recent years some studies showed high sensitivity of Bacterial Meningitis Score (BMS) for differentiation between viral versus bacterial meningitis. The main objective of our study was to assess the effectiveness of using BMS in clinical practice. We retrospectively analyzed 169 medical records of children from 1 month till 14 years admitted in Iashvili children's central hospital with diagnosis of meningitis during 2014. The inclusion criteria included the age, diagnosis of meningitis in previously healthy children, absence of sepsis. Record of the patients who received antibiotics before lumber puncture were excluded. Totally medical records of 139 patients with meningitis were included for analyses. Majority of patients were boys 61,8 % (n=86) , mean age was (4,8± 2,2 years). The viral meningitis were diagnosed in 84,8% (n=118). The retrospective analyses showed that risk of BM was significantly related to the BMS score. The majority of patients (94,1%) with BMS score < 1 have viral meningitis. In patients with BMS >2 the 68,2 % were diagnosed with bacterial meningitis and 31,8 % have viral meningitis. So, BMS score can help physicians in decision making according antibiotic therapy

ESPID-0183
DIAGNOSTIC TOOLS

COMPARISON OF MOLECULAR DIAGNOSIS FOR PNEUMOCOCCI AS AN ETIOLOGIC AGENT OF OTITIS MEDIA WITH EFFUSION

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Purpose: Although culture-based bacterial detection is reliable for diagnosing otitis media, the increased culture-negative middle ear fluids (MEFs) of otitis media with effusion (OME) due to treatment of antibiotics remains unsolved for the impact of vaccine against pathogens of OME.

Methods: To assess whether a molecular diagnosis can be applied to rapidly and directly detect *Streptococcus pneumoniae* in MEFs, polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP), which are specific for pneumococcal *lytA* gene, were comparatively tested for both specificity and sensitivity against *S. pneumoniae* in MEFs and then these assays were applied in the pneumococcal detection in the clinical MEFs.

Results: PCR and LAMP showed approximately 10^4 colony forming unit (CFU) and less 10 CFU of their sensitivities against *S. pneumoniae*, respectively, whereas both assays did not amplify nucleic acid at over 10^6 CFU of *H. influenzae* or *M. catarrhalis*. In their clinical application with 22 culture-negative MEFs of the OME, twelve were positive in LAMP (54.5%). Of twelve LAMP-positive samples, only three MEFs were positive in PCR (13.6%). The remaining ten MEFs were double-negative (45.5%). Statistically the efficiency of LAMP in detecting pneumococcal DNA is more significant than that of PCR ($P < 0.01$).

Conclusion: Conclusively LAMP has a high resolution to detect nucleic acid equivalent to less 10 CFU of *S. pneumoniae* in MEFs without any cross-reaction with other otitis media pathogens. We suggest the potential application of LAMP for diagnosing pneumococcal etiology in OME and evaluating the impact of pneumococcal conjugate vaccine against OME.

ESPID-0784
DIAGNOSTIC TOOLS

DIAGNOSTIC MANAGEMENT OF FEBRILE CHILDREN AND SEPSIS6 GUIDELINE RECOMMENDATIONS:PROSPECTIVE OBSERVATIONAL STUDY

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Background

The UK SEPSIS6 guidelines recommend a strategy for management of febrile children presenting with clinical features indicative of increased risk of serious bacterial infection. We compared the management of febrile children in our paediatric emergency department (ED) with the UK SEPSIS6 recommendations.

Methods

In this prospective observational study, we collected data on febrile children aged 1 month – 16 years presenting to St. Mary's Hospital London, November – December 2014. We measured adherence to the recommended SEPSIS6 actions within 1 hour of presentation: high flow O2; intravenous or intra-osseous access and blood tests including culture; IV or IO antibiotics; fluid resuscitation; senior clinician review; early inotropic support.

Results

Of 800 children with fever, 345 (43%) presented with NICE guideline amber or red warning signs. Median age was 27 months. 141 (41%) fulfilled SEPSIS6 criteria, defined as ≥ 2 of temperature ≥38.5, tachycardia, prolonged capillary refill or altered mental state. Only 3 patients (2%) were managed according to SEPSIS6 ≥5 recommendations. 10 children received iv antibiotics (7%), 5 (4%) were fluid resuscitated, 6 (4%) received O2, and 15 (11%) were reviewed by a senior clinician. No patient received inotropes or was admitted to PICU. 47 (33%) were admitted.

Conclusions

Although 41% of febrile children fulfilled SEPSIS6 criteria, a minority was managed to their recommendations, with no evidence of adverse outcome in the 98% who were not managed thus. SEPSIS6 recommendations may place unacceptable burden on resources, and require further validation before being recommended in a paediatric ED setting.

ESPID-0820
DIAGNOSTIC TOOLS

APPLICABILITY OF MOLECULAR TECHNIQUES FOR THE DIAGNOSIS OF CENTRAL NERVOUS SYSTEM INFECTIONS IN CHILDREN

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BACKGROUND AND AIMS:

Viruses are a common cause of CNS infection. Our aim was to study the presence of virus in CSF samples from children with suspected CNS infection by means of a multiplex PCR plus low density microarray.

METHODS:

Retrospective, descriptive study of hospitalized patients with symptoms suggestive of CNS infection and whom CSF analyses were performed, including a panel of 9 neurotropic (enterovirus and herpesvirus 1 to 8) viruses between October-2010 and April-2014.

RESULTS:

96 CSF samples corresponding to 94 patients were analyzed. 61.4% of the patients were males, aged from 7 days to 15 years (median 62 months). 30/96 samples (31.3%) tested positive for at least one virus. The results and the associated diseases are described in the table below:

	EV	**HHV-6**	**HHV-7**	**EV+ HHV-7**	**EV+HHV-7+EBV**	**VEB**
Aseptic meningitis	**9**	**1**	**1**	**2**	**1**	
Encephalitis/meningoencephalitis	**2**		**4**	**3**		**1**
Kingella kingae meningitis		**1**				
Muscle contractions		**1**				
Basilar-type migraine		**1**				
Miller-Fisher syndrome			**1**			
Cephalea/meningeal syndrom	**1**					
Fever without a source	**1**					

Enterovirus (EV), human herpes virus 6, 7 (HHV-6, HHV-7), Epstein-Barr virus (EBV).

CONCLUSIONS:

1. Molecular techniques for the detection of neurotropic viruses are applicable in the etiological diagnosis of CNS infection.

2. As expected, enteroviruses are commonly associated with the presence of aseptic meningitis.

3. In our series, in cases of encephalitis or meningoencephalitis, HHV-7 is most commonly found.

4. We also have found > 1 virus in cases of aseptic meningitis and encephalitis or meningoencephalitis and the presence of virus in processes without inflammatory reaction.

ESPID-0130
DIAGNOSTIC TOOLS

SERIAL MEASUREMENTS OF PLASMA LIPID CONCENTRATIONS IN NEONATAL INFECTIONS

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Background-aims: Circulating lipids play a vital role in hostdefense. However, the diagnostic value and possible aberration of circulatinglipid levels during neonatal infection have been minimally studied.

Methods: Plasma triglycerides, total-cholesterol(total-C), HDL-C and LDL-C levels were determined in 51 term neonates withinfection (21 of them were septic) and in 20 healthy term neonates of similarpostnatal age and gender distribution, as controls. Lipid concentrations wereserially measured on days 0, 1, 2, 3 and 7 following admission in all infected neonates,and once in controls.

Results: In infected neonates, total-C and HDL-C levelson admission (day-0) were significantly lower than in controls (p=0.01 andp=0.008, respectively), whereas triglycerides and LDL-C levels did not differsignificantly between patients and controls. Total-C levels were also lower ininfected neonates than in controls on day-1 (p=0.001), but increased afterwardsand did not differ than levels in controls on days-2, -3 and -7. HDL-C levelsin infected neonates were significantly lower than in controls on day-1 (p=0.003),day-2 (p=0.004) and day-3 (p=0.002), but not on day-7 (p>0.05). Total-C andHDL-C on admission correlated negatively with serum CRP levels (r_s=-0.46,p<0.001 and r_s=-0.55, p<0.001, respectively).

Conclusions: This is the first study showing that Total-Cand HDL-C levels are reduced in the acute phase of neonatal infection andcorrelate negatively with serum CRP levels, but increase later reaching to the controllevels when infection subsides. Total-C and HDL-C levels may be used ascomplementary biomarkers in the diagnostic workup of neonatal infection.

ESPID-0132
DIAGNOSTIC TOOLS

CIRCULATING GHRELIN AND PEPTIDE PYY (3-36) LEVELS IN NEONATAL INFECTION: ASSOCIATIONS WITH FEVER CHANGE DURING THE COURSE OF INFECTION

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Background: Studies in animals and human adults haveshown that the gastrointestinal tract-derived hormones ghrelin and peptide YY,that participate in the regulation of food intake and energy balance, may alsoplay roles in the inflammatory response. However, their involvement in neonatalinfection or sepsis is not known.

Methods: Plasma ghrelin and peptide YY 3-36 (PYY3-36)levels were determined by ELISA in 36 term neonates with febrile infection (22of them were septic) and in 20 healthy term neonates of similar postnatal ageand gender distribution, as controls. Ghrelin and PYY3-36 levels were seriallymeasured on days 0, 1, 2, 3 and 7 following admission in all infected neonates,and once in controls. Associations of ghrelin and PYY3-36 levels with clinicaland laboratory parameters, including anthropometrics, fever, leukocyte andplatelet counts, serum glucose and CRP levels, were assessed.

Results: Plasma ghrelin levels were significantlyhigher in infected neonates than in controls at each study day ($p=0.009$),whereas PYY3-36 levels did not differ significantly between patients andcontrols at any day. In infected neonates, ghrelin levels on admissioncorrelated negatively with serum glucose levels ($p=0.002$), whereas fever changeduring the course of infection was significantly associated with change of ghrelinlevels on repeat measurements ($p<0.01$). Receiver operating characteristicanalysis of ghrelin levels resulted in significant areas under the curve (AUC)for detecting infected neonates on admission (AUC=0.728, $p=0.005$).

Conclusions: Circulating ghrelin, but not PYY3-36, is anearly marker of neonatal infection, possibly reflecting and/or participating inthe inflammatory process.

ESPID-0025
DIAGNOSTIC TOOLS

APPLICATION OF DIFFERENT SCORING SYSTEMS AND THEIR VALUE IN PEDIATRIC INTENSIVE CARE UNIT

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Background: Little is known on the impact of risk factors that may complicate the course of critical illness. Scoring systems in ICUs allow assessment of the severity of diseases and predicting mortality. ***Objectives:*** Apply commonly used scores for assessment of illness severity and identify the combination of factors predicting patient's outcome. ***Methods:*** we included 231 patients admitted to PICU of Cairo University, Pediatric Hospital. PRISM III, PIM2, PEMOD, PELOD, TISS and SOFA scores were applied on the day of admission. Follow up using SOFA score and TISS. ***Results:*** There was positive correlations between PRISM III, PIM2, PELOD, PEMOD, SOFA and TISS on the day of admission, and the mortality rate ($p<0.0001$). TISS and SOFA score had the highest discrimination ability (AUC: 0.81, 0.765; respectively). Significant positive correlations were found between SOFA score and TISS scores on day 1, 3 and 7 and PICU mortality rate ($p<0.0001$). TISS had more ability of discrimination than SOFA score on day 1 (AUC: 0.843, 0.787; respectively). ***Conclusion:*** Scoring systems applied in PICU had good discrimination ability. TISS was a good tool for follow up. LOS, mechanical ventilation and inotropes were risk factors of mortality.

ESPID-0076
DIAGNOSTIC TOOLS

CSF FERRITIN AS A MARKER FOR BACTERIAL MENINGITIS IN CHILDREN

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Background and aims: Rapid differentiation between bacterial and aseptic meningitis, and the need for immediate antibiotic treatment in the former, is crucial in the prognosis of these patients. Ferritin is one of the most sensitive biochemical markers investigated in cerebrospinal fluid (CSF) for the early diagnosis of bacterial meningitis. The aim of this study was to evaluate the diagnostic capability of CSF ferritin in differentiating bacterial and viral meningitis in the pediatrics setting.

Methods: A cross-sectional study was carried out in the referral Children's Medical Center Hospital, Tehran, during 2008 and 2009. In this study, CSF samples from 42 patients with suspected meningitis were obtained and divided into two meningitis groups, bacterial (n = 18) and viral (n = 24). Ferritin and other routine determinants (i.e., leucocytes, protein and glucose) were compared between the two groups.

Results: Ferritin concentration in the bacterial meningitis group was 106.39± 86.96 ng/dl which was considerably higher than in the viral meningitis group (10.17±14.09, $P < 0.001$). Mean CSF protein concentration and cell count were significantly higher in the bacterial meningitis group and showed a positive correlation with CSF ferritin.

Conclusion: This study suggests that CSF ferritin concentration is an accurate test for the early differentiation of bacterial and aseptic meningitis; however, further investigation on a larger cohort of patients is required to confirm this finding.

ESPID-0024
DIAGNOSTIC TOOLS

ULTRASOUND IN DETECTION OF ELEVATED INTRACRANIAL PRESSURE IN CHILDREN WITH MENINGITIS

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Our goal was to investigate the sensitivity of the ultrasound investigation of optic nerve sheath diameter (ONSD) in detetction of elevated intracranial pressure in children with meningitis.
Methods. 24 patients (age 6 months - 12 years, 14 boys, 10 girls) were enrolled, all admitted to the ICU with meningitis (11 aseptic and 13 bacterial). 6 patients were conscious and 18 in coma. 2 patients died, 22 recuperated. Measurement of ONSD was performed with the Mindray M7 device, 7.5-MHz linear probe with beam focused on the retrobulbar area. The ONSD was measured 3 mm behind the optic disc, with measurements performed in the transverse and sagittal planes of both eyes. Final ONSD value was calculated by averaging 4 measured values. Measurements were performed at 2 time points: at admission and when the clinical course of the disease changed (e.g. coma resolved or worsened).
Results. Mean ONSD was 5.49 mm for OD & 5.29 for OS, range 3.9-7.2 mm. There was a significant decrease of mean ONSD with clinical improvement (regaining of consciousness or recuperating): mean decrease to 5.0 OD & 4.9 mm OS. In 2 patients who died, ONSD increased beyound 6 mm on both eyes (6.5 mm OD & 6.4 mm OS in one and 7.1 OD & 7.2 OS in another). **Conclusions.** Repetitive ONSD measurement proved sensitive in the monitoring of clinical condition in children with meningitis. We propose that ONSD changes in this population may reflect changes of intracranial pressure.

ESPID-0117
DIAGNOSTIC TOOLS

EVALUATION OF AID LINE PROBE ASSAY FOR RAPID DETECTION OF BACTERIAL MENINGITIS PATHOGENS IN CEREBROSPINAL FLUID SAMPLES IN CHILDREN

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This study aimed to evaluate and compare the AID line probe assay (LPA) with conventional multiplex PCR for *Streptococcus pneumoniae* (Sp) and real-time PCR for *N. meningitidis* (Nm) and *H. influenzae* type b (Hib) in CSF samples in children. The AID LBA consists of 2 strips to detect 16s universal bacterial DNA, Sp, Hib, Nm, 11 serotypes of Sp, 2 penicilin resistance genes for Sp and 5 serogroups of Nm. Of 751 CSF samples, 431 (57%) were negative, 127 (17%) were Sp, 53 (7%) were Hib, 41 (5%) were Nm, 2 were positive for both Sp and Hib, and 2 were positive for both Hib and Nm. In 95 (13%) CSF samples we detected strip banding in 16sDNA. Sensitivity of LPA for Sp, Hib and Nm were 74%, 95%, and 83%, respectively. Sensitivity of LBA for Sp serotype 4, 6A/6B, 9V/9A, 14, 18, 19F, 23F, 3, 19A, 1, 5 and 7F were found to be 100% (2/2), 80% (4/5), 50% (1/2), 100% (4/4), 60% (3/5), 72% (8/11), 100% (6/6), 100% (1/1), 0% (0/4), 70% (7/10), and 0% (n=0), respectively. Sensitivity of LBA for Nm serogroup A, B, C and W were found to be 100% (1/1), 38% (9/24), 100% (2/2) and 0% (0/1), respectively. We conclude that LBA is helpful tool for the rapid detection of bacterial meningitis pathogens in children.

ESPID-0930
DIAGNOSTIC TOOLS

EVALUATION OF A MULTIPLEX PCR FOR DIAGNOSIS OF LATE ONSET SEPSIS IN PRETERM INFANTS

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Background and aims
Late onset sepsis (LOS) occurs frequently in preterm infants and requires rapid and accurate diagnosis. Blood culture suffers from a long turnaround time; PCR could provide a rapid additional tool. We clinically evaluated the diagnostic performance of a newly developed multiplex PCR that detects the 8 most prevalent bacterial pathogens (panel: coagulase negative staphylococci, *Staphylococcus aureus, Enterococcus faecalis, Streptococcus agalactiae, Escherichia coli, Klebsiella spp., Pseudomonas aeruginosa and Serratia marcescens*). This assay requires limited hands-on time and provides species-specific results within 4 hours.
Methods
We prospectively included 91 episodes of suspected LOS in preterm infants admitted to our NICU. A blood sample for PCR was obtained together with blood culture prior to initiation of antibiotic therapy. Blood culture and PCR were compared. The study was approved by the Institutional Review Board and parents provided written informed consent.
Results
Blood culture was positive in 60 and negative in 31 episodes, while PCR was positive in 53. For monomicrobial infections (n=85) PCR demonstrated a sensitivity of 75%, specificity 81%, PPV 88% and NPV of 68% compared to blood culture. Six episodes were polymicrobial, of which 3 were detected by PCR only. For example, PCR detected *Klebsiella*, *Enterococcus* and *Streptococcus* in a neonate with NEC while blood culture only grew lactobacilli.
Conclusions
We clinically evaluated a newly developed multiplex PCR. PCR had a high PPV and sensitivity, and detected additional cases of LOS. This study demonstrates that multiplex PCR is a useful additional diagnostic tool for rapid diagnosis of LOS.

ESPID-0565
DIAGNOSTIC TOOLS

HOW SERIOUSLY DO TURKISH MOTHERS TAKE FEVER?

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Background and aims: One of the most common problems of childhood period is fever. Fever is a symptom that can be managed by parents at home and its complications can be prevented with early intervention. This study was aimed at identifying Turkish mothers' knowledge of and attitudes towards fever.

Methods: The study was conducted with 172 mothers who have children 0 to 10 years of age and visited Yozgat Family Health Centre during October-December 2014. Prior to the study, the approval of institution and verbal consent of the mothers were taken. The questionnaire form was used to collect data. The data was assessed through percentages.

Results: It was found that, of the mothers, 68.0% stated that fever stemmed from infection, %87.2 stated that high fever was harmful for the child, and 70% said that high fever might cause convulsion in child. Of the mothers, 34.9% specified that they were reducing fever with their own methods; of these 16.3% gave their children a warm shower, 7% applied compress with water with vinegar and took their clothes off as a way to reduce fever, 30% stated that they immediately saw a doctor. In this study, 67.2% of the mothers stated that they did not have sufficient knowledge of fever and nearly all of them stated they had anxiety over fever.

Conclusions: It was found out that mothers were experiencing anxiety over fever and they needed more information. Informing mothers on managing fever will contribute to prevention of incorrect practises.

ESPID-0524
EPIDEMIOLOGY AND PUBLIC HEALTH

CHARACTERISTICS OF TRANSIENT AND CHRONIC POSTINFECTIOUS CYTOPENIAS IN CHILDREN ACCORDING TO THE ASSOCIATED INFECTIOUS AGENTS.

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Background and aims: Acquired postinfectious cytopenia in childhood is common. We aimed to assess the aetiology, duration and outcome of febrile cytopenia in hospitalized previously healthy children.

Methods: We evaluated 116 children with postinfectious cytopenia (mean±SD age 4.0±3.8years), admitted to a paediatric ward during a two-year period, using inflammation markers, cultures and serological tests. Neutropenia was characterised as mild (absolute neutrophil count,ANC:1.001-1.500/μL), moderate (500-1.000/μL) or severe (<500 cells/μL). Anaemia was defined as mild (Hb:10−11.4 g/dL), moderate (7-9.9 g/dL) and severe (<7g/dL). Thrombocytopenia was characterised as mild (platelet count:50.001-150.000/μL), moderate (20.000-50.000/μL) and severe (<20.000/μL).

Results: In 74 (63.8%) cases an infectious agent was identified, i.e.44.8% viral, 11.3% bacterial, 7.7% parasitic. In 28.4% patients one cell line was affected, while in 71.6% ≥2 cell lines. In 82.75% cases cytopenia was transient (duration \<180 days), while in 17.24% it was chronic (duration>180 days). The transient cytopenia subgroups exhibited a difference in severity (p=0.018), (mild: bacterial subgroup, moderate:viral and parasitic) and in the number of affected cell lines, i.e.predominantly two in the viral and bacterial subgroups and pancytopenia in the parasitic subgroup (p=0.001). The chronic group had severe cytopenia (p=0.004) with ≥2 cell lines affected, while the transient had mild-to-moderate cytopenia, with 1-3 cell lines affected. Both groups were associated with viral infections and were in overall good condition.

Conclusion: Childhood cytopenia during febrile illness is usually transient, of short duration, mild/moderate severity, benign course and usually resolves spontaneously. However, patients with severe cytopenia affecting ≥2 cell lines, need further evaluation and follow-up.

ESPID-1079
EPIDEMIOLOGY AND PUBLIC HEALTH

CLINICAL AND DIAGNOSTICAL PARTICULARITIES OF FIRST INFECTION WITH EBV WITH HEPATITIS IN CHILDREN

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Introduction. During the last period the annual average incidence of infectious mononucleosis (MI) increased significantly to 4.42 - 5.4 per 100,000 people for the period from 2012 to 2013.

The purpose of the study. Evaluation of the clinical and diagnostical particularities of MI with Epstein-Barr virus (EBV) serologically confirmed in children.

Materials and methods. The study included 45 children aged from 1 to 18 years old with MI of EBV was established based on serological markers, hospitalized during January 2013 to March 2014.

The study results. The clinical picture was characterized by: fever - 100%, nasal obstruction - 86.7%, eyelid edema - 55.6%, toxic syndrome - 77.7%, purulent tonsillitis - 86.7%, lymphadenopathy - 100%, hepatomegaly - 71.1%, splenomegaly - 68.9% and rash - 11.1% with discharge persistence of hepatomegaly - 62.5% and splenomegaly 41.9%. Laboratory tests detected leukocytosis - in 91.1% of cases, lymphocytosis and monocytosis - 68.9%, atypical lymphocytes - 31.1% and accelerated ESR - 64.4%, the high level of ALT - 71.1%, the high level of AST – 95.5% persisting at discharge (the high level of ALT -33.3% and AST - 51.1%). The disease evolved in the medium form at 68.9% and severe form – 31.1% of patients. The treatment included antibiotics (91.1%), corticosteroids (55.5%), recombinant interferon α2β (66.7%), etc., for about 10 days Complications and deaths have not been recorded.

Conclusion: MI with EBV had an acute and benign evolution, requiring surveillance because the persistence of clinical and laboratory changes.

ESPID-0816
EPIDEMIOLOGY AND PUBLIC HEALTH

SEROTYPES CAUSING INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN UNDER 5 YEARS OLD IN CATALONIA, SPAIN (2012-2013)

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Invasive pneumococcal disease (IPD) is a major cause of morbidity and mortality among children. The objective of this study was to determine the circulating serotypes of *Streptococcus pneumoniae* and penicillin non-susceptibility in children under 5 years old, after pneumococcal conjugate vaccine 13-valent (PCV13) introduction, in a community with vaccination coverage around 50%.

We analysed all notifications of IPD reported at the Microbiological Reporting System of Catalonia (2012-2013). IPD was defined as isolation or detection by PCR of *S. pneumoniae* in any normally sterile site. Clinical and microbiological data collected were: clinical presentation, hospitalization, vaccination, serotype and antibiotic sensitivity.

265 cases were diagnosed of IPD (81.1% by culture) in children <5 years old. The incidence was 31.7 per 100.000 persons-year. Pneumonia was the most-frequent clinical manifestation with 187 (70.6%) cases, and empyema occurred in 23.8% of them. PCV13 serotypes represented 60.5%. Serotypes 1(15.8%), 3 (11.4%), 19A (10.5%) and 24F (10.5%) were the most frequent. Hospitalization rate was 73.6% (197 cases; and one patient with serotype 24F died). Of the 113 vaccinated cases, 75 (66.4%) received at least 1 dose of PCV13. In these cases, the most common serotype was 24F (14.6%). Of 189 strains analysed, 70 (37.1%) were penicillin non-susceptible, of which serotype 24F was the most frequent (32.9%). All serotype 24F strains were penicillin non-susceptible.

After the introduction of PCV13 in children, the PCV13 serotypes remain high with predominance of serotype 1. 24F is one of the main circulating serotype with all strains penicillin non-susceptible.

ESPID-0985
EPIDEMIOLOGY AND PUBLIC HEALTH

SALMONELLA INFECTION IN NORTHERN SPAIN: VARIATION OF THE STRAINS ISOLATED AND THEIR ANTIMICROBIAL SUSCEPTIBILITY OVER AN 11-YEAR PERIOD

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Background and aims:
Salmonellosis is an important problem in terms of public health. The aim of this study is to analyze *Salmonella spp* isolates in children and their antimicrobial susceptibility in a region in Northern Spain.
Methods:
Descriptive retrospective study of *Salmonella spp* isolates and their susceptibility to antibiotics in pediatric patients (0-14 years old) between 2003 and 2013 in Gijón (Spain), with a population around 303,000.

Results:
A total of 1041 *Salmonella spp* isolates were registered during this period (98.3% from stool cultures). Patients' mean age was 4 years (95% CI: 3.8-4.2). Since 2008 a shift in the *S. enteritidis* vs *S. typhimurium* rate was found (80.6% vs 28.9% in 2003-2007; 21.3% vs 54.7% from 2008); there was an outbreak of Salmonella enterica serotype Poona in 2011. Antimicrobial susceptibility results were available from 900 strains (86.5%). Resistance rates to ampicillin increased (25.6% to 44.1%) and to ciprofloxacin decreased (21.8% vs 11.2%) between the two study periods. Overall, 13.6% of *S. enteritidis* and 68.2% of *S. typhimurium* strains were non-susceptible to ampicillin. Resistance rates to cefotaxime (0.7%), amoxicillin-clavulanic (2.7%), and trimethoprim-sulfamethoxazole (4.1%) remained stable during the study.
Conclusions:

S. typhimurium is replacing *S. enteritidis* as the most frequent Salmonella strain isolated in children, resulting in an increase in ampicillin resistance. Most Salmonella strains remain susceptible to cefotaxime, amoxicillin-clavulanic, and trimethoprim-sulfamethoxazole.

ESPID-0698
EPIDEMIOLOGY AND PUBLIC HEALTH

IS THERE EVIDENCE FOR HAV CHILDHOOD VACCINATION IN EUROPE?

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Background

We reviewed HAV seroprevalence data and HAV vaccination policies in the EU/EEA to support decisions on prevention strategies.

Methods

We systematically reviewed the literature and institutional websites for HAV seroprevalence records in all languages from 1975 to 2014, excluding high-risk groups and non EU/EEA studies. We extracted and analysed seroprevalence data by age, year and country. We attributed country endemicity profile (WHO criteria) and used seronegativity at 15 years as susceptibility marker. We surveyed EU/EEA countries on HAV vaccination policies.

Results

We identified 4283 articles, screened full-text 442 and included 220. In 2014, EU/EEA presents very low (n= 21), low (n=5) and intermediate (n=1) endemicity profiles. In 2000-2013 HAV seroprevalence in 15 years olds ranged from 1% to 62% (data from 16 countries). We estimate HAV seroprevalence among 15-year olds to be currently <10% in 10 EU/EEA countries. Nordic countries show the lowest seroprevalence with an increasing gradient towards South and East Europe.

HAV universal childhood vaccination is recommended in 4 countries, all at very low endemicity. All countries recommend vaccination for travellers and 5 for second generation migrants and adoptees' families.

Conclusions

Susceptibility at 15 years is high in EU/EEA most countries, but presents high variability, including evidence of local virus circulation in some countries. Emerging risk factors linked to increasing movement of people and food importation from both inside and outside the EU/EEA pose new risks of exposure to HAV. HAV prevention policies in some EU/EEA countries could be revised according to the new evidence.

ESPID-0052
EPIDEMIOLOGY AND PUBLIC HEALTH

THE ECONOMIC BURDEN OF CHILDHOOD INVASIVE PNEUMOCOCCAL DISEASE AND PNEUMONIA IN TAIWAN.

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Background and aims: Invasive pneumococcal disease (IPD) and pneumonia are the most important causes of morbidity and mortality in children in both developed and developing countries. The treatment of IPD and pneumonia is a major economic burden on healthcare systems and families. The purpose of this study was to estimate the economic burden of IPD and pneumonia among younger children in Taiwan.

Methods: We used a cost-illness approach to identify the cost categories for analysis in this study according to various perspectives. We obtained hospitalization, outpatient, and emergency department visit data from the National Health Insurance Research (NHIR) database for children less than 5 years of age from January 2008 to December 2008. A prospective survey was administered to the families of the patients to obtain detailed personal costs.

Results: The total annual social and hospital costs for IPD were US $4.3 million and US $926,000, respectively. The total annual social and hospital costs for pneumonia were US $150 million and US $170 million, respectively. On average, families spent US $653 or US $218 when their child was diagnosed with IPD or pneumonia, respectively. This cost represents approximately 27%–81% of the monthly salary of an unskilled or service worker.

Conclusions: these data emphasize the need for a safe and effective pneumococcal vaccine to reduce the economic burden associated with pneumococcal disease.

ESPID-0609
EPIDEMIOLOGY AND PUBLIC HEALTH

THE CHANGES IN THE OUTBREAK OF ROTAVIRUS GASTROENTERITIS IN CHILDREN AFTER INTRODUCTION OF ROTAVIRUS VACCINES IN KOREA: A RETROSPECTIVE STUDY AT A TERTIARY HOSPITAL

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Purpose: This study aimed to examine the changes in the outbreak of acute gastroenteritis, rotavirus gastroenteritis after the introduction of the rotavirus vaccine in Korea.
Methods: The current study investigated the number of inpatients in the pediatric ward of Inje University Sanggye Paik Hospital during the periods of 2005–2006 and 2011–2012. A retrospective analysis was conducted on the medical records of 2,840 patients <5 years of age who were hospitalized at Inje University Sanggye Paik Hospital in these time periods.
Results: When we compared 2 separate sets of data from before (2005–2006) and after (2011–2012) vaccine introduction, there were statistically significant decreases in the number of patients who were hospitalized for acute gastroenteritis across all of the groups of patients <5 years of age except those <2 months of age. The number of patients with rotavirus gastroenteritis in all age groups declined except for children <2 months of age and those 2–5 months of age.
Conclusion: These results show that after the introduction of a rotavirus vaccine in Korea, the incidence of rotavirus gastroenteritis decreased in 6–59-month-old patients hospitalized for acute gastroenteritis.

ESPID-0669
EPIDEMIOLOGY AND PUBLIC HEALTH

METHODS WHICH MOTHERS HAVING CHILDREN 0 TO 6 YEARS OF AGE THINK AS EFFECTIVE TO PROTECT CHILDREN AGAINST INFECTION

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Background and aims: Infections in infants and children are widely seen in the early years of life in particular. Measures to protect children against infections are important for reducing frequency of infections and complications. This study was conducted to identify the methods which mothers having children 0 to 6 years of age think as effective to protect children against infections.

Methods: The study was carried out with 144 mothers having children 0 to 6 years of age who visited Yozgat Public Hospital Children's Unit between November-December 2014. Prior to study institution's approval and mothers' verbal consent were taken. The questionnaire form was used to collect data. The data was assessed through percentages.

Results: It was found that, of the mothers participating the study, 63.6% were in the 26-35 age group, 24.7% were graduates of vocational school, 80.5% did not work. In the study, it was also found that, 58.4% of the mothers' children had infection previously, %20.8 had infection in every 2-3 weeks and the most common case was upper respiratory tract infection(67.5 %). Of the mothers, 77.9% stated vaccination, 51.9% keeping children away from crowded environment, 51.9% boiling feeding bottle, 65.5% breastfeeding, 71.4% airing child's room often, and 68.8% paying attention to hand hygiene as affective measures to protect children from infection.

Conclusions: It was shown that mothers had insufficient knowledge about methods of protecting children from infection. Training mothers on this subject is considered to be effective in reducing the frequency of infection in children.

ESPID-0661
EPIDEMIOLOGY AND PUBLIC HEALTH

VARICELLA VACCINATION MIGHT RESULT IN INEQUALITY IN HEALTH BENEFITS BETWEEN GENERATIONS

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Background
After primary varicella-zoster virus (VZV) infection, the virus persists in latency. Subsequent reactivation results in herpes zoster (HZ). It has been hypothesized that exogenous boosting by VZV reduces the probability of VZV-reactivation. Therefore, universal varicella vaccination may increase HZ incidence due to reduced VZV circulation in the population. To inform decision-making, we conducted cost-effectiveness analyses of varicella vaccination including effects on HZ.

Methods
Statistical analyses were based on a dynamic transmission model, using Dutch VZV seroprevalence and HZ incidence data. In a scenario analysis, we considered four vaccination coverages of a two-dose vaccination program (12 months and 4 years of age). The scenarios differed by whether or not including exogenous boosting effects on HZ, and presence or absence of vaccine VZV reactivation.

Results
All models showed a decrease in varicella after introduction of vaccination. Without exogenous boosting, vaccination (95% coverage) is expected to be cost-effective or even cost-saving. In contrast, in models with boosting, vaccination (95% coverage) is either not cost-effective within 180 years (with vaccine VZV reactivation) or cost-effective only on the very long term (>130 years, without vaccine VZV reactivation), because of increased HZ. Furthermore, disadvantages for unvaccinated birth cohorts out-weigh health benefits for vaccinated cohorts.

Conclusions
Cost-effectiveness of varicella vaccination depends strongly on its impact on HZ, and the time perspective. Our findings reveal ethical considerations as varicella vaccination might result in inequality in health benefits between generations: birth cohorts born just before introduction of vaccination might pay the price for health gain among vaccinated cohorts.

ESPID-0662
EPIDEMIOLOGY AND PUBLIC HEALTH

COST-EFFECTIVENESS EVALUATION OF ALTERNATIVE MENINGITIDIS ACWY CONJUGATE (MENACWY) VACCINATION IN THE KINGDOM OF SAUDI ARABIA (KSA)

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Background and aims:

Neisseria meningitidis causes life-threatening cases of invasive meningococcal disease (IMD). In the Kingdom of Saudi Arabia (KSA) specifically, the annual Hajj is associated with high risk of IMD outbreaks. This study assessed the cost-effectiveness of different MenACWY vaccination scheme compared with the current routine 9-12months MenACWY scheme.

Methods:

An annual population static model reproduced variable annual epidemiologic IMD patterns over a 100-year time horizon, from 1995 to 2002 reported KSA IMD incidence. Vaccination effectiveness was based on KSA IMD serogroup and age distribution, expected vaccine effectiveness, duration of protection, and vaccine coverage rate. Lifetime costs and quality-adjusted life-years (QALYs) were assigned to each model-projected IMD based on international literature adapted to KSA. A vaccine price of $22.2/dose was assumed (3% discount rate). Lifetime costs, QALYs and the incremental cost-effectiveness ratios (ICER) compared with the current vaccination was calculated for each scenario (routine 9-12months, 12months+14years, 9-12months+14years, 2-4-6-12months+14years).

Results:

The 12months+14years vaccination scheme dominates the current (9-12months) scheme (more QALYs and lower costs with 262 IMD cases prevented) while a 9-12months+14years scheme results in an ICER of $377,242/QALY (-374 IMD). Implementing an additional 14years booster-dose to a full infant vaccination (2-4-6-12months) scheme lead to an ICER of $553,636/QALY (-767 IMD).

Conclusions:

Adding an adolescent MenACWY vaccine booster-dose to the current or to a full infant vaccination scheme was modelled not to be cost-effective in KSA (ICER>3 gross domestic product/capita [$77,556]) while switching the current routine 9 months dose to an adolescent booster dose would save lives and money.

ESPID-0683
EPIDEMIOLOGY AND PUBLIC HEALTH

ESTIMATING THE COST IMPACT OF A PREFILLED SYRINGE ADMINISTRATION FOR THE HEXAVALENT VACCINE IN VALENCIA, SPAIN

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BACKGROUND AND AIM: Vaccination programs should be highly efficient. As the vaccines are given repeatedly to most of the children, any improvement may produce a big saving. The aim was to assess the economic impact for the health system if a prefilled syringe (Hexyon™) was used instead of a vial & syringe that needs reconstitution (Infanrix-Hexa™).

METHODS: A cost minimization analysis was performed. We assumed both vaccines were equally efficacious and safe, at the same price. Time used for reconstitution was measured in 55 nurses (reconstitution of 455 vaccines). Cold chain cost was calculated using the volumes of the vials and of the fridges. An approximation of the programmatic errors (injection of a vaccine without reconstitution) was obtained of mixing the number of cases declared to the system and those that the nurses reported in a survey.

RESULTS: Reconstitution time was 70.2 sec (95%CrI: 68.6-72.0). Cost of a primary care nurse hour: 22.0€. Cost for a programmatic error: 308€. Boxes for Infanrix-Hexa™ halved the volume (67 vs 160 cm3), and therefore the cost.

For a two dose schedule, a population of 47931 children (2011) and 97% coverage of hexavalent vaccines, using a prefilled syringe would save the health system 53807 € per year. This comes from: -53685€ for the time saved, -2570€ for avoidance of the programmatic errors and +2448€ for the cold chain.

CONCLUSIONS: Using prefilled syringes would save resources to the health system, and avoid programmatic errors.

ESPID-0473
EPIDEMIOLOGY AND PUBLIC HEALTH

EPIDEMIOLOGICAL REPORT OF INVASIVE PNEUMOCOCCAL DISEASE IN A PRIVATE HOSPITAL OF BUENOS AIRES, ARGENTINA IN COMPARISON WITH PUBLIC HOSPITALS

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Background and aims: Invasive infection by *S. pneumoniae* is a frequent cause of mortality in children. The aim of this study was to analyze *S. pneumoniae* serotypes in invasive disease at a private hospital and compare them to those obtained at public hospitals.
Methods: 47 patients admitted during 2007-2014 with documented Invasive Pneumococcal Disease in usually sterile fluids were studied. All isolates were identified according to standard methods and sent to INEI-ANLIS "Dr. Carlos G. Malbrán" Institute for serotyping with Neufeld-Quellung reaction. Each case was compared 1:1 to another unvaccinated child of similar age, pathology and geografphic region, admitted at public hospitals.
Results: Most frequent diagnosis were: pneumonia 30, meningitis 6 and bacteremia 6. Serotypes more frequently found at the private hospital were: 1 (n:15), 5 (n:8) and 19A (n:5); in hospital controls: 1 (n:13), 5 (n: 7), 14 (n:6). Serotype 1 was associated with pneumonia (p=0.028)
Rates of hospitalization in subsequent years were: 36.7%00, 37.5%00, 35.4%00, 15.0%00, 15.5%00, 16,5%00, 19.5%00 and 23.1%00.
There were more patients fully vaccinated during the period 2010-2014 (15/21) than between 2007-2009 (4/26) (p 0.001) No patients developed invasive disease due to serotypes included in vaccination.
Conclusions:
1. Risk of hospitalization due to Invasive Pneumococcal Disese was strongly reduced after the introduction of new conjugate vaccines in the private practice.
2. Most frequently isolated serotypes were not included in PCV-7 vaccine.
3. Proportion of pneumonia/pleural effusion due to serotypes 1 and 5 was high in both groups.
4. Serotype 1 was associated with lung infection.

ESPID-0899
EPIDEMIOLOGY AND PUBLIC HEALTH

PERSONAL ATTITUDES AND MISCONCEPTIONS TOWARDS VACCINATIONS AMONG SCHOOL TEACHERS IN NORTHERN ITALY

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Introduction. School is reputed as pivotal for health education. Past researches have shown that schoolteachers' (ST) interventions maximize the consent for vaccination programs. The aim of this study was to evaluate knowledge and attitudes of ST regarding vaccinations.
Subjects and Methods. In this case control study, 334 school professionals (153 ST and 181 controls from technical personnels) responded to a modified version of Luraschi & Pellegri questionnaire assessing their attitude towards vaccination and general vaccination related knowledge.
Results. In general, 83.5% of subjects were "favorable to vaccinations", with ST showing a significantly higher unconditioned attitude towards vaccination (39.2% vs 29.8%, $p < 0.05$). The main reasons for declining vaccination were: to avoid shots/medications (13.7%), the risk of side effects (4.6%) and the uselessness (1.9%), with no differences between cases and controls. The main reason to be vaccinated were to avoid getting vaccine preventable diseases (VPD, 39.9%) and to avoid transmitting VPD (73.7%, $p < 0.05$). On the other hand, in 28.3% of cases (vs 15.5% of controls, $p < 0.05$) vaccinations are suspected to be more strictly associated with economic interests than to medical necessities. Main informational sources were General Practitioners (60.1%), conventional media (36.6%) and new media (15.7%, $p < 0.05$): among the latter, misconceptions of economic interests and uselessness were significantly more frequent ($p < 0.0001$).
Conclusions. Despite the small sample size, this study suggests a generally sufficient knowledge of the vaccination practices and policies among ST but also stresses the potentially conflicting role of the new media.

ESPID-0533
EPIDEMIOLOGY AND PUBLIC HEALTH

CLINICAL RESEARCH DURING EPIDEMICS: IDENTIFYING ETHICAL, ADMINISTRATIVE, REGULATORY AND LOGISTICAL ISSUES RELEVANT TO PARTICIPATION OF CHILDREN

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Background and aims

Rapid up-scaling of clinical research is central to ensuring an adequate response in an epi/pandemic situation. We aimed to identify a number of key barriers (in particular ethical, administrative, regulatory and logistical (EARL) barriers) in conducting epidemic research and offer some possible solutions to the currently fragmented research response in Europe. We examined barriers of particualr relvance to paediatric research.

Methods

We conducted an early and comprehensive scoping exercise to identify potential barriers to pandemic research. We triangulated data from a series of qualitative interviews with relevant key Member State (MS) professional stakeholders in the field; via an on-line survey and via secondary data on clinical trial authorisation and ethical approval processes in each MS. This data collection included the specific area of paediatric research which offered some particular problems and ‘solutions’.

Results

Our analysis shows that there are numerous vital issues requiring future consideration in relation to public engagement; processes of recruitment; clarification of appropriate levels/ methods of consent; allocation of funding resources; a lack of uniformity regarding ethical approval systems and variance in procedures among and within MS countries. The inclusion of vulnerable populations must be specifically considered.

Conclusion

Children can be critical in the spread of an epi/pandemic and extrapolation of findings from adults to children is often impossible. Our findings suggest the importance of

addressing EARL barriers, such as ethics, recruitment and consent issues, as many may be particular obstacles to research involving children in future epi/pandemics.

ESPID-0425
EPIDEMIOLOGY AND PUBLIC HEALTH

HUMAN RHINOVIRUS INFECTION IN YOUNG CHILDREN HOSPITALIZED WITH ACUTE WHEEZE IN BULGARIA.

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Objective and Aims:
Human Rhinovirus (HRV) is an important respiratory virus responsible for childhood wheezing illnesses, especially for asthma. The aim of the study was to elucidate the association of HRV with two previously identified asthma-related single nucleotide polymorphisms in chromosome 17 - ORMDL3 (rs8076131 G>A) and GSDMB (rs 2305480 C>T), as well as, with severity of clinical manifestation, family history of asthma and risk of recurrent wheezing.
Materials and Methods:
Medical history and nasal samples were collected prospectively from 30 children less than 3 years of age (21 boys and 9 girls), presenting to hospital with an wheezing episode. Nasal washes were evaluated using real-time reverse transcriptase polimerase chain reaction (PSR) and indirect immunofluorescence assay. All children were genotyped by PSR-restriction fragment length polymorphism. The results were compared with the clinical data.
Results:
The HRV detection rate among participants was 26.66% (n=8). The found relationship between rhinovirus infection and family history for asthma was:OR 3.2, CI 1.8 - 6.62. HRV positive infants were more likely to have recurrent wheezing (p=0.04). Genotype A/A was a possible risk factor for rhinovirus wheezing in elderly children (p=0.05). Homozygous for T-allele had more early age of first wheezing (p=0.02) and no one of them were infected with HRV.
Conclusions:
The data confirmed the association among rhinovirus infection during infancy and family history for asthma, genotype A/A (rs 8076131 G>A) and increased risk of recurrent wheezing.
The study was financially supported by research grant, 2014y, Medical University, Sofia.

ESPID-0165
EPIDEMIOLOGY AND PUBLIC HEALTH

ESTIMATING THE IMPACT OF HERD IMMUNITY IN PAEDIATRIC VACCINATION FOR INFLUENZA

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Backgroundand aims: The indirect effect ofinfluenza vaccination is widely accepted and modelling provides a way toanalyse the impact in different settings.

Methods:A dynamic transmission model simulates the directand indirect effects of influenza, for an age stratified cohort (<2, 2-4,5-17, 18-64 and 65 years and over) on a daily cycle over a 5 year horizon. Allowingdirect cost-effectiveness comparisons of annual paediatric vaccination (APV) inEngland and Wales, with various levels of coverage.

Results: APV may offer wider protection in the susceptibleand older age groups (18 – 65 and those 65 years and older) – impacting on overall influenzainfections and associated clinical consequences (hospitalisations, primary careconsultations and influenza related mortality). Comparing APV coverage rates of10% and 50% – demonstrates an overall reduction of 25% in the number influenzainfections (consistent with reduction seen in 18-65 year olds alone). Further analysisof coverage between 60% and 100% provides reduction of 4 -15%. These resultsare coupled with annual savings between €1,412 and €5,900 (10-50% coverage: €1,412-3,942and 60-100%: €4,473-5,900). This modelcan be easily adapted for other countries with limited data.

Conclusions: APV is a relevant strategy that mayhave the potential to provide wider protection against seasonal influenza inthe total population, even with low coverage. Herd immunity increases theclinical and economic benefits of paediatric vaccination for all achievable coverageRates; greatest reduction observed in the number of influenza infections occursbetween 10% and 50% coverage.

ESPID-0723
EPIDEMIOLOGY AND PUBLIC HEALTH

VIEWS OF MOTHERS ON THE ROLE OF TOYS IN THE SPREAD OF INFECTION IN CHILDREN: A QUALITATIVE STUDY

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Background: The lack of sufficient awareness and vigilant in selection, use and hygiene of the toys which are meant to be useful in supporting mental, physical and psychiosocial development of children can actually be the source of contracting infections. This study was designed to detect the views of the parents about the role of toys in spreading childhood infections.

Methods: The interviews were performed with 11 mothers having children aged between 0 to 6 years at Yozgat State Hospital Social Pediatrics Policlinic between 10 to 14 November 2014. Informed consent of each subject and approval of local ethical committee were obtained accordingly.The mothers' verbal consents were obtained .The data were analyzed by using content analyses method.

Results: This study, general views of 7 mothers, showed that continuous hands in contact with toys, frequent fall of toys and hosting of several microorganism on toys may play role in the development and spreading of childhood infections. Four mothers said that they paid extra attention to the suitability of toys for relevant age group, five mothers considered educational, qualitative, washable, safety, and anti-allergic aspects of toys while buying them. Seven mothers said that they washed all toys once a week to reduce infection risk. Three mothers said that they washed toys in washing machine, and cleaned the hard plastic toys by boiling or brushing with water with soap.

Conclusions: We detected that mothers need more knowledge related to the usage, hygiene and selection of toys.

ESPID-0684
EPIDEMIOLOGY AND PUBLIC HEALTH

YOGA IN THE POSTNATAL PERIOD IMPROVES SUCCESS RATE OF BREASTFEEDING IN PREMATURE BABIES

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Exclusive breastfeeding in the first six months of life followed by continued breastfeeding till 2 years of age has been recommended by the WHO as beneficial to babies. Breastfeeding promotes immunity and lowers the risk of severe infections. However, the incidence of successful exclusive breastfeeding is declining due to various reasons including early discharge, maternal stress and lifestyle diseases. Forty seven mothers of babies less than 2 months of age born prematurely (late preterms, 34 to 36 weeks gestation) , who were using formula in addition to breastfeeds were counseled extensively about lactation for a week by experts, but they continued to feed formula to their infants. Yoga was recommended to all mothers for decreasing stress and to keep fit. Of these, twenty one mothers agreed and joined yoga sessions. They did yoga (breathing exercises, asanas and sun salutations) for 1 hour a day, 3 days a week, for 1 month. At the end of one month, 18 out of 21 mothers who attended yoga (86%) were exclusively breastfeeding. Only 2 out of 26 mothers (8%) who did not join yoga were exclusively breastfeeding at this time.

Mothers who did yoga reported greater confidence and less stress, therefore leading to better latching-on during lactation. In addition to lactation counseling, use of yoga for stress reduction in lactating mothers may be an adjunctive method to establish breastfeeding, and improve immunity in infancy. This may be even more important in mothers of premature infants who experience greater stress and issues with bonding.

ESPID-1025
EPIDEMIOLOGY AND PUBLIC HEALTH

THE CONCENTRATION OF SERUM VITAMIN D3 IN CHILDREN HOSPITALIZED FOR VARIOUS REASONS IN THE PEDIATRIC WARD IN POLAND.

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Background

Despite numerous preventive strategies in recent years, vitamin D deficiency in infants still appears to be a global health problem. However data from some countries (including Polish) are still insufficient.

Aim of the study

To determine the vitamin D3 status of in children admitted to the pediatric ward, regardless of the cause of hospitalization.

Material and methods

The study involved 1143 children aged 1 month to 18 years admitted to the Clinical Department of Paediatric in Bielanski Hospital, in the period from 01-10-2013 to 30-09-2014, including 570 girls and 573 boys. Measuring the concentration of 25(OH)D levels in serum were performed by using the system Liaison XL.

Results

Mean concentration of 25(OH)D in the whole group was 26.26 ng/ml. Status of 25(OH)D in thewhole group is given in Table 1,and the concentrations of different age groups are listed in Table 2.

Table 1 - Status of 25(OH)D in the whole group [ng/ml]

25(OH)D	<10	10-20	20-30	30-50	>50		TOTAL
NUMBER OF PATIENTS	53	293	406	368	23		**1143**
PERCENTAGE	4,64%	25,63%	35,52%	32,20%	2,01%		100%

Table 2 - Status of 25(OH)D in different age groups [ng/ml]					
	<10	10-20	20-30	30-50	>50
>10 years	**12,55%**	46,15%	33,60%	**7,69%**	0,00%
5-10 years	7,04%	43,66%	35,21%	12,68%	1,41%
3-5 years	3,26%	36,41%	42,39%	17,93%	0,00%
3 years	1,85%	24,07%	39,81%	32,41%	1,85%
2 years	**0,53%**	6,38%	39,89%	50,53%	2,66%
1 year	1,09%	4,38%	28,10%	**61,31%**	5,11%

Conclusions

The study, involving a large number of the population of Polish children, showed that the optimal (30-50 ng/ml) concentration was found in 32,2% infants. However,if we exclude from the analysis the youngest children (1-3 years), the optimal concentration was observed only in 12.22% of children, which is consistent with previous reports. It seems particularly important to increase the pressure on the promotion of vitamin D3 supplementation in a group of older children.

ESPID-1006
EPIDEMIOLOGY AND PUBLIC HEALTH

NEONATAL SEPSIS AND EPIDEMIOLOGICAL TRENDS AMONG NEWBORNS IN A COUNTRY REFERRAL HOSPITAL IN NORTHERN KENYA

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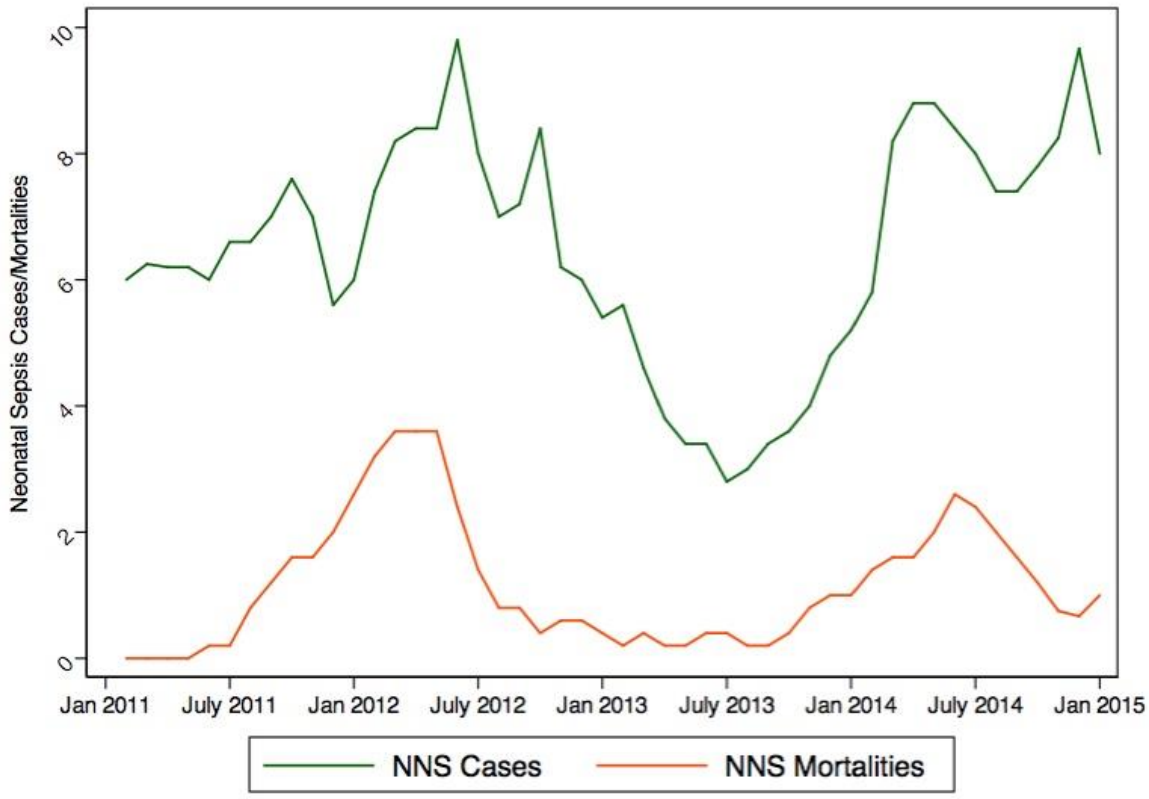
Infection remains the leading cause of neonatal mortality in developing countries. In Kenya, about 20% of neonatal deaths are attributable to sepsis. We aim to look at the epidemiological pattern of neonatal sepsis in a county referral hospital in Kenya. Retrospective data was collected for all admissions to the Newborn unit between 2011 to 2014 at Nanyuki Teaching and Referral Hospital. We calculated monthly rates of neonatal sepsis cases, mortalities, and case fatality rates for all admissions. We then plotted a monthly time series of sepsis cases and mortalities to determine if there was a seasonal trend over the four-year period. The epidemic time series was plotted and smoothed using a seasonal moving average estimator in Stata 12.1.There were 1262 admissions to the Newborn Unit during the 4 year period. 23.9% of admissions had a diagnosis of neonatal sepsis. The overall mortality rate of admissions was 24.7%, whereas mortality attributed to sepsis was 18.2%. We observed a biannual peak in sepsis cases, with peaks in July 2012 and July 2014. Case fatality rates were highest in March 2012 (66.6%), July 2012 (50%), July 2014 (50%) and August 2014 (50%).



The overall rate of neonatal mortality due to sepsis in this hospital is comparable to the national average. Our study indicates that sepsis cases correspond to a strong bi-annual pattern rather than a yearly one, with intermediate years yielding few sepsis cases. From this, we predict low sepsis rates in 2015, with a peak of cases in July 2016.

ESPID-0604
EPIDEMIOLOGY AND PUBLIC HEALTH

ESTIMATING THE SEROINCIDENCE OF PERTUSSIS IN JAPAN

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Despite relatively high vaccination coverage of pertussis for decades, the disease keeps circulating among both vaccinated and unvaccinated individuals and a periodic large epidemic is observed every 4 years. To understand the transmission dynamics, specific immunoglobulin G (IgG) antibodies against pertussis toxin (PT) have been routinely measured in Japan. Using the cross-sectional serological survey data with a known decay rate of antibody titers as a function of time since infection, we estimate the age-dependent seroincidence of pertussis The estimated incidence of pertussis declined with age, the shape of which will be extremely useful for reconstructing the transmission dynamics and considering effective countermeasures.

ESPID-1068
EPIDEMIOLOGY AND PUBLIC HEALTH

METHICILIN RESISTANT STAPHYLOCOCCUS BACTEREMIA AND SEPSIS IN CHILDREN AT THE UNIVERSITY HOSPITAL CENTER IN TIRANA, ALBANIA.

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Background Methicillin resistant staphylococcal bacteremia and sepsis are a major pediatric health care problem despite the availability of new antibiotics. In our country the incidence of methicillin-resistant staphylococcus bacteremia and sepsis was increased in the last years. Some of the reasons are broadly using of intravenous catheter for the treatment, using of invasive diagnostic procedures and the low social-economic conditions.

The aim of the study was to determine the incidence and pattern of methicillin resistant staphylococcal bacteremia and sepsis in pediatric group at tertiary hospital in Tirana, Albania.

Methods: This was a retrospective study performed in Pediatric Infectious Diseases Services**,** University Hospital Center Tirana in the period of January 2010 to January 2012. Positive culture was found in 246 patients aged below 14 years with a total of 6582 admissions in the period.

Results: The highest incidence of bacteremia and sepsis was found in patients under one years old 142 cases (57, 9%), majority of patients were male 150 cases(61%).Staphylococcus aureus was the most common isolated pathogen 92 cases (37,2%) among other staphylococcus group. Prematurity and malnutrition were associated in the majority of case in (18, 5%), respiratory tract infections were found in (13, 7%) as the most common primary focus

Conclusions: Staphylococcus aureus is the most common isolated pathogen, the most common primary focus are respiratory tract infections and the most common risk factors were prematurity and malnutrition

ESPID-0307
EPIDEMIOLOGY AND PUBLIC HEALTH

MARSHALL SYNDROME. CASE SERIES

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Background and aims. PFAPA is a chronic auto-inflammatory condition including recurrent fever episodes, aphthous stomatitis, pharyngitis, adenitis. A**uthors emphasize PFAPA patients peculiarities. Methods. Authors analyzed PFAPA children regarding diagnosis and evolution: symptoms onset age, duration between episodes and between disease onset and its confirmation.** Authors also compared 2 groups („PFAPA group" versus "non-PFAPA group") to identify a sensitive biological marker for disease. Both groups were tested for procalcitonin, CRP, TNF-alpha (serum values). Inclusion criteria: patients up to 10 years of age, patients between febrile attacks, patients with negative procalcitonin value. Exclusion criteria: patients during febrile attacks. Results. **34 patients were included in study.** Mean age disease debut was 42.23 months. Duration from symptoms onset to diagnosis confirmation was 46.29 months, suggesting PFAPA is under-diagnosed. Authors noticed decreasing of period regarding last 12 included children (34.91 months) as compare with first 22 studied cases (52.5 months) due to improvement of PFAPA awareness among general practitioners (GP). Average period between fever attacks was 7.1 weeks. Authors analyzed 2 groups: „PFAPA group" represented by 6 patients and „control group" (4 non-PFAPA patients). Both group patients have high values for TNF-alpha, without statistical significance. Mean CRP value for PFAPA patients was 19,72 as compare to 5.04 in non-PFAPA patients. Conclusions. 1.Authors remarked a low suspicion index for PFAPA diagnosis; 2.PFAPA awareness improvement is mandatory in order to avoid antibiotics; 3.TNF isn't useful to appreciate PFAPA evolution; 4.CRP remains a sensitive marker for disease activity in PFAPA patients, even out of fever attacks.

ESPID-0857
EPIDEMIOLOGY AND PUBLIC HEALTH

CLINICAL, SEROLOGICAL AND EPIDEMIOLOGICAL FEATURES OF ENDEMIC HEPATITIS A IN LEON, NICARAGUA: 315 CASES REPORTED MAY 2006 TO JUNE 2010

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Background and Objectives**:** To document endemicity and disease burden of hepatitis A in the study area of an observational vaccine trial in León, Nicaragua, a viral hepatitis screening project was initiated.

Methods: All children, adolescents and young adults in the city of León (≈250,000 inhabitants) presenting with jaundice and/or other clinical signs of hepatitis were offered at the community health centers free serologic screening (hepatitis A, B and C) and blood tests for liver enzymes and bilirubin. Clinical and socioeconomic data were collected in a questionnaire. The serodiagnosis of acute hepatitis A was confirmed by anti-HAV IgM testing.

Results: Of 558 subjects enrolled between May 2006 and June 2010, 315 (56.5%) were diagnosed with hepatitis A, 86% of them ≤ 10 years and none >20 years of age. No severe cases were seen, none of the patients had to be hospitalised. Apart from the usual symptoms and signs of hepatitis A (fever, jaundice, pale stool, dark urine, nausea, vomiting, anorexia) moderately raised liver enzymes and bilirubin was seen in 2/3 of patients. Diagnosis was in 89% of cases done within 11 days after start of symptoms. Transmission occurred throughout the year, with highest incidences from October to March. Socioeconomic factors, such as poor sanitary conditions and crowding, were the main risk factors.

Conclusions: Hepatitis A is still highly endemic in the study area, with the majority of infections occurring in young and school age children and a low socioeconomic level being a risk factor. No severe pathology was seen.

ESPID-0823
EPIDEMIOLOGY AND PUBLIC HEALTH

SEROEPIDEMIOLOGICAL STUDY OF B. PERTUSSIS IN CHILDREN IN CZECH REPUBLIC

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Introduction and methods: Pertussis incidence is increasing in children population since 1993 in Czech Republic. This trend continues despite high vaccination coverage (97-100%).

This study was designed as a part National Serological Study of the representative population sample of children from 1 to 18 years. In 1769 children IgG against B. pertussis toxin was estimated by a commercial enzyme-linked immunosorbent assay (Sekisui Virotech). Titer ≥5 IU/ml was applied to indicate seropositivity in vaccinated population. However, there are no reliable measurements of protective immunity against pertussis. Pertussis vaccination status all of examinated children was analysed concurrently.

Objectives: To specify the proportion of sufficient antibody response in vaccinated population; to evaluate the persistence of antibodies; to compare seropositivity with specific morbidity rate in age groups.

Results: Total 84,2% of children showed serological response after vaccination. Despite of only 84.2% of 1-year old children received complete vaccination, all of them (100%) reached seroconversion. Serological analysis in age groups confirmed that antibody levels decrease with time since last pertussis vaccination. The highest morbidity was reported in 10-14 age group long-term. After introduction of vaccination in age 10-year (2009) the highest incidence shifted to 15-19 age. However, seropositivity is also affected by morbidity in this age.

Conclusion: Serological response after acellular pertussis vaccination shows high seroconversion but rapid decline of antibody levels. Seroconversion cannot be seen as a indicator of protection against infection but as immune response evidence to vaccination. It can be assumed that the incidence of pertussis will continue.

ESPID-0866
EPIDEMIOLOGY AND PUBLIC HEALTH

THE PREPARE PROJECT: DETERMINING THE PREVALENCE OF INFECTIOUS SYNDROMES WITH EPI/PANDEMIC POTENTIAL IN A EUROPEAN NETWORK OF PEDIATRIC TERTIARY CENTRES.

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BACKGROUND AND AIMS

Pandemic preparedness of pediatric tertiary centres currently is fragmented across Europe. This study aimed to assess the characteristics and potential of the pediatric nodes of the PREPARE (http://www.prepare-europe.eu) (Platform for European Preparedness Against (Re-)emerging Epidemics) network.

METHODS

The pediatric PREPARE network presently includes 21 hospitals from 13 countries. They were asked in summer 2014 to review retrospective one-year admission and emergency department (ED) consultation counts and to conduct a prospective short epidemiologic survey (SES) on patients presenting with specified infectious syndromes (fever, sepsis, rash, respiratory, gastrointestinal or neurological symptoms) during a defined timeframe (72-hours for ED and 2-weeks for acute admissions).

RESULTS

Eighteen of 21 centres completed the survey. Results for each survey are shown in **Table 1** and **2.** The relative predominance of gastrointestinal infections may be related to seasonality. Overall, a mean of 440 patients with clinical syndromes of potential epi/pandemic relevance are seen every day in ED and 2400 are admitted every month in the network.

CONCLUSIONS

A SES can be considered an inexpensive and feasible method to assess broad patterns of infectious syndromes with epi/pandemic potential in our network because of the high amount of children seen presenting with these syndromes. Pediatric syndromic surveillance based on pediatric centres should be a crucial component of pandemic preparedness.
Table 1:

RETROSPECTIVE COUNTS			
	Average n beds/centre (range)	Total acute admissions/year	Average annual bed rotation index
Acute admissions	145 (30-437)	126,129 (902-23,113)	48.3 (7.5-164.8)
PICU admissions	16 (7-40)	12,170 (205-1,717)	44.4 patients/bed (11.1-102.3)
Emergency consultations	n/a	576,469 (0-83,374)	n/a

Table 2:

PROSPECTIVE SURVEY		
	2-WEEK ADMISSIONS SURVEILLANCE	72-HOURS ED SURVEILLANCE
TOTAL PATIENTS	3,816	4,048
PATIENTS WITH SYMPTOMS OF AN INFECTIOUS DISEASE	1,192 (31%)	1,567 (28%)
SEPSIS	69 (5.8%)	27 (1.7%)
RESPIRATORY	319 (26.8%)	379 (24.2%)
GASTROINTESTINAL	433 (36.2%)	425 (27.1%)
RASH	110 (9.2%)	280 (17.9%)
FEVER	201 (16.9%)	425 (27.1%)
NEUROLOGICAL	60 (5%)	31 (1.9%)

ESPID-0767
EPIDEMIOLOGY AND PUBLIC HEALTH

MOLECULAR EPIDEMIOLOGY OF NOROVIRUS IN ACUTE GASTROENTERITIS CHILDREN IN MANADO, INDONESIA

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Background and aims

Noroviruses have been known as one of the leading cause of viral gastroenteritis for children under five years old. In Indonesia, most of the studies conducted previously were focusing at rotavirus. Epidemiological data regarding noroviruses has been scare. The aim of this study is to investigate norovirus incidence and genotype variations in Indonesia.

Methods

Four hundred forty one fecal specimens were collected from hospitalized children age one month up to 13 years old, with diagnosis acute gastroenteritis. Sample collection was conducted in Manado, North Sulawesi, from April 2013 to July 2014. Noroviruses were identified by multiplex RT-PCR and semi-nested PCR. Sequence analysis was performed for further genotyping.

Results

Norovirus GI was detected in 1.1% and norovirus GII was detected in 16.6% of the specimens. Sequence analysis were conducted to five positive samples of norovirus GI, and fifty two positive samples of norovirus GII. For genogroup I, three genotypes were found, norovirus GI.6 (n=3), norovirus GI.1 (n=1), and norovirus GI.3 (n=1). For genogroup II, norovirus GII.4 Sydney 2012 strain was the predominant genotype (n=34). Other genotypes found in this study were norovirus GII.17 (n=5), norovirus GII.14 (n=2), norovirus GII.3 and GII.1 (n=1). This study is the first to report noroviruses genotyping from human samples in Indonesia

Conclusions

Results from this study indicated that norovirus GII is also one of the leading cause of gastroenteritis in paediatric patients, and contribute to the burden of diarrheal disease in Indonesia.

ESPID-0891
EPIDEMIOLOGY AND PUBLIC HEALTH

RISK FACTORS RELATED TO HOSPITALIZATION IN CHILDREN WITH ACUTE GASTROENTERITIS

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Present retrospective study was performed to review factors influencing hospitalization of children with acute gastroenteritis (AGE). We review 1057 records of children (> 1 month) admitted to ER with AGE in 2014. Age distribution - 54% under one, 34% 1-5 years old, 12% above 5. 56% of patients were males. 27% children were hospitalized, 73% of them were under one year. 73% of patients were from Tbilisi, the rest from different regions of Georgia. 51 % of patients from regions were hospitalized, versus 23% of children from Tbilisi. Patients discharged from ER had no (13%) or moderate (87%) dehydration on admission. Hospitalized patients had either moderate (47%) or severe (53%) dehydration on admission. Rehydration in severe dehydration was started with IV infusion, only 2% of patients receive enteral rehydration with nasogastric tube (insertion of IV catheter failed), while in moderate dehydration 31% receive ORS and 69% - IV infusion (inability to drink adequate amount of ORS or vomiting). In 29% of patients AGE was caused by bacterial infection. The reasons for hospitalization was severe bacterial infection (19%), severe dehydration regardless of treatment (20%), inability to drink water/vomiting during mild/moderate dehydration (26%), place of residence Hospitalization (17%), lack of mother's ability to take care of childe and very low socioeconomic status of family (18%).

So, we conclude that hospitalization during AGE is related to patients age, hydration status, ability of patient to tolerate oral rehydration, family social status, place of residence and presence of bacterial infection.

ESPID-1007
EPIDEMIOLOGY AND PUBLIC HEALTH

THE NEW MENINGITIS B VACCINE: IMMUNIZATION - PARENTAL INFORMATION

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Background and aims

To investigate the immunization coverage with type B meningitis vaccine in children in Greece, given that the MenB vaccine is not yet included in the National Vaccination Program. In Greece, type B Neisseria is responsible for 61% of meningitidococcal meningitis.[1]

Methods

Immunization data were collected through pediatric vaccination cards, in children who were admitted in the Pediatric Emergency Department, in 2 University Hospitals in Greece. The sampling took place throughout the first week of January (5-8/1) 2015. We included in the sample one child for every four, of those admitted in the department, and whose parents agreed to undertake the questionnaire. Children with known allergies in vaccination and children with chronic diseases were excluded.

Results

There were 64 children included in the study. The mean age was 7.6 ± 0.5 and 73% were boys. 94% of children had been vaccinated with MenC and of those over 11 years, 30% were vaccinated with fourfold Neisseria vaccine (A,C,Y,W135). Although in 16% of children the MenB vaccine has been planned, only 2% have been vaccinated.

Conclusion

The coverage with type B meningitis vaccine was about 2%. Only very few parents were informed about this new vaccine (16%). The reasons of both inadequate pediatric information and low vaccination coverage should be explored. There is a need for a national strategy plan in order to increase the vaccination coverage with type MenB.

[1]Source :ΚΕΕΛΠΝΟ, Data 1998-2011

ESPID-1059
EPIDEMIOLOGY AND PUBLIC HEALTH

ROTAVIRUS GASTROENTERITIS IN A NEONATAL UNIT OF A GREEK TERTIARY HOSPITAL: CLINICAL CHARACTERISTICS AND GENOTYPES

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Introduction: Rotavirus (RV) infection in neonatal age can be mild or even asymptomatic. Several studies have reported that RV is responsible for 31-87% of pediatric nosocomial diarrhea and causes gastroenteritis outbreaks in pediatric and neonatal units.

Objectives: Study clinical characteristics, genotypes and risk factors of RV infection in neonatal age.

Methods: A prospective study was conducted from April 2009 till April 2014 in the neonatal special care unit of the largest tertiary pediatric hospital of Greece. Fecal samples and epidemiological data were collected from each neonate with gastrointestinal symptoms. RV antigen was detected with a rapid immunochromatography test. RV positive samples were further genotyped with RT-PCR and sequencing using specific VP7 and VP4 primers.

Results: Positive for RV were 130 samples and 47% were hospital acquired. Mean age of onset was 17 days. Seasonality of RV infection did not differ significantly throughout the year with the exception of 5 sporadic outbreaks. Genotypes found during the study period were G4P[8] (46,5%), G1P[8] (14,5%), G2P[4] (9,5%), G3P[8] (8,5%), G12P[8] (6%), G12P[6] (5%), G9P[8] (1,5%) and mixed or uncommon strains (8,5%). RV cases presented with: diarrhea (57%), feeding intolerance (42%), fever (37%) and vomiting (25%) whilst 1/3 of cases were asymptomatic. Comparing community with hospital acquired cases no significant differences were found.

Conclusions: Significant incidence of nosocomially transmitted RV infection in neonatal age including asymptomatic illness exists. Genotypes causing nosocomial outbreaks are not different from community strains. Circulating vaccines can be effective in preventing nosocomial RV infection through herd immunity.

ESPID-1008
EPIDEMIOLOGY AND PUBLIC HEALTH

SUSCEPTIBILITY TO MEASLES, MUMPS, RUBELLA AND VARICELLA IN YOUNG ADULTS

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Background and aims:

Childhood vaccination rate is known to be satisfactory high in Saxony. Possible gaps in immunity of young parents may nevertheless pose a risk to unborn children or children of very young age. We therefore aimed to investigate humoral immunity and vaccination status in young adults.

Methods:

368 samples, from individuals aged 19 to 29 years, were consecutively collected between January 2013 and April 2014. Measles, mumps, rubella and varicella IgG was assessed by Elisa and neutralization assay.

Results:

Only 54% of individuals had detectable immunity to all four viruses. Lack of immunity for the individual viruses ranged from 3% to 25%. Overall immunity was highest for varicella but mainly due to wild virus infection. Catch-up vaccination, recommended for young adults with only one documented measles or rubella vaccination, was absent in 14%.

Conclusions:

The findings indicate a gap in collective immunity against the vaccine preventable diseases measles, mumps and rubella in the young adult age-group. Information programs are warranted to close these gaps.

ESPID-0941
EPIDEMIOLOGY AND PUBLIC HEALTH

THE EFFECTIVENESS OF AN EDUCATIONAL LECTURE ON YOUNG WOMEN'S ATTITUDE TO VACCINATIONS IN POLAND

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Many vaccines (e.g. acellular pertussis, conjugated pneumococcal and rotaviral vaccines) are not reimbursed and administered on parents' demand in Poland. At the same time anti-vaccinist's movement rises unreasonable concerns regarding vaccines safety and efficacy, therefore education of the parents is necessary.

The aim of our study was to assess how effectively the participation in a lecture about vaccinations changes the attitude to immunization of Polish women.

METHODS: 484 women (age: 29±3 years; 68% pregnant; 44% mothers of infants) attending the educational lecture were examined before and after the lecture with dedicated questionnaire using visual analogue scales (VAS 150 mm) assessing their subjective perception of their knowledge about immunizations, the safety, efficacy and the need of vaccinations. The lectures were given by different physicians experienced in field of immunizations in 11 largest Polish cities. Women also assessed how they liked the lectures.

RESULTS: Respondents assessed their knowledge of vaccinations significantly higher (101±23 vs. 69±31 mm) and perceived vaccinations as more needed (116±26 vs. 107±32 mm) and safer (104±26 vs. 87±30 mm) after vs before the lecture. Women who did not like the lectures and evaluated them below the median (122 mm) had similar results. The results depended upon the lecturer and the city.

CONCLUSION: Educational lectures may positively change the attitude to vaccinations of Polish women in child-bearing age and result in increased rate of voluntary immunized children in Poland. This educational intervention may be effective even in women with negative attitude to vaccines.

ESPID-0413
EPIDEMIOLOGY AND PUBLIC HEALTH

EPIDEMIOLOGICAL CHARACTERISTICS IN RECENT THREE MYCOPLASMA PNEUMONIAE PNEUMONIA EPIDEMICS IN A SINGLE HOSPITAL IN KOREA

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Background and aims: *Mycoplasma pneumoniae* pneumonia (MPP) epidemics occur in cycles of 3-4 years in Korea. Here, we evaluated the epidemiological characteristics of MPP in Daejeon, Korea, from 2003 to 2012.

Methods: We retrospectively examined the medical records of 779 children (age, 0-15 years) with MPP and performed a comparative study across 3 recent epidemics.

Results: The mean age and male-to-female ratio were 5.0 ± 2.2 years and 1:1, respectively; most cases were observed in autumn. There were 3 epidemics during the study period (2003, 2006-2007, and 2011). We found no differences in mean age, male-to-female ratio, hospitalization duration or rate of seroconverters during hospitalization among 3 epidemics. All 3 epidemics began in early summer and peaked in September 2003 and 2011, and in October 2006. The peak pattern of epidemics gradually decreased until the following year's spring season, although the 2006 epidemic extended into 2007. The peak age of the children in 2003 and 2006 were 3-6 years (57.5% and 56%, respectively), but that in the 2011 epidemic, was 1-4 years (46.5%). The proportions of children aged $\leq$ 2 years were 20%, 15.7% and 28.8%, whereas the proportions of children aged $\geq$ 10 years were 5.2%, 13.8% and 14.8% of total patients in the 2003, 2006 and 2011epidemics, respectively.

Conclusions: MPP epidemics occurred every 3-4 years. The pattern of the 3 recent epidemics was similar with regard to demographic characteristics and seasonality, with certain variations such as duration of the epidemic and age distribution in each epidemic.

ESPID-0402
EPIDEMIOLOGY AND PUBLIC HEALTH

COMMUNITY ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCAL SCALDED SKIN SYNDROME: CLINICAL FEATURES, TREATMENT AND OUTCOME

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Purpose : Staphylococcal scalded skin syndrome (4S) is a well known disease defined by clinical, microbiological and histological criteria caused by Staphylococcus aureus. We investigated the clinical features of staphylococcal scalded skin syndrome.

Methods : We reviewed retrospectively medical records of 111 patients diagnosis of staphylococcal scalded skin syndrome who were admitted to Changwon Fatima hospital, Korea from February 2002 to August 2014. These patients were divided into 3 clinical types; generalized type, intermediate type, abortive type. Age, sex ratio, clinical manifestations, laboratory findings, response to therapy and prognosis were investigated.

Result : 1)The mean age of patients was 2.53years, ranging from 20 days to 7 years. Male-to-female ratio was 1.58:1. 2) By clinical types, 9 patients were in the generalized type (8%), 73 patients in the intermediate type (65.8%), 29 patients in the abortive type (26.2%). The coexisting diseases were variable, including conjunctivitis (36 cases), atopic dermatitis (12 cases), otitis media (1 case). On laboratory findings, most of patients didn't have leukocytosis or increased C-reactive protein. 4) A total of fifty one Methicillin Resistant Staphylococcal Aureus (MRSA) strains were isolated from September 2003 through August 2014. Fourteen strains were positive for exfoliative toxin B gene by PCR and negative for enterotoxin, toxic shock syndrome toxin and Panton-Valentine leukocidin genes. 5) The mean duration of admission was 6.4 days. Patients were treated with vancomycin or amoxacillin/clavulanate or ampicillin/sulbactam or cefuroxime without significant sequelaes.

Conclusion : Recently, Staphylococcal scalded skin syndrome caused by exfoliative toxin B produced by CA-MRSA in Changwon in Korea has been increasing.

ESPID-0774
EPIDEMIOLOGY AND PUBLIC HEALTH

DECREASE OF STREPTOCOCCUS PNEUMONIAE (SPN)-ASSOCIATED PAEDIATRIC PARAPNEUMONIC EMPYEMA (PPE/PE) AND INCREASE OF STREPTOCOCCUS PYOGENES (SPY)-ASSOCIATED PPE/PE IN GERMANY, 2010-2014

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Introduction

An increase in the incidence of PPE/PE has been observed in several countries. We investigated the incidence and pathogens of paediatric PPE/PE in Germany.

Methods

Between October 2010 and June 2014 nationwide hospital-based PPE/PE surveillance has been conducted using the German Surveillance System for Rare Paediatric Diseases (ESPED). Children ≥7 days or necessitating pleural drainage were included. Bacterial pathogen detection from pleural fluid by eubacterial 16S-rDNA PCR and pneumococcal serotyping was offered.

Results

821 children with PPE/PE (median age: 5 years; IQR 3-9) were included. Culture or PCR from blood or pleural fluid resulted in the identification of bacterial pathogens in 256 (31%) children with PPE/PE: *SPN* in 130 (51% of 256) and SPY in 42 (16%). SPN were serotyped in 45 cases: serotype 1 45%; serotype 3 24%; serotype 7F 13%; other serotypes 20%. From 2010 to 2014 the proportion of SPN-associated PPE/PE decreased from 60% to 34% whereas SPY-associated PPE/PE increased from 10% to 21%, and PPE/PE associated with other pathogens (OP) increased from 24% to 45%. The overall PPE/PE-incidence decreased from 15.8 in 2010 to 13.2 cases/10^6 children in 2014. Incidence of SPN-PPE/PE decreased from 3 to 1.3 cases/10^6 children, whereas SPY- and OP-PPE/PE-incidences increased from 0.4 to 0.8 cases and from 1.1 to 1.7 cases/10^6 children respectively.

Conclusion

Although a decrease in paediatric PPE/PE was observed, further surveillance is necessary to detect increase of PPE/PE due to new SPN-serotypes or other pathogens.

ESPID-0947
EPIDEMIOLOGY AND PUBLIC HEALTH

NATIONAL VACCINATION COVERAGE STUDY OF CHILDREN 2-3 YEARS OLD ATTENDING NURSERIES-KINDERGARTENS IN GREECE

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Background:

In countries lacking vaccination registries, studies assessing vaccination coverage are important. The study aimed to estimate complete and timely vaccination coverage of preschool children aged 2-3 years old.

Methods:

Geographically stratified cluster sampling was implemented. Prefectures were considered as strata, based on NUTS-3 classification. Nurseries-kindergartens were the primary sampling units consisting "clusters" of children (final sampling units). They were selected by simple random sampling from the complete national list for 2012-2013 school year in each prefecture (sampling frame).

Results:

Vaccination coverage with "classic" vaccines (DTaP, IPV, MMR), was very high. Overall, 99.5% and 95.8% of children were vaccinated with 3 and 4 doses of DTaP respectively. IPV coverage, with 2 doses until 12 months and 3 doses until 24 months was 99.1% and 99.0% respectively. Vaccination with the first dose of MMR reached 97.3%. Although coverage with 3 doses of HepB vaccine was high (96.2%), delayed schedule initiation and completion in the first year remained. Hib vaccination surpassed 99% for the first 3 doses. Despite high coverage with PCV (first 3 doses exceeded 95%) only 62.3% have concluded 4 doses until the second year. Totally, 89.6% have received one dose of MenC over the age of 12 months while 92.0% were vaccinated with one dose for varicella.

Conclusions:

Vaccination coverage with recommended vaccines is maintained at high levels in children aged 2-3 years in Greece. However, due to economic crisis intense efforts must be taken in order to sustain these satisfactory results.

ESPID-0957
EPIDEMIOLOGY AND PUBLIC HEALTH

NATIONAL VACCINATION COVERAGE STUDY OF CHILDREN 2-3 YEARS OLD ATTENDING NURSERIES-KINDERGARTENS IN GREECE: ARE THERE VACCINES OF LOWER PRIORITY?

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Background:

In countries lacking vaccination registries, studies are a means to assess vaccination coverage. The study aimed to estimate complete and timely vaccination coverage of preschool children aged 2-3 years old.

Methods:

Geographically stratified cluster sampling was implemented. Prefectures were considered as strata, based on NUTS-3 (Nomenclature of territorial Units for Statistics) classification. Nurseries-kindergartens were the primary sampling units consisting "clusters" of children (final sampling units). They were selected by simple random sampling from the complete national list (public and private) for 2012-2013 school year in each prefecture (sampling frame).

Results:

Overall, the level for basic vaccination of children aged 2-3 years old in Greece was very high. Vaccination coverage with DTaP, serving as a marker, was 99.5% (95%CI: 99.1-99.7) and 95.8% (95%CI: 94.8-96.6) with 3 and 4 doses respectively. Vaccination coverage for hepatitis A was found significantly lower compared to other vaccines of the NIP: 79.5% (95%CI: 77.4-81.5) with one dose and 41.7% (95%CI: 39.3-44.1) with 2 doses. Vaccination coverage with one dose of flu vaccine was very low (23.1%, 95%CI: 21.0-25.3). Immunization against Rotavirus was similarly low as only 19.5% (95%CI: 17.7-21.4) of the study population were covered with 2 doses of monovalent or 3 doses of pentavalent vaccine.

Conclusions:

Vaccination coverage with most of the vaccines included in the Greek NIP is high while vaccines for hepatitis A, flu and Rotavirus seem to be considered of lower

priority leading to suboptimal coverage levels. These facts are important for decisions considering vaccine implementation.

ESPID-0049
EPIDEMIOLOGY AND PUBLIC HEALTH

4-YEAR TREND OF STAPHYLOCOCCUS AUREUS INFECTIONS IN A JAPANESE PEDIATRIC HOSPITAL

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Background and Aims

Staphylococcus aureus can cause severe infections in children. We conducted this study to elucidate the trends of Staphylococcus aureus infections in tertiary pediatric hospital in Japan.

Methods

We collected the culture data and medical charts of inpatients of Nagano Children's Hospital from October 2010 to September 2014. And we reviewed all the cases of Staphylococcus aureus infections.

Results

During study period, there had been 90 infections due to Methicillin-sensitive Staphylococcus aureus (MSSA) and 39 infections due to Methicillin-resistant Staphylococcus aureus (MRSA).

83% of MSSA infections and 92% of MRSA infections were health care-associated (HA), namely post-operative surgical site infection, central line-associated blood stream infection, ventilator-associated pneumonia. About MSSA, there was apparent increase of community-acquired (CA) infections in 2014. For MRSA, only 3 were CA, namely external ear infection, osteomyelitis and bacterial tracheitis. There found no increase of total number of S. aureus infections per year.

Conclusions

Admissions due to CA MSSA infection had increased significantly during the study period. The introduction of Hib vaccine and pneumococcal conjugate vaccine for Japanese children might have affected this epidemiological trend.

ESPID-0086
EPIDEMIOLOGY AND PUBLIC HEALTH

FEASIBILITY OF IPV CAMPAIGNS IN NIGERIA TO ENABLE GLOBAL POLIO ERADICATION

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BACKGROUND

Poliomyelitis is an acute inflammation of the spinal cord resulting mostly in acute flaccid paralysis .The GPEI has prevented about 9 million cases of polio and about 1.5 million deaths since 1988. Its current end game strategic plan has objectives of strengthening immunisation systems and withdrawing OPV. To enable this, IPV is to be introduced in all countries routinely and in some campaigns. This research was done to ascertain the feasibility of using IPV in campaigns in Nigeria

METHODS

A cross sectional survey was carried out using a structured questionnaire to assess the knowledge and perceptions of vaccination programme managers in Sokoto State of Nigeria regarding potential challenges of using IPV in campaigns and ways of nullifying those threats. Analysis was descriptive, and was done using Microsoft Excel.

FINDINGS

All respondents had knowledge of the PEI. While 83% recognized the absence of IPV in Nigeria's routine immunisation programme due to local unavailability; they accepted a need for mass IPV campaigns. In past vaccination, the challenges recognized are same as for an IPV campaign and included financial and logistic challenges, cold chain constraints and mobilization of the population to be vaccinated. They felt that those factors among others would be key to a successful IPV campaign.

CONCLUSION

IPV campaigns are feasible in Nigeria, but a lot is needed for success in terms of strong governance mechanisms, efficient coordination, and collaboration with partners, scale up of vaccination infrastructure, a clear accountability framework and effective population mobilisation.

ESPID-0731
EPIDEMIOLOGY AND PUBLIC HEALTH

IMPACT ON EVERYDAY LIFE AND FINANCES OF AFFECTED FAMILIES OF CHILDREN WITH ROTAVIRAL INFECTION HOSPITALIZED IN UNIVERSITY CHILDREN'S HOSPITAL IN LATVIA

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Background. Rotavirus is the leading cause of acute gastroenteritis in childrenworldwide. The incidence of rotaviralgastroenteritis has significantly increased in last 10 years in Latvia.

Aims. To assessthe impact on everyday life activities and finance of parents and other familymembers of children with rotaviral gastroenteritis hospitalized in UniversityChildren's Hospital.

Methods. Dataassociated with the burden of rotaviral gastroenteritis were extracted from questionnairescompleted by parents (n=165) of children aged 1-133 months hospitalized in University Children'sHospital within the time period of June 2013 – February 2014. Parents wereasked to evaluate the impact of child being sick with acute gastroenteritis ontheirs and other family member's everyday life and finance.

Results. Results showed that 81,2%(n=134) parents wereforced to change their everyday plans and activities: more frequently changesinvolved work plans 43%(n=71), free timeactivities 46,7%(n=77), house work 50,9%(n=84) and study plans 12,1%(n=20). Inmore than half of the cases 55,7%(n=92) a parent or other family member wasabsent from work because of the child's rotaviral gastroenteritis; 27,9%(n=46)of cases missing work caused financial losses. Additional financial expenseswere also evaluated: more frequently due purchase of medication and products ofhygiene 55,1%(n=91), cleaning anddisinfection products 16,4%(n=27), cost of a parent staying in hospital30,3%(n=50), nanny services 7,3%(n=12).

Conclusions. Rotaviral gastroenteritis has considerable adverse impact on everydaylife activities and finance of parents and family members of children withrotaviral gastroenteritis hospitalized in University Children's Hospital.

Granted by Riga Stradins University.

ESPID-0426
EPIDEMIOLOGY AND PUBLIC HEALTH

FACTORS ASSOCIATED WITH EARLY APPLICATION OF OSELTAMIVIR IN CHILDREN WITH INFLUENZA VIRUS INFECTION AND OUTCOME.

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Aims: Following recommendation by the National Institute for Health and Care Excellence early oseltamivir use is recommended for children at risk because of co-morbidities as there is evidence for reduction of duration of illness.

We investigated factors associated with the use of oseltamivir and subsequent respiratory outcome in children with influenza virus infection.

Methods: Retrospective study of children attending a District General Hospital with influenza virus infection over a five year period with comparison of groups with and without early application of oseltamivir (within 24 hours of arrival to hospital) regarding age, gender, co-morbidities, type of virus, respiratory support required and duration of stay.

Results: We included a total of 70 children, 39 received oseltamivir. Patients receiving oseltamivir had a median age of 35 months (range 7 to 180), patients without oseltamivir treatment had a median age of 16 months (range 7 to 138) (p=0.004). There was no significant difference in gender, comorbidities (20/39 in patients treated with oseltamivir and 11/31 in patients not treated with oseltamivir), requirement for respiratory support (13/39 in patients with and 6/31 in patients not receiving oseltamivir) or duration of stay in hospital between groups. Two patients receiving oseltamivir but none in the group without oseltamivir treatment required mechanical ventilation. Patients without oseltamivir treatment were significantly more likely to be infected with influenza B virus.

Conclusions: Patients treated with oseltamivir were significantly older and less likely to have influenza B virus infection in our study population.

ESPID-0706
EPIDEMIOLOGY AND PUBLIC HEALTH

INJURY EXPERIENCES AND PRECAUTIONS TAKEN BY NURSES WORKING IN PEDIATRIC WARDS TOWARDS PENETRATIVE/INCISIVE TOOLS

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Background and aims: Health professionals are under the risk of several occupational hazards during their practice. In United States, approximately 600.000-800.000 percutaneous injuries take place every year. It is also a very important issue in our country. This study was carried out to detect the frequency of needle prick injury and the measures taken to prevent these events among nurses working in pediatric wards.

Methods: The study was carried out in Karadeniz University Farabi Hospital. The study included 72 nurses working in pediatric wards. Informed consent and approval of local ethical committee were obtained accordingly. The data were analyzed with number, percentage, and chi-square tests.

Results: 67.6% experienced needle prick injury during their professional life of nurses. 20.3% claimed that they experienced injury with contaminated tool and 16.0% said that they reported their injury officially. Most of the injuries took place at the time of closing needle head, drawing medication from vials, removing head of vials, or removal of needle from syringe. 31.4% of the nurses clean the relevant area with bethadine solution, 25.9% with drap water, 18.9% with medical dressing. 58.1% of the nurses reported that they did not have sufficient knowledge about this issue.

Conclusions: This study showed that the frequency of penetrative/incisive tool injuries were high but the rate of reporting the relevant injuries was low. These results indicated that education on this issue was necessary to increase awareness and to reduce incidance of injuries among nurses.

ESPID-0511
EPIDEMIOLOGY AND PUBLIC HEALTH

PREPAREDNESS FOR SERIOUS CROSS-BORDER HEALTH THREATS IN CEVAG COUNTRIES – THEORY AND REALITY

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Background: CEVAG (Central European Vaccine Awareness Group) is a vaccine advocacy team of experts from Central and Eastern European countries (Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Slovenia and Turkey), regularly meeting twice/year. They have evaluated their relevant countries preparedness for ebola and the other serious emerging cross-border health threats.

Methods: Data have been collected on the relevant countries available public health preparedness and response plans, awareness, surveillance, logistic plans, laboratory diagnostic and clinical capacities related to an emerging health threat, including systems for identification and management of patient under investigation for Ebola virus.

Results: Each country has definite response plan to all probable threats, but marked differences could be detected in risk communication to both the public and the medical communities, in the laboratory diagnostic methods (BL4 labs are extremely limited and frequently external European laboratory capacities are utilized) and in dedicated clinical isolation capacities.

Conclusion: In all CEVAG countries the public health network is pro-actively dealing with preparedness to unexpected emerging health threats, though capacities for an adequate response varies. According to our opinion, public awareness even within the medical communities of this region is far less, than optimal, regarding the seriousness of a possible imported case – continuous medical education is urgently needed.

ESPID-1023
EPIDEMIOLOGY AND PUBLIC HEALTH

MYCOPLASMA PNEUMONIAE LOWER RESPIRATORY TRACT INFECTION EPIDEMIC IN SLOVENIA IN 2014

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Background and aims: Mycoplasma pneumoniae (MP) is a common cause of community-acquired lower respiratory tract infections (LRTI) in children. The aim of our study was to characterise the MP epidemic presenting in Slovenia from October to December 2014.

Methods: We collected data of children younger than 15 years which presented to our clinic with signs of LRTI and tested positive for MP by polymerase chain reaction (PCR) from nasopharyngeal swabs during the MP epidemic in 2014.

Results: A total of 247 children (male 53.0%, mean age 7.1, SD 3.2) were PCR positive for MP during the epidemic, compared to 101 in the rest of the year. They all presented with signs of LRTI, a mean duration of the disease prior to diagnosis of 7.6 days (SD 4.1 days) and mildly raised inflammatory markers (median CRP 21, IQR 8-41; median leukocytes 9.5, IQR 6.6-12.5). When performed, X-ray showed pulmonary infiltrates in 90.0% and pleural effusion in 30.0%. 95.6% of patients were given antibiotic treatment, of those 74.0% midecamycin as a first choice antibiotic, 25.1% azithromycin and 0.9% doxycycline. We observed deterioration on therapy in 4.5% of patients; no macrolide resistance was suspected in these cases. 19.4% required hospital care with a mean duration of stay of 2.6 days (SD 2.5 days), of which 22.9% needed oxygen support.

Conclusions: MP epidemics occur in our environment at intervals of 4 to 7 years. During the

last epidemic, antibiotic treatment was successful in most cases and a low percentage of
children required hospitalisation.

ESPID-1030
EPIDEMIOLOGY AND PUBLIC HEALTH

ARE MYCOPLASMA PNEUMONIAE INFECTIONS TREATED DIFFERENTLY DURING AN EPIDEMIC?

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Background and aims: During epidemics, higher number of patients and differences in clinical phenotype may lead to different treatment and outcome. We assessed if Mycoplasma pneumoniae (MP) lower respiratory tract infection (LRTI) treatment and outcome differed during a recent epidemic.

Methods: We retrospectively analysed data of all children younger than 15 years who presented to our clinic with signs of LRTI and tested positive for MP by PCR from nasopharyngeal swabs in 2013 and 2014. We compared patients who presented during the epidemic from October to December 2014 with those treated previously.

Results: 247 children (mean age 7.1, SD 3.2) were PCR positive for MP during the 3-monthly epidemic compared to 132 (mean age 6.9, SD 3.6) in previous 21 months. There was a higher incidence of boys during the epidemic (53.0% vs 38.6%, p=0.008). The groups did not differ in clinical and laboratory characteristics. Antibiotic treatment differed significantly. Midecamycin was the most common choice during the epidemic (74.0%) and azithromycin in other patients (58.9%). Deterioration on therapy was low in both groups (4.5% vs 5.0%). A lower percentage of children was hospitalised during the epidemic (19.5% vs 34.1%, p=0.002), with no difference in the length of hospital stay or the need for oxygen therapy.

Conclusions: During the epidemic, antibiotic choice was different and a lower percentage of children required hospitalisation. No differences in outcomes were observed. It is important that reasons for observed differences are evaluated and an optimal clinical path is defined.

ESPID-0963
EPIDEMIOLOGY AND PUBLIC HEALTH

INCIDENCE OF SHINGLES IN A REGION WITH UNIVERSAL 2-DOSE VARICELLA VACCINATION PROGRAM, NAVARRE, SPAIN, 2006-2013

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BACKGROUND

Navarre introduced chickenpox vaccination in the childhood vaccination schedule in 2007, with two doses. There is concern whether chickenpox vaccination might increase the incidence of shingles, due to the absence of contact with the wild virus and the consequent reduction of boosters of immunity.

AIM

The aim of this study is to describe the evolution of the incidence of shingles seven years after the beginning of the vaccination programme (period 2006-2013).

METHODS

Data were obtained from the automatic notification of electronic clinical reports of primary healthcare, diagnose S70 (shingles) according to the International Classification of Primary Care, Second Edition (ICPC-2). Duplicated cases and cases with diagnose of “postherpetic neuralgia” were excluded. Population data were obtained from the National Statistics Institute (INE). Incidence comparison was performed with χ^2 test with Yates’s correction o Fisher's exact test..

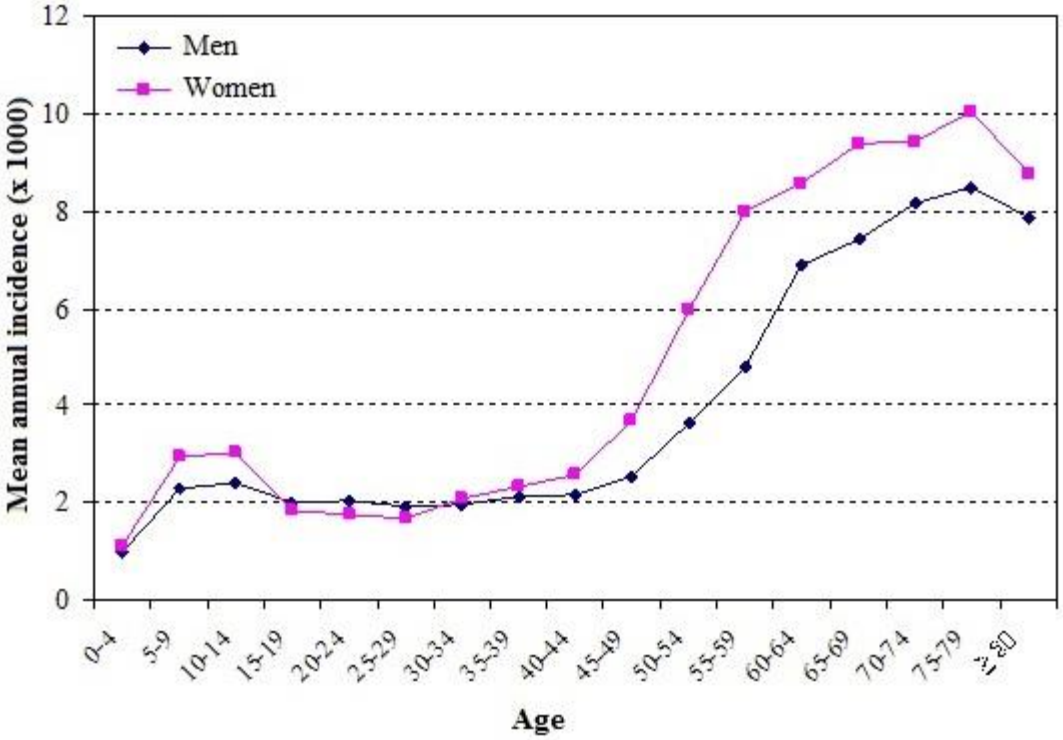
RESULTS

Shingles median incidence in the period was 4.1 cases per 1000 inhabitants. It was significantly higher in women (4.6 per 1000) than in men (3.5 per 1000). 65% of cases were observed in people over 50 years. Compared with 2006 shingles incidence was 7,6% lower in 2013. In chickenpox-vaccinated cohorts (children aged 1-9), shingles incidence decreased 58.9%. Incidence reduction was also registered in almost all age groups, except in adults over 75 years, in which incidence increased. Of those, it was significantly higher in people over 80 years.

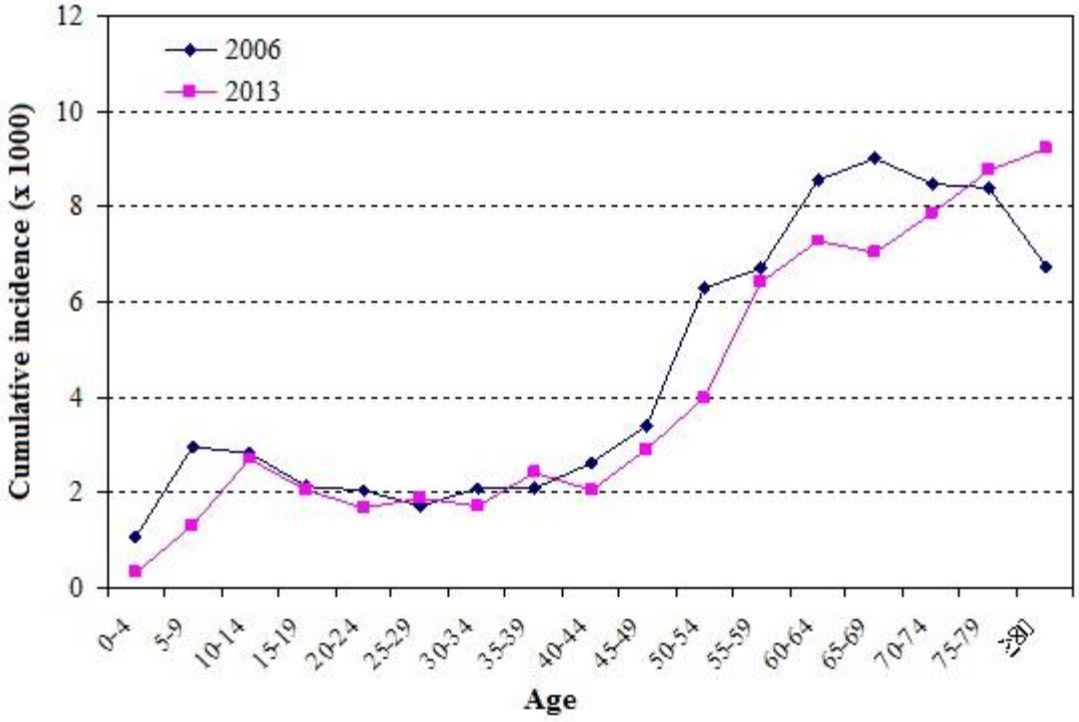
CONCLUSIONS

Up to 7 years follow-up incidence of shingles remains stable or even lower. Further follow-up is needed to assess incidence trends of shingles.

Mean annual incidence by sex and age, 2006-2013



Incidence of shingles by age, Navarra, 2006 vs. 2013



ESPID-0087
EPIDEMIOLOGY AND PUBLIC HEALTH

MOLECULAR EPIDEMIOLOGY AND GENETIC CHARACTERIZATION OF MEASLES VIRUS IN IRAN IN 2013-2014

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Background and aims: Molecular epidemiology of measles viruses (MV) helps to identify transmission pathways of the virus and to document the interruption of endemic virus circulation. We carried out a phylogenetic analysis of measles virus circulating in Iran over the period 2013–2014.

Methods: Specimens of serum, throat swab and urine from suspected cases of measles were collected from different provinces of Iran. All sera were screened for measles IgM specific antibody using ELISA kits. Virus isolation was performed on throat swabs and urine of confirmed serologically measles cases. For virus isolation, the specimens were inoculated onto mycoplasma free Vero/hSLAM cell line. Partial nucleoprotein gene segments of MV were amplified by RT-PCR. PCR products were sequenced in both directions. Sequenced data were analyzed by Bioinformatics software.

Results: A total of 98 cases of measles were serologically confirmed. 17 sequences (17.4%) were obtained from viral isolates using cell culture and the 81 (82.6%) were obtained directly from specimens. The age of cases ranged from 2.5 month to 44 years. The vaccination history showed that among all confirmed cases, 8 (8.16%) had been vaccinated, 83 (84.7%) had not been vaccinated, and 7 (7.14%) had unknown vaccination status.

?Conclusions: In spite of progress in measles surveillance, outbreaks were reported from some parts of Iran over the last 2 years. Genotypes B3 (92.86%), D4 (5.1%) and D8 (2.04%) were detected mainly in non-vaccinated persons. This information is valuable to inform vaccination strategies with a focus on those populations who remain susceptible to measles infection.

ESPID-0699
EPIDEMIOLOGY AND PUBLIC HEALTH

ETIOLOGY OF ANAEMIA AMONG YOUNG CHILDREN (AGE UNDER FIVE YEARS) IN SOUTH INDIA

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Background and aims: Globally, severe anaemia is one of the critical public health problems in developing countries. About 89 million children are living with anaemia in India. The present study examined the prevalence of anaemia with review of existing program of the anaemia among children in South India.

Methods: The study has used recently available fact sheet of District Level Household and Facility Survey (DLHS-4, 2012-13) which was conducted during 2012-13 and National Family Health Survey (NFHS-3) data (2005-06). Bivariate and chi-square test have been used.

Results: The prevalence of severe anaemia (haemoglobin level, below 7g/dl) is 21.2% in Andhra Pradesh followed by Telangana (13.3%) and Karnataka (14%) among children (under age five years). On this contrast, the lowest prevalence of severe anaemia is 3% in Kerala and Tamil Nadu (3.7%). Previous literature have shown that children's anaemic mothers, less educated mothers and mothers belongs to the lowest quintile are the contributing factors for the severe anaemia among children. The study has found that huge geographic variations of severe anaemia among children in Southern India.

Conclusion: The present study found that the prevalence of severe anaemia is high in Andhra Pradesh and Telangana. Through, previous literature study found that most of the program was focussed on providing iron folic tablets that were not sufficient for the reduction of anaemia. Hence, study has recommended that there is need to monitor the program at ground level and provide active training facility to resources person of the program.

ESPID-0221
EPIDEMIOLOGY AND PUBLIC HEALTH

OUTBREAK OF ENTEROVIRAL MENINGITIS IN NORTHEASTERN POLAND DURING THE SUMMER SEASON 2014

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Background and aims

Enteroviruses are the most common cause of viral meningitis worldwide and may cause local outbreaks. Central Nervous System infection is usually mild but occasionally may lead to severe complications or even death. Our goal was to determine the epidemiology, characteristics and clinical outcome of patients with enteroviral meningitis admitted to The Medical University of Bialystok Children's Clinical Hospital, from January 2013 to December 2014.

Methods

Retrospective analysis of medical records of children diagnosed with enteroviral meningitis. Enteroviral RNA was detected in cerebrospinal fluid samples by polymerase chain reaction. To determine virus type, viral culture was performed.

Results

A total of 292 children were included. In 2014 a 35-fold increase in the total number of enteroviral meningitis was observed, as compared to 2013 (284 vs 8). Most cases (81.7%) were admitted from June to August. All age groups were affected, with substantial number of children aged 10 years and older (44%). Males accounted for 64.8% of cases. In majority of patients (85.6%) CSF protein concentration was within normal range (<60mg/dl) and in 45% of cases pleocytosis exceeded 100 cells. Enterovirus Echo 30 was identified as the etiologic agent of the outbreak. The median length of stay was 7 days. As many as 96.8% of children recovered within 10 days. No severe complications were observed.

Conclusions

The outbreak followed patterns observed worldwide. We recorded surprisingly high number of children over 10 years of age, what may reflect a lack of previous exposure to Echo 30 in this population.

ESPID-0302
EPIDEMIOLOGY AND PUBLIC HEALTH

THE DIRECT AND INDIRECT COSTS OF UNCOMPLICATED VARICELLA TREATMENT IN SLOVAKIA IN CHILDREN

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Background and aims: Varicella belongs to the most common infectious diseases globally. Around 18,000 cases are annually reported in Slovakia. The aim of this work was to analyze direct and indirect costs for treatment of uncomplicated varicella in Slovakia in the age group under 14-year-old children in 2012.

Methods: Data of the infection incidence were obtained from Epidemiological information system of the Slovak Republic. Direct costs included costs for outpatient treatment and the average capitation payment in individual age groups. Indirect costs included costs for contribution to family member home care and loss of productivity during 10-day treatment.

Results: Average costs per one case of uncomplicated varicella in children represented EUR 12.14 which means an increase by more than 100 % compared to 2007 (EUR 5.97). The average costs for contribution to family member home care reached EUR 75 per case. Loss of productivity what is unformed gross domestic product during the 10-day absence from work for parents taking care of a sick child (aged 1-14 years) reached EUR 356. Total indirect costs reached EUR 431 per one case which is 20 % more than in 2007 (EUR 359).

Conclusion: Treatment costs for varicella rise each year because of increasing mainly indirect costs. Indirect costs in Slovakia represent about 97 % of total costs, which is the highest proportion in comparison with other countries.

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contract No. APVV-0096-12 (EPIBIOMAT).

ESPID-0543
EPIDEMIOLOGY AND PUBLIC HEALTH

S.PNEUMONIAE CARRIAGE AND FREQUENCY OF SEROTYPES IN CHILDREN UNDER 25 MONTHS IN A THE REGION OF BLIDA (ALGERIA)

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Aim:

Estimate of *S.pneumoniae* carriage frequency inchildren under 25 months in theregion of Blida. Determine the serotypesof strains and their resistance to antibiotics.

Method:

For a period of six months, wecollected 335 nasopharyngeal swabs,from unvaccinated children against pneumococcal disease, the average agewas 9.5 months. We excludedall feverish children, sufferingfrom acute respiratory infection orwho have received antibiotic therapyduring the last 7 days. Parental consent is requested foreach sample. Identification of pneumococcalstrains is based on standard tests. The determination ofserotypes was made by serotype-specificantisera (Staten Serum Institute). The MICinterpretive criteria follow thestandards CLSI (2014).

Results:

Sixty-seven S. pneumoniae strains were isolated. Thefrequency of pneumococcal carriage in the region of Blida is estimated at 20%[CI: 15,7- 24.2]. The serotypes found are: 19F (13.4%), 6B (10%), 14 (9%), 23F(9%), 19A (6%), 11A (6%) and 29 (6%). The number of PSDP is 43 (64%) ofpneumococcal CMI ≥0.125 mg / ml. Resistance to other antibiotics: amoxicillin3%, 4% for cefotaxime, erythromycin 50% and 24% for cotrimoxazole. Noresistance to fluoroquinolones or glycopeptides.

Conclusion:

The carriagefrequency of *S.pneumoniae* within thestudied population was 20%, of which 64% of PSDP; vaccine serotypes represent49 and 61% respectively for VPC10 and VPC13. A cross-regional study onpneumococcal carriage is necessary in Algeria, before introduction and monitoring ofpneumococcal vaccination.

ESPID-0233
EPIDEMIOLOGY AND PUBLIC HEALTH

CHARACTERIZATION AND VARIATION OF MACROLIDE RESISTANCE IN GROUP A STREPTOCOCCI ISOLATED FROM CHILDREN WITH PHARYNGITIS IN JAPAN.

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【Objective】The aim of this investigation is to determine characterization and variation of popular macrolide resistant Group A streptococci (GAS) strains in southwestern Japan.
【Background】The drug of first choice for pharyngitis was penicillin, but for penicillin allergy patients, treated by macrolide. A rate of macrolide resistant GAS has tended to increase.
【Methods】 All of 302 GAS strains were isolated from pharyngitis patients of children between 2011 and 2013. Macrolide and clindamycin susceptibility testing was performed and macrolide-resistant strains were extracted. Thus, *emm* and T serotyping were performed, and macrolide-resistant genes<erm<> (</erm<><erm<></erm<><*erm*<>*erm*</*erm*<><*erm*<>*B, ermTR, mefA, msrD)*</*erm*<><erm<> were detected by the PCR method. Further analysis of chromosomal DNA was carried out by PFGE.
【Results】The macrolide-resistant strains were 126 strains. Seventy-seven strains of these strains possessed *mefA* gene (that had also *msrD*), and 47 strains possessed *ermB*. T-serotype and *emm* type were detected 12 and 7 types, respectively. And the predominant types were T12 and T1, similarly *emm*12 and *emm*1. The predominant types of *emm*-T types were *emm*1-T1 and *emm*12-T12. The strains possessed *mefA* had majority of T1 types, and similarly *ermB* had majority of T12 type. We identified 15 distinct PFGE clusters. *emm1*-T1 strains had two of PFGE clusters, and *emm*12-T12 had 7 clusters, whereas we found that one cluster had 4 *emm*-T types (*emm*75-T4, *emm*75-T25, *emm* st1815-T25, *emm* st1815-T5/27/44).
【Conclusion】Plural molecular characterization of macrolide resistant GAS strains were detected. It suggests that each strain has obtained macrolide resistant individually.</erm<><*erm*<>
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ESPID-0811
EPIDEMIOLOGY AND PUBLIC HEALTH

OUTBREAK OF MEASLES IN A NURSERY IN FLANDERS - THE IMPORTANCE OF TIMELINESS OF VACCINATION AND PROMPT REPORTING OF CASES

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Background and aims

Despite a vaccination coverage of 96.6% against measles in Flanders, an outbreak of 33 cases occurred in a nursery in April 2014. We investigated this cluster by source and contact tracing and checking the vaccination status in order to hold further spread of measles and to find the reasons why this occurred.

Methods

Following notification of two cases of measles in babies from the same nursery, we investigated children and staff of the nursery and their household contacts on clinical measles. We screened staff and unvaccinated children and their mothers by oral swab tests (PCR and ELISA for IgM and IgG). Unvaccinated children older than 6 months were given an MMR vaccine.

Results

Out of 34 unvaccinated children younger than 16 months, 28 cases were found. In due time vaccination might have avoided 6-10 cases. Two of five adult cases had received 2 vaccines.

The genotype found was D8, very similar to the genotype circulating in the Zeeland Province in the Netherlands in 2013-2014. The first case in this outbreak – a staff member - had visited this province a week before getting ill, which makes it most probable she was the source of the outbreak.

Conclusions

Young children remain a highly vulnerable group for measles when a case is introduced into the group. This might be a key issue for the measles elimination goal of WHO. Timeliness of vaccination is of upmost importance to avoid spread. Prompt reporting of measles cases allows to take appropriate measures.

ESPID-0486
EPIDEMIOLOGY AND PUBLIC HEALTH

USING BEXSERO® TO HELP REDUCE THE BURDEN OF MENINGOCOCCAL B DISEASE – VACCINATION STRATEGIES

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Background:
Meningococcal disease remains a significant public health burden in many countries. Following widespread successful use of MenC vaccines, MenB disease now predominates in European Union (EU) countries particularly in infants. In 2013, Bexsero® (Novartis Vaccines and Diagnostics Srl, Italy) became the first broad-coverage vaccine licensed for active immunization against MenB disease in EU. Bexsero is now also licensed in Australia, Canada, Chile, Uruguay and Brazil.

Methods:
We outline strategies to help reduce the burden of MenB disease using Bexsero.

Results:
Infants plus catch-up program: Most MenB cases occur in infants/young children, with a smaller peak in adolescents/young adults. The latter group also acts as a transmission reservoir. Modelling studies suggest vaccinating both groups potentially delivers the greatest reduction in MenB disease. Such a vaccination program was implemented in Saguenay-Lac-Saint-Jean, Québec in 2014.

Infants-only program: The UK Joint Committee on Vaccination and Immunisation recommends routine Bexsero vaccination for infants, without a catch-up program. This strategy was formulated on the basis of cost-effectiveness modelling and the perceived need to offer protection to all infants.

Outbreak control: Outbreaks of meningococcal disease at two USA universities prompted the deployment of Bexsero by CDC under an Investigational New Drug protocol.

Medically at-risk groups: Bexsero has been recommended for individuals at increased risk of meningococcal disease. Definitions of high-risk groups and availability of public funding vary by country/region.

Conclusion:
While different strategies have been employed, the maximum reduction in disease is expected with a combined infant/adolescent program that could be accelerated through various catch-up programs.

ESPID-0953
EPIDEMIOLOGY AND PUBLIC HEALTH

ACCURACY AND PITFALLS OF THE CURRENT CASE DEFINITION TO DIAGNOSE PERTUSSIS IN COSTA RICAN CHILDREN: RESULTS FROM A CASE-CONTROL STUDY

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Background and aims: With the classic pertussis case definition some infants will escape from diagnosis if laboratory confirmation doesn't occur. Our main objective was to analyze this definition and it usefulness in Costa Rican patients.

Methods: Case-control study performed in a second level hospital. Cases were defined as ambulatory and hospitalized patients aged <12 years with PCR-confirmed pertussis obtained from nasopharyngeal aspirates, from Jan-1-2006 to Dec-31-2010. Controls were defined as children with respiratory disease with a negative pertussis-PCR during the same period. A descriptive analysis and evaluation of sensitivity, specificity and predictive values of the current case definition findings was calculated.

Results: 97 cases and 117 unmatched controls were enrolled, with a median age of 1.9 years. No significant differences were found in appearance of symptoms and clinical signs as well as laboratory results or radiographic findings. Only 10 cases had a history of ≥ 2w cough. Current case definition for children >1 y was 97% specific (95%CI 83-99) but only 3% sensitive (95%CI 1-16), with 50% positive predictive value (95%CI 9-91) and 49% negative predictive value (95%CI 37-62). For infants, it was 12% sensitive (95%CI 5-25), 95% specific (95%CI 88-98), 56% PPV (95%CI 27-81) and 67% NPV (95%CI 58-75). The most sensitive variable in infants was paroxysms (35% 95%CI26-51) and stridor (32% 95%CI15-90) in older children.

Conclusion: In this population, the current case definition was not sensitive for early clinical pertussis diagnosis, particularly in children ≥1 year of age and those with <2-week cough.

ESPID-1050
EPIDEMIOLOGY AND PUBLIC HEALTH

DECREASING NUMBER OF HOSPITALIZATIONS DUE TO RHEUMATIC FEVER AND ACUTE GLOMERULONEPHTRITIS AT COSTA RICA'S NATIONAL CHILDREN'S HOSPITAL: A FOUR-DECADE EXPERIENCE

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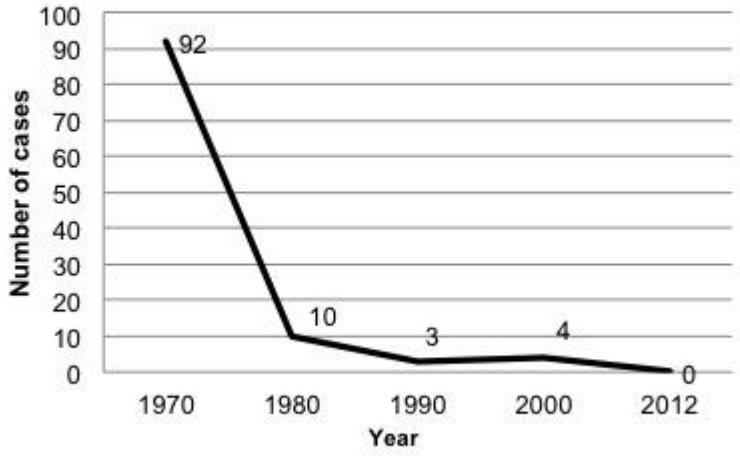
BACKGROUND AND AIMS: The morbidity and mortality attributed to Group A Streptococcus (GAS) associated-diseases is considerable in developing countries, particularly for rheumatic fever (RF), rheumatic heart disease (RHD), and acute glomerulonephritis (AGN). In Costa Rica, Kawasaki disease replaced RF as the leading cause of pediatric acquired cardiac disease during the last three decades. Our main objective was to describe the successful story of specific public health interventions to fight these diseases: nationwide availability of penicillin treatment protocols for children with acute tonsillitis/pharyngitis and impetigo following experts recommendations, improved sanitary and socio-economic conditions, and improved laboratory capacities.

METHODS: Retrospective descriptive study of hospital discharge databases for children <13 years of age with a diagnosis of RF/RHD and AGN, between 1970-2012 and 1967-2012, respectively, at the only national pediatric tertiary referral academic hospital of Costa Rica.

RESULTS: An important and sustained decrease in the number of hospitalizations due to RF and AGN has been seen at our institution during the last four decades (Figures 1 and 2).

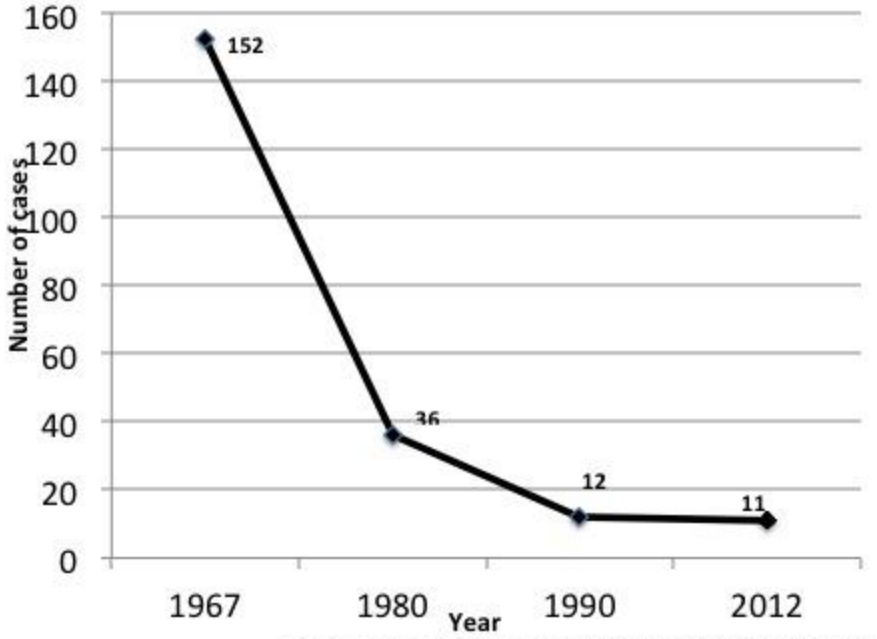
CONCLUSIONS: This is an example where in the absence of an available vaccine for a specific microorganism (GAS), specific public health interventions and prevention programs can impact positively in the fight against a specific disease in a developing country.

Figure 1. Number of hospital discharges due to new onset cases of rheumatic fever, Hospital Nacional de Niños "Dr. Carlos Sáenz Herrera", Costa Rica.1970-2012



Source: Department of Health Statitstics and Registries, 2012

Figure 2. Number of hospital discharges due to acute glomerulonephritis, Hospital Nacional de Niños "Dr. Carlos Sáenz Herrera", Costa Rica.



Source: Department of Health Statitstics and Registries, 2012

ESPID-0852
EPIDEMIOLOGY AND PUBLIC HEALTH

A DESCRPITIVE COHORT OF RHEUMATIC HEART DISEASE PATIENTS FROM THE CARDIAC CLINIC AT THE MEDICAL RESEARCH COUCNIL UNIT, THE GAMBIA

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Background: Rheumatic heart disease (RHD) is the leading cause of cardiac death and disability in children and young adults. It results from valvular damage caused by an exaggerated immune response to Group A streptococcus (GAS) infections, usually during childhood and adolescence. There is little data on either the burden of RHD or knowledge of prevalent GAS strains in sub-Saharan Africa.

Aims: Our analysis aimed to establish the number of patients with RHD from our out-patient department (OPD) and the age and severity of disease at presentation.

Methods: Retrospective analysis of children seen in OPD at Medical Research Council Unit, The Gambia, from 2002-2014, to assess symptoms, severity at presentation and cardiac lesions on echocardiography.

Results: Of 91 records found, 64 met our inclusion criteria. Median age at presentation was 11 years (IQR 5-18) and 65% were female. Common presenting features were dyspnoea (62.5%), cough (59.4%) and chest pain (46.9%). Severity of symptoms at presentation were quantified using the modified Ross score: class I (11.9%), class II (40.7%), class III (15.2%), class IV (32.2%). 53% had single valve involvement, 37.5% had two valves affected and 9.5% had triple valve involvement. The most common finding was mitral regurgitation (62), followed by aortic regurgitation (24), tricuspid regurgitation (12) and mitral stenosis (7).

Conclusion: The young age of presentation with severe cardiac disability illustrates the urgent need for surveillance studies to assess both the burden of RHD and the prevalence of circulating GAS strains to inform secondary prevention programmes and future vaccine studies.

ESPID-0603
EPIDEMIOLOGY AND PUBLIC HEALTH

EPIDEMIOLOGY CHARACTERISTICS OF HFMD IN CHILDREN IN SHANGHAI,2014

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Background: We investigated the epidemiological data of all hand,foot,and mouth disease(HFMD) outpatient cases in Shanghai,2014.

Methods: The epidemiological characteristics of HFMD outpatient cases diagnosed in Children's Hospital of Fudan University were analyzed retrospectively, including gender, age, place of residence, disease duration, detection of peripheral blood EV71-IgM.

Results: (1)A total of 19208 patients were diagnosed with HFMD in 2014. Of 19208 HFMD cases, 11693 patients are boys and 7515 girls, with a male-to-female ratio 1.56:1. (2)The incidence rates of HFMD for age group ≥0.5,0.5 to 1,1 to 3,3 to 5,and >5,years were significantly different, with the peak incidence rates in the age groups 1 to 3 years(9289/19208,48.3%),3 to 5 years(5889/19208,30.7%); HFMD occurred throughout the year, with occurring in January(265,1.4%),February(233,1.2%),March(1111,5.8%), April(2402,12.5%),May(2281,11.9%),June(3000,15.6%),July(2666,13.9%),August(1486,7.7%),September(1823,9.5%),October(1871,9.7%),November(1062,5.5%),December(1008,5.3%); Of 19208 HFMD cases, 17734 patients(92.3%) are Shanghai residents, with the highest proportion in Minhang District(6748/17734,38.1%),followed by Songjiang District(16.7%),and other districts(45.2%). (4) The average duration of the initial treatment is 1.53±1.20d(M 1d); Among the 17955 patients detected peripheral blood EV71-IgM,3567 cases were positive(19.8%),with the EV71-IgM positive duration 1.67±1.26d(M 1d).

Conclusions: Incidence of HFMD was highest in 1-3 years old children, with males being predominant. HFMD cases have increased in March ,with peak occurring in June and July. The highest incidence rate areas are located in urban fringe areas. Peripheral blood EV71-IgM detection may provide basis for early diagnosis of HFMD.

ESPID-0931
FUNGAL INFECTIONS

CANDIDA BLOOD STREAM INFECTIONS OF NEONATES IN NEONATAL INTENSIVE CARE UNIT (NICU),HAMAD MEDICAL CORPORATION (HMC), QATAR BETWEEN 2004-2010

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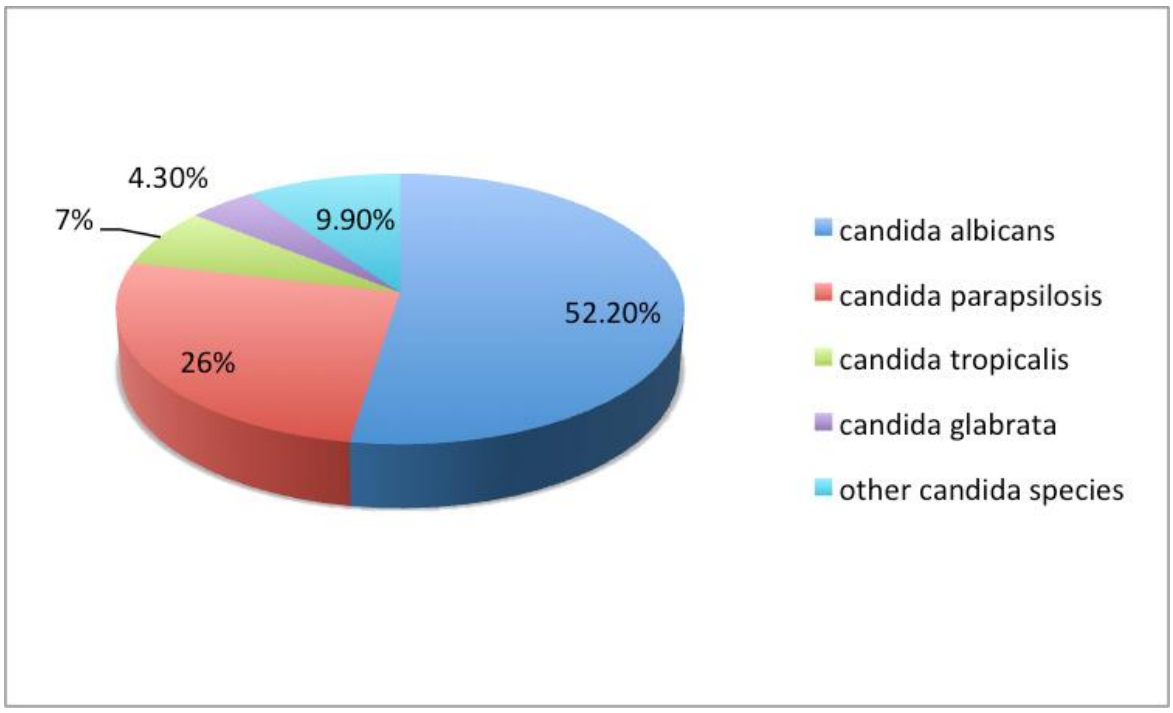
Background : Candida blood stream infections is an important neonatal infections that causes high morbidity and mortality among very low birth weight infants (VLBW) and extremely low birth weight infants (ELBW).Candida Albicans is the most prevalent species but the isolation of nonalbicans species is increasing.
Aim:Measure the prevalence of invasive Candida infection in NICU at HMC,Identify the distribution of Candida species,describe historical risk factors , clinical features, and attributable mortality.
Method :we conducted a retrospective chart review on neonates with candidia blood infections between 2004-2010,We developed data extraction sheet which included;Demographic,Species and susceptibility of Candida,Risk factors for Candida infection,Investigations &Treatment given, attributed death was calculated as death within 3 days of postive culture for Candida.
Results :Total number of subjects were 90,median mother age is 28.1years(17-40), 55.1% male and 44.9% female, median birth weight is 980gm (480-4030), median gestational age 27 weeks (23-40weeks).
Prevalence of neonatal candida infections decreased from 1.1% in 2005 to 0.5% in 2010. prevalence is higher in gestational age 21-28 weeks.Candida species were C albicans at 57.8% compared to C nonalbicans 42.2%.



clinical presentation were nonspecific but 76% had thrombocytopenia.looking at risk factors;—17% were on postnatal steroids,35% had a previous positive bacterial culture and 100% were on some kind of antibiotic.58.9% survived, 28.9% died because of candida blood infection and 12.2% died for other causes.
limitation of the study: restropective, looked only at positive blood culture which underestimate the burden of the disease.we didn't compare our patients with neonates who didn't have candida blood infections.

ESPID-0410
FUNGAL INFECTIONS

VITAMIN D MEDIATED HYPERCALCEMIA IN AN IMMUNOCOMPETENT CHILD WITH DISSEMINATED CRYPTOCOCCOSIS

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Cryptococcus neoformans is an opportunistic yeast commonly found in soil contaminated by bird feces throughout the world . Cryptococcosis continues to cause significant morbidity and mortality in immunocompromised as well as immunocompetent patients . Hypercalcemia has been described in variety of granulomatous diseases and fungal infections. However, hypercalcemia in disseminated cryptococcosis in a child is rare. We report a 7-year-old immunocompetent child who initially presented with fever and severe pain abdomen, severe hypercalcemia with increased serum vitamin D concentration and suppressed parathyroid hormone. Disseminated cryptococcosis was diagnosed as the cause of hypercalcemia. Successful treatment resulted in the resolution of hypercalcemia.

ESPID-0107
FUNGAL INFECTIONS

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS MASQUERADING AS PULMONARY TUBERCULOSIS IN A 10 YEARS OLD GIRL.

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Introduction: Allergic bronchopulmonary aspergillosis is an immunologically mediated lung disease that is caused by hypersensitivity to antigens of the genus Aspergillus. We present an unusual pediatric patient with severe allergic bronchopulmonary aspergillosis that masqueraded as pulmonary tuberculosis.

Case: A 10 years old girl was referred with history of cough and weight loss since one month. Patient was evaluated for tuberculosis with normal sputum examination , negative mantoux test and family history. Xray chest showed bilateral infiltrates with dense opacities in the right lower lobe. Complete blood count showed high total leukocyte count with 56% eosinophil count and normal ESR suggesting pulmonary eosinophilic syndrome. CT chest clinched the diagnosis with presence of bronchoceles with bilateral segmental atelectasis suggestive of allergic bronchopulmonary aspergillosis. IgE and allergen specific IgE Aspergillus Fumigatus levels came out to be very high. She was started with oral steroids and responded very well with resolution of cough, weight gain and clearance of infiltrates on chest Xray.

Conclusion: The remarkable radiological similarity to pulmonary tuberculosis has important clinical implications in our country as patients with allergic bronchopulmonary aspergillosis often receive antituberculous therapy. CT chest is crucial to the diagnosis of allergic bronchopulmonary aspergillosis.

ESPID-0409
FUNGAL INFECTIONS

INTERFERON-GAMMA IMMUNOTHERAPY IN A PATIENT WITH REFRACTORY DISSEMINATED CANDIDIASIS

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Background and aims: Despite advances in supportive care and novel antifungal agents,mortality due to invasive *Candida* infectionremains high. A three-year-old boy with disseminated *C. dubliniensis* infection during induction chemotherapy for acutelymphoblastic leukemia deteriorated, despite resolution of neutropenia and optimalantifungal treatment. Monocyte HLA-DR (mHLA-DR) expression was extremely low,suggesting immunoparalysis.

Methods:IFN-g was started as salvage therapy three times per week.Immune status was monitored regularly and cytokine responses were determinedbefore and during treatment.

Results: Last resort adjunctive immunotherapy with IFN-g resulted in normalization of mHLA-DR expression, and cytokine responseswere also partly restored. This restoration of innate immune functionsparalleled and likely contributed to clinical recovery.

Conclusion: Our observation warrants further study in pediatricpatients with invasive fungal infections who deteriorate despite optimalantifungal treatment, in which immunotherapy with IFN-γ may be considered asadjuvant salvage therapy.

ESPID-0942
FUNGAL INFECTIONS

HISTOPLASMOSIS AND TUBERCULOSIS - CO-INFECTION OR SUPERINFECTION?

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African Histoplasmosis is caused by *Histoplasma capsulatum var. duboisii*. It is a fungal, invasive and endemic infection.The clinical spectrum is broad and ranges from asymptomatic infection to severe disseminated disease. Infection by Mycobacterium tuberculosis has increased at the cost of developing countries.The authors describe the case of a 12 years boy, with no known personal history, transferred to Oporto from Guinea Bissau by cutaneous lesions ulcerated and exudative, containing pus and hard consistency at the level of ganglion chains associated with asthenia, anorexia and intense cervical pain, with 2 years of evolution. Chest CT-Scan reveal one consolidation area in the left lower lobe associated with peripheral micronodules. Ganglionic histological examination showed fungal infection by *Histoplasma spp duboisii variant*. Serology for HIV were negative and the research of Koch bacillus in gastric juice was positive. Radiological examination showed lytic lesions at the skull. Fulfilled therapeutic with antituberculosis and antifungals (Posaconazole "of-label"). Guinea Bissau, an underdeveloped country, has one of the lowest levels of human development. So, due to limited resources of sanitation and hygiene, Tuberculosis and Histoplasmosis become endemic in this region and provide greater individual susceptibility to the disease. Are rare references to African histoplasmosis during HIV infection, in contrast to that found in classical variant. Note that both are endemic in the same region. Thus, regardless of the temporal sequence of occurrence of infections: histoplasmosis and tuberculosis, is a causal link between both, doubt remains: reactivation of latent tuberculosis infection by histoplasmosis vs opportunist Histoplasma in a patient with tuberculosis.

ESPID-0864
FUNGAL INFECTIONS

CASE REPORT ABOUT FALSE POSITIVE ASPERGILLUS-AG TESTS IN NEONATES AND PREMATURE INFANTS

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Background. Infections on neonatal intensive care units are still a challenge concerning diagnosis and effective treatment. Whereas clinical and paraclinical parameters for the diagnosis of bacterial infections in neonates are well established, the detection of fungal infection, especially concerning Aspergillus spp. remains difficult. Fungal infections are rare and show regional differences in prevalence. The Platelia™-Aspergillus-Antigen-ELISA test (Bio-Rad) is well evaluated in adult medicine as diagnostic tool for the detection of infection with Aspergillus spp.. Our goal is to provide data regarding its use in (preterm) neonates.

Methods and results. Starting from an index patient with continued respiratory symptoms and positive Platelia™-Aspergillus-Antigen-ELISA test, we report about an assumed outbreak of Aspegillus-infections in the patients on our NICU. None of the 8 patients tested 1 to 2 times during an environment examination showed clinical signs of fungal infection that would explain the highly positive test results found in 6 of them. When assessing different explanations it became obvious that all patients receiving formula or fortified breast milk had positive test results, whereas patients receiving pure breast milk had negative test results. In a third step we directly tested the different types of nutritive substances used on our NICU and could reproduce the link between positive test results and formula/fortifier.

Conclusions. Considering our findings we suggest that the Platelia™-Aspergillus-Antigen-ELISA test may only be used in neonates when fed pure breast milk to prevent false-positive test results.

ESPID-0202
FUNGAL INFECTIONS

POSTOPERATIVE KERATITIS DUE TO PAECILOMYCES IN AN IMMUNOCOMPETENT CHILD; THE SUCCESFUL TREATMENT OF A RARE PEDIATRIC CASE

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Introduction: Fungal infections like *Paecilomyces* keratitis have become an important recently. Corneal cultures should be performed on fungal media such as Sabouraud dextrose agar (SDA). **Case:** A-14-year-old boy with a history of acute hydrops due to keratoconus in the right eye that was treated by keratoplasty. He had given prednisolone acetate 1% drops postoperatively. On the 30th day after the surgery he complained of severe pain, redness and decreasing vision in the right eye. On slit lamp examination, there was a 3x3 mm central abscess in the right eye. On the microscopic examination of the corneal scrapings that revealed a septate and branching fungal hyphal structures. Mold colonies appeared on SDA.
On examination of fungal culture, the obverse site of the colony was flat, powdery, velvety, and yellowish; reverse site was white to pinkish in color and fungal identification was reported as *Paecilomyces species* by microbiology laboratory. Antifungal therapies was rearranged with topical and systemic voriconazole and oral terbinafine. Repeat fungal cultures were turned to negative due to applied antifungal therapies agents. Clinical improvement was observed and corneal lesion healed with a vascularized scar tissue. Voriconazole and terbinafine were discontinued after 6 weeks and 2 weeks from the start, respectively. **Conclusion:** We want to draw attention once again to the increase in fungal keratitis caused by unusual agents such as *Paecilomyces*. Voriconazole was effective in treating this severe keratomycosis caused by *Paecilomyces species.*

ESPID-0660
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

SEPSIS AFTER SEVERE HEAD TRAUMA IN CHILD: A CASE REPORT

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Background and aims: One of the most common and life threatening complications after major surgeries is sepsis. The aim of this study is to plan and implement nursing actions with case management on child with severe head trauma.

Method: The data for the study is comprised of files and medical reports of a nine year old child who was admitted to Yozgat Public Hospital Emergency Room with head trauma on 16th.09.2014. Verbal and written consents of the child's family were taken.

Result/Case:9 year-old T.S was run over by a reversing car on a snowy road after school and had a head trauma. T.S was taken to the hospital by an ambulance. Conscious but agitated upon arriving, the patient had visible dent fracture in his skull, subarachnoid hemorrhage, contusion on the left temporoporietal area, and a cut on his left ear. Flap on his dent area, galeal graft on his temporal region was applied and his left ear was repaired. Having been monitored at surgery intensive care unit for two days, T.S developed sepsis. His treatment continued at neurosurgey service for 24 days.

Conclusion: The child has to be put in stable condition and fluid has to be given, and he should be reassessed with clinical parameters like oxygenation. Urination, mental state, vital findings, nausea-vomiting, pupil changes and convulsion all should be monitored. Surgical incision area should be watched for flow and smell. Proper treatment and nursing approach in this case can reduce mortality and possible complications in the future.

ESPID-0932
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

NEONATAL INFECTION SURVEILLANCE IN GREECE - DATA FROM A EUROPEAN NETWORK

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Background & Aims

Data on the pathogens causing infections in the Neonatal Intensive Care Units (NICUs) in Greece are limited. Equally, the emergence of multi-drug resistant pathogens highlights the importance of establishing a comprehensive national surveillance system. This study aims to describe the epidemiology of neonatal infections in Greek NICUs as captured by the neonIN database.

Methods
NeonIN is an international web-based surveillance database for culture proven neonatal infections. Cases from participating Greek NICUs from January 2012 to October 2014 were extracted. Early-onset sepsis was defined as occurring within 48 hours of birth.

Results There were 259 episodes (involving 238 infants) from 11 NICUs in Greece. Overall incidence was 54/1000 NICU-admissions. *Coagulase-Negative Staphylococcus* (CoNS) (86, 33%) was the most common Gram-positive organism. Amongst Gram-negatives, *Enterobacteriaceae* (97, 37.4%) were the commonest pathogens with *Klebsiella spp* (40, 15 %) most frequently isolated.

There was no resistance among CoNS to teicoplanin or vancomycin documented. Resistance among *Enterobacteriaceae* to at least one aminoglycoside was recorded in 47% (46 /97), to 3rd generation cephalosporins in 31.9% (31/97) and to carbapenems in 10% (10 / 97). Enterococcal resistance to vancomycin was 18.7% (3/16 cases).

Conclusions
CoNS and *Enterobacteriaceae* were the most common bacteria isolated in Greek NICUs. High rates of resistance to aminoglycosides, 3rd generation cephalosporins and carbapenems were detected. Continuous surveillance at a national level will enable a better understanding of the disease and antibiotic resistance burden.

ESPID-1005
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

GRAM NEGATIVE BACTERIA CAUSING LATE-ONSET NEONATAL SEPSIS-A COMPARISON BETWEEN TWO EUROPEAN COUNTRIES

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Background and aims: Neonatal infection due to Gram-negative (GN) pathogens is increasing. The epidemiology may differ across Europe. This study compares the distribution, demographics and antibiotic resistance patterns of the GN pathogens responsible for late-onset sepsis (LOS) between the United Kingdom and Greece using data from the neonIN surveillance network. **Methods:** neonIN is an international web-based surveillance database for culture proven neonatal infections. Infection episodes from January 2012 - October 2014 were extracted. Late-onset

sepsis (LOS) was defined as occurring after 48 hours of birth. **Results:** A total of 304 episodes of infection (involving 294 infants) were recorded. The incidence of LOS due to GNs was 19.9/1000 neonatal admissions in Greece versus 4.5/1000 in the UK (p-value < 0.001). The commonest GN pathogen in Greece was *Klebsiella* spp (39/90, 43 %) whereas in the UK it was *E. Coli* (71/214, 33%). Details of demographics by country are shown in Table-1, while Table-2 compares the antibiotic resistance rates to at least one aminoglycoside, 3rd generation cephalosporin and carbapenem by pathogen and country.

Table-1	**UK** **n=214**	**Greece** **n=90**
Number of participating units	27	10
Incidence of LOS (/1000 neonatal admissions)	4.5	19.9
Sex (males)	137 (64.0%)	66 (73.3%)
Gestational Age at birth*(weeks)	27 (24-30)	34 (31-38)
Birth weight*(g)	910 (662-1350)	2105 (1300-3190)
PNA*(days)	20 (10-40)	16 (9-28)
Central line in-situ	148 (69.2%)	16 (17.7%)
Treated for meningitis	26 (12.2%)	8 (8.9%)

* Median (IQR). PNA: postnatal age

Table-2	**GN pathogen**	**Antibiotic Resistance**	**UK**	**Greece**	p value
	Klebsiella spp	aminoglycosides (gentamicin)	4/38 (10.5%)	18/35 (51.4%)	< 0.001
	Klebsiella spp	3rd generation cephalosporins (cefotaxime)	0/10	3/12(25%)	NS*
	Klebsiella spp	carbapenems (meropenem)	0/22	1/17 (5.8%)	NS
	E. coli	aminoglycosides (gentamicin)	13/19 (22%)	4/28 (14.2%)	NS
	E. coli	3rd generation cephalosporins (cefotaxime)	2/6 (33.3%)	1/3 (33.3%)	NS
	E. coli	carbapenems (meropenem)	0/31	0/14	NS
	Enterobacter spp	aminoglycosides (gentamicin)	0/27	1/12(10%)	NS
	Enterobacter spp	3rd generation cephalosporins (cefotaxime)	2/9 (22.2%)	7/7 (100%)	0.003
	Enterobacter spp	carbapenems (meropenem)	0/22	3/6 (50%)	0.006

*NS = not significant

Conclusion:

Variations in disease burden, pathogen distribution and antibiotic resistance patterns exist between these two countries. Continuous surveillance is vital to develop effective antibiotic stewardship programmes and infection control policies.

On behalf of the Neonatal Infection Surveillance Network (neonIN)

ESPID-0722
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

HAND HYGIENE COMPLIANCE AMONG HEALTHCARE WORKERS IN NEONATAL INTENSIVE CARE UNIT

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Background: Compliance with hand hygiene (HH) protocols among healthcare professionals in NICU is recognized as one of the most important means of preventing hospital acquired infections. This study estimated HH compliance among health care workers (HCWs).

Methods: An observational study design was carried out in neonatal intensive care unit (NICU) at the University Hospital in Erzurum. The population for the survey was comprised of HCWs. Unobtrusive observation of patient contact, hand hygiene practices, and hand washing technique among HCWs. Data was collected with a health worker HH compliance form, based on World Health Organization guidelines. Well-trained infection control nurses during their routine visits made observations during December 2014. The moment the observer identified an indication; it was counted as an opportunity, which there should be a corresponding positive or negative action (hand washing).

Results: The present study included 54 observations collected from the NICU. In the research, it was observed that only 46 health personals (8.5%) washed their hands but the other health professionals who had came to the clinic for various processes didn'4 wash their hands. It was determined that the contact time between a baby and any health person had been 7.41±7.10 s and the mean hand washing time had been 12.06±8.67 s.

Conclusion: In the research, it was observed that the hand hygiene compliance of the other health professionals who was not a health staff was insufficient. According to the findings, we proposed to organize the regular educations on hand hygiene compliance.

ESPID-0871
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

HAND HYGIENE COMPLIANCE MONITORED BY VIDEO SURVEILLANCE IN A TERTIARY NICU IN INDIA

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It is well known that good compliance with hand hygiene is essential to prevent nosocomial sepsis and improve outcomes in NICU. As per CDC, the barriers to hand hygiene include lack of education, skin irritation by disinfectants, shortage of supplies, improper prioritization, forgetfulness and high workload or overcrowding. Recommendations to improve hand hygiene include ongoing education, routine observation, reminders and feedback, rewards, and avoiding irritant chemicals / overwork / crowding.
In most Indian NICUs suboptimal patient-nurse ratio due to varied reasons (migration, shortage of trained personnel, fewer NICUs etc) increases workload of nurses. With this drawback, 57 NICU nurses from 4 hospitals in Chennai were surveyed on methods to improve compliance with hand hygiene. On a score of 1 to 5, they were asked about the effectiveness of various measures, and scores of $\geq$3 were considered positive responses.
Results of nurses survey to assess best methods to improve hand hygiene compliance:

Method	Number of nurses opting		Major Comments
Ongoing education	35/57	63%	"we know, but logistics prevent compliance"
Camera surveillance	54/57	95%	"pushes us to do it despite workload' "we do not feel it offending -for the sake of patients,"
Reducing workload	46/57	81%	"not feasible in near future"
Rewards / penalties	16/57	28%	" not ethical"
Others	10/57	17%	

As recommended, video cameras were installed in one NICU, and supervisors / physicians monitored hand hygiene compliance at random. Hand hygiene compliance improved from 55% to 89% 3 weeks later. Feedback from nurses is essential to devise such infection-control protocols.

ESPID-0098
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

KNOWLEDGE AND ADHERENCE OF THE MEDICAL STAFF OF PEDIATRIC WARDS AT KING ABDULAZIZ UNIVERSITY HOSPITAL TO INFECTION PREVENTION AND CONTROL STANDARDS

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Background and aims:

Proper implementation of infection prevention and control measures is critical to prevent the possible spread of infections in health care facilities. This study was conducted to assess knowledge and adherence of medical staff to standard precautions for infection prevention and control (SPIPC) in the general pediatric wards of King Abdulaziz University Hospital, Jeddah.

Methods:

Self-administered questionnaire for WHO main SPIPC, was administered to the medical staff. For more reliable assessment, direct observation of practices of health care workers was carried out by research team on multiple occasions, and the observations of parents of admitted children on the adherence of medical staff to some of the main SPIPC were recorded by a simple abbreviated questionnaire.

Results:

Proper awareness and knowledge about infection prevention and control policy with the need for regular training were reported by 57-90% of medical staff; with higher rates of knowledge found in nurses and specialists than in residents and interns. Proper practices for the main SPIPC especially hand hygiene of the medical staff were noticed in all occasions (100%) of direct observations. Hand hygiene compliance was confirmed by observations provided by 93% of parents. The practice of wearing masks was recorded in 66.7% of direct observations and 46.5% of parental observations.

Conclusions:

In this study, the knowledge and adherence of medical staff to SPIPC was adequate (in line with international standards). Areas for improvement in some aspects of

SPIPC were identified to ensure better prevention of life-threatening emerging infections in hospital settings.

ESPID-0219
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

SOME FEATURES OF HEALTHCARE ASSOCIATED ROTAVIRUS ENTERITIS IN PRESCHOOL KIDS FROM BUCHAREST ROMANIA. 2009 – 2014

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Aim: analyze healthcare associated rotavirus enteritis in preschool children

Methods: electronic records retrieved of preschool patients discharged from 500 beds infectious and tropical diseases university clinic with a diagnosis of Rotavirus enteritis (ICD code: A08.0). Cases were allocated in two epidemiological categories as either community associated (COMMRE) (when diarrhea was present at hospital admission) or healthcare associated (HCARE) when diarrhea appeared after 2 days from hospital admission. Excessive duration of hospitalization was defined as any duration longer than the value iterated at percentile 75 of respective time series.

Results

A total of 2220 cases codified A08.0 was discharged between 2009 and 2014; from these 167 cases (7.5%) were classified as HCARE.

The prevalence of HCARE in infants under one (15.0 %) was significantly higher than in age group 1-5 years (6.6%) (RR: 2.21; 95%CI: 1.48 – 3.30; p: 0.0001351)

The prevalence of excessive duration of hospitalization in HCARE (72.5%) was significantly higher than in COMMRE (16.14 %): (RR: 4.49; 95%CI: 3.92 – 5.15; $p < 0.0001$)

Conclusions: prevention of HCARE in preschool children is important as it saves important health resources represented by excessive long hospitalization. Universal rotavirus vaccination is the best preventing intervention.

ESPID-0338
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CHARACTERISTICS AND RISK FACTORS FOR MULTIDRUG-RESISTANT BLOOD STREAM BACTERIAL INFECTION IN NEWBORNS ADMITTED IN LEVEL III NEONATAL UNIT NEW DELHI

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Background and Aim: 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 identify factors associated with its development.

Methods: 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, 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. Risk factors were evaluated using Univariate and Multivariate Logistic regression Analysis.

Results: Sixty nine out of (6.8%) out of total of 1012 blood cultures sent grew organisms. Forty three (62.3%) were MDR. Birth weight, gestation, ventilation, ventilation duration, asphyxia, surfactant administration, antenatal steroids, central catheters, total parenteral nutrition or duration of stay had no influence on occurrence of MDR. Administration of breast milk significantly reduced the incidence of MDR. Multivariate logistic regression analysis confirmed that breast milk had independent significant protective effect (O.R. 0.216 C.I. 0.072-0.646 p 0.006).

Conclusions: Multidrug-resistant blood stream infection occurred at high rates in sick neonates in the NICU. Breast milk had protective effect.

Risk Factors for MDR BSI

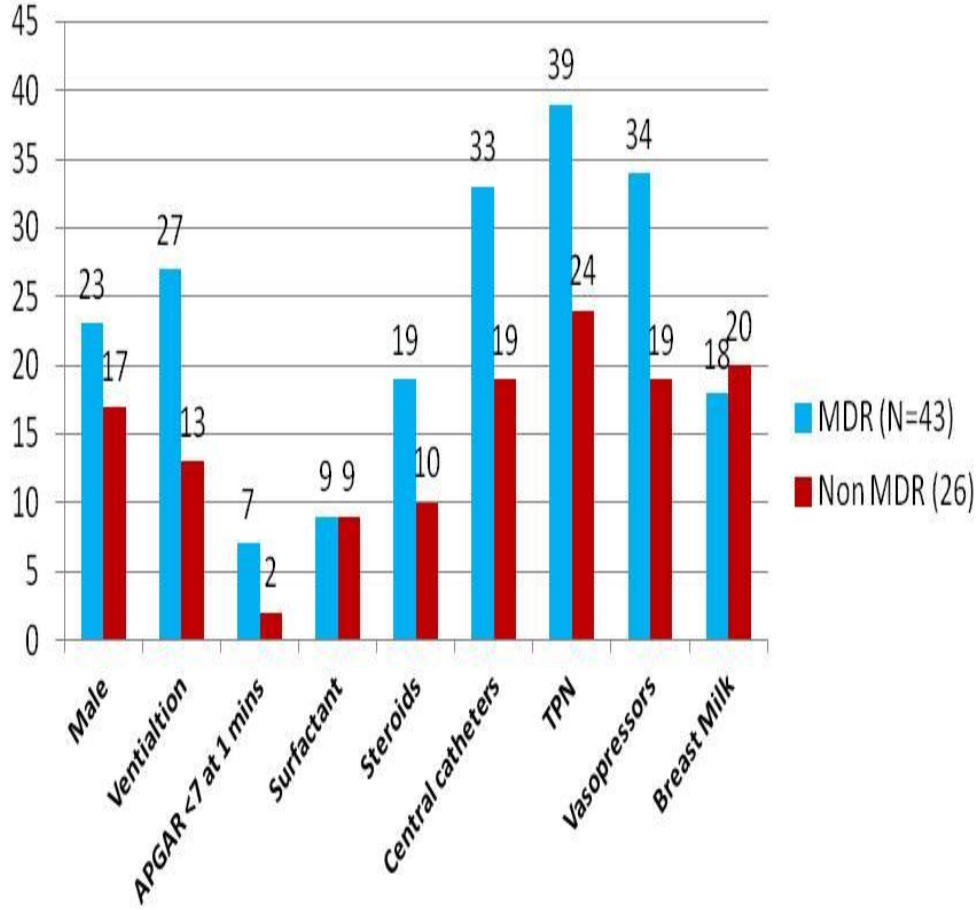

Table 1. Univariate analysis

Variable	MDR (n=43)	Non-MDR (n=26)	O.R	Confidence interval		P Value
Male Sex	23	17	0.609	0.223	1.665	0.334
Gestation (weeks)	32.33 (3.778)	32.35 (4.372)	0.999	0.883	1.130	0.983
Duration of stay (Days)	26.95 (21.881)	32.73 (21.303)	0.988	0.966	1.010	0.284
Ventilation	27	13	1.687	0.629	4.526	0.299
Duration of ventilation	4.91 (9.446)	7.54 (15.498)	0.982	0.944	1.023	0.385
Vasopressors	34	19	1.392	0.447	4.335	0.568
APGAR <7 at 1 Min	7	2	2.333	0.446	12.200	0.315
Surfactant	9	9	0.500	0.168	1.490	0.213
Steroids	19	10	1.267	0.469	3.420	0.641
Central catheter	33	19	1.216	0.397	3.721	0.732
TPN	39	24	0.813	0.138	4.779	0.818
Breast Milk	18	20	0.216	0.072	0.646	0.006

Table 2. Multivariate Logistic Regression analysis

Factors	Odds ratio	Confidence Interval		P Value
Breast Milk	0.216	0.072	0.646	0.006

Multivariate regression analysis revealed that breast milk was protective. It decreased the risk of infection with MDR organisms significantly.

ESPID-0974
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION CAUSED BY PANTOEA AGGLOMERANS: A CASE REPORT

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Background and aims: *Pantoea agglomerans*, a gram negative bacillus in the *Enterobacteriaceae* family, has been isolated from feculent material, plants and soil. Numerous *Pantoea* species are known as causative agent in plant diseases and used as biopesticides in the agricultural industry. *Pantoea* species rarely can cause pneumonia, urinary tract infections, surgical site infection and catheter-related bloodstream infections, sepsis and peritonitis.

Case: We reported a case of a 3-month-old boy who presented with growth retardation. The baby was diagnosed as truncus arteriosus type-1. Since fever developed in the boy on the 25th postoperative day, blood cultures were taken. Then *Pantoea agglomerans* was isolated in the blood cultures. The patient was diagnosed as central line-associated bloodstream infections. Central line was replaced. Vegetation was not seen by echocardiography. According to antibiogram combined with meropenem and amikacin therapy were administered for 14 days after first sterile blood culture. Bacteremia did not repeat. He was successfully treated.

Conclusions: *Pantoea agglomerans* should be kept in mind as one of the possible pathogens causing catheter-related infections.

ESPID-0841
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

NOSOCOMIAL BLOODSTREAM INFECTIONS NOT ASSOCIATED WITH A CENTRAL VENOUS CATHETER IN A GENERAL PEDIATRIC UNIT: A 10 YEARS RETROSPECTIVE STUDY

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Background and aims: Most of the studies concerning pediatric nosocomial bloodstream infections (nBSIs) target the central line-associated infections. The aim of this study was to provide data of nBSIs not associated with central venous catheter.

Patients and Methods: All the children < 18 years, without central venous catheter, hospitalized in the general pediatric unit of the Robert Debré Hospital (Paris) between October 2003 and December 2013 who had ≥ 1 nBSI were included. nBSI was defined by the presence of ≥ 1 positive blood culture for noncommensal bacteria at least 48 hours after admission.

Results: 33 children were included with a median age of 20 months (IQR1-3: 6 months-9 years). The incidence of nBSIs was 0.32 for 1000 hospitalization days. 51% of patients were hospitalized for gastrointestinal or respiratory diseases. The median duration of hospitalization before the first positive blood culture was 8 days [2;30 days]. Of the 33 nBSIs, a total of 22 (67%) were caused by Enterobacteriaceae (32% of them carrying extended spectrum betalactamases), 5 (15%) by Acinetobacter sp., 4 (12%) by Pseudomonas sp. and 4 (12%) by *Staphylococcus aureus*.

Complication occurred in eight patients (24%): 6 superficial venous thrombosis, one osteomyelitis and one muscle abscess. All the children had peripheral venous catheters that were not adapted to the child's weight in 54% of cases.

Conclusion: nBSIs may lead to severe and complex infections. A case control study is ongoing to better understand the risk factors of such infections and particularly the impact of peripheral venous catheters.

ESPID-0634
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS IN A TERTIARY REFERRAL PEDIATRIC CANCER CENTER IN RUSSIA

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BACKGROUND AND AIMS

Central lines (CLs) are essential for the modern cancer care in children. However, CLs are subject to potentially life-threatening complications, including central line–associated bloodstream infections (CLABSIs). *There are no* data available on the epidemiology of CLABSIs for pediatric hematology/oncology in Russia. The study's aim was to determine the rate of CLABSIs in the Russia's largest pediatric cancer center.

METHODS

Active surveillance for CLABSIs was conducted for 7 months (March – September 2014) in 6 units: 3 oncology, 1 immunology and 2 bone marrow transplantation departments (BMTU). CLABSIs were prospectively identified using the Centers for Disease Control's and Prevention National Healthcare Safety Network's definitions. Unit-specific rates of CLABSI (per 1000 CL days) and device utilization (DU) ratios (CL days per patient days) were calculated.

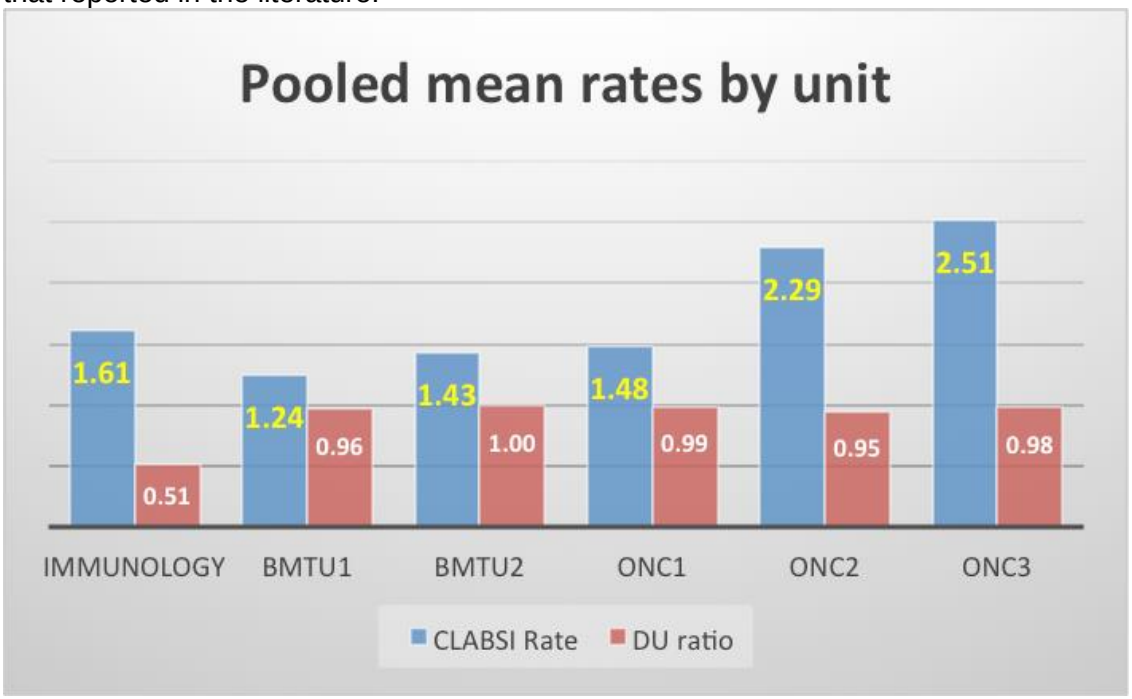
RESULTS

47 CLABSIs were detected. Unit-specific pooled mean CLABSI rates ranged from 1.24/1000 catheter days (0.0 – 3.31/1000) in the BMTU-1 up to 2.51/1000 catheter days in the oncology-3 unit (0.0 – 8.86/1000) (Figure). DU rates varied from 0.51 (immunology department) to 1.0 (BMTU-2). The most frequent microorganisms isolated were *Klebsiella pneumoniae* and *Achromobacter spp*. (19.1% each), followed

by *Escherichia coli* (10.6%), *Streptococcus pneumoniae* (8.5%) and *Staphylococcus aureus* (8.5%). There was an outbreak due to *Achromobacter spp*. from the identified single source in oncology-3 unit.

CONCLUSIONS

CLABSI rates were relatively low and similar to published data from the United States for this population with DU being high. The microbiology of CLABSI was similar as that reported in the literature.



ESPID-0366
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

QUALITY INITIATIVE TO DECREASE HOSPITAL ACQUIRED INFECTION IN A TERTIARY CARE UNIT IN INDIA : A NEONATAL COLLABORATIVE

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Background: Bloodstream infections (BSI) are an important cause of neonatal mortality worldwide and are an important contributor to healthcare infections. There is urgent need for simple and cost effective interventions to reduce hospital acquired infection especially in resource limited setting.

Methods: This multi-centric study was conducted across six centers in India as part of quality initiative in collaboration with ACCESS health international (Indian School of Business) which is supported by Institute of healthcare Improvement (Massachusetts), between January 2013 to June 2014. Neonates were screened as per modified NEOKISS criteria for hospital acquired infection. The evaluation was done by sepsis screen along with blood culture. Patient were diagnosed as Microbiological BSI,Clinical BSI and CLABSI as per standard definition.Process measures audits were done.

Results: Out of 1549 admission over 1.5 years, 220 babies were screened for suspected 406 episodes. There were 107/406 (26.36%) microbiological BSI, 112/406 (27.58) clinical sepsis and 187/406(46.06) no sepsis. Staphylococcos (26.17%) and Candida (25.23%) were predominant pathogen followed by Kleibseilla (19.62%). There was consistent decline observed in BSI rates over 18 months (14.3 to 3.5/1000 patient days) and CLABSI (40.8 to 19.1/1000 catheter days). Audit of processes measures revealed compliance for hand hygiene/glove use (66.82 %), aseptic non touch technique (65.65%) and central line insertion bundle (85.41%) along with availability of hand rub at 95% of time.
Conclusion:Quality initiative and continued surveillance of processes for infection control results in consistent decline in BSI and CLABSI rates.

ESPID-0186
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

MOLECULAR CHARACTERIZATION AND RISK FACTORS FOR CARBAPENEM-RESISTANT GRAM-NEGATIVE BACILLI COLONIZATION IN CHILDREN: EMERGENCE OF NDM-PRODUCING ACINETOBACTER BAUMANNII IN A NEWBORN INTENSIVE CARE UNIT IN TURKEY

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Background: This study examined the molecular characteristics and risk factors for nosocomial colonization with carbapenem-resistant Gram-negative bacilli (CR-GNB) in hospitalized pediatric patients in a tertiary university hospital's pediatric units in Turkey.

Methods: A prospective case-control study was performed at a university hospital in Istanbul, Turkey.

Results: A total of 1840 rectal swab specimens were collected from all 762 hospitalized children between March 2013 and October 2013. Among them, 176 (23%) patients were colonized with CR-GNB. Of these, 72 (9%) patients were colonized with carbapenem-resistant Enterobacteriaceae (CRE), 138 (18%) with CR-nonfermenter Gram-negative bacilli (CR-NF) and 34 (4%) with both. The control group consisted of noncolonized patients. The median CR-GNB colonization time was 10 days (range 1-116). The median duration of rectal colonization with CR-GNB was 8 days (range 1-160). NDM (31%) was the second most frequent carbapenemase identified in *A. baumannii* isolates, and has not previously been detected in Turkey. All of the 17 patients colonized with NDM-producing *A. baumannii* were newborns in the neonatal intensive care unit (NICU). Independent risk factors for CR-GNB colonization were age under 1 year (odds ratio [OR]: 2.0, p=0.048), nasogastric tube placement (OR:5.1, p=0.001), presence of underlying chronic diseases, (OR :3.2, p=0.001), ampicillin usage (OR:3.1, p=0.012), surgical intervention (OR:2.9, p=0.007), and carbapenem use (OR:2.5, p=0.01).

Conclusions: This is the first description of NDM in *A.baumannii* in newborn units and in our country. Carbapenem usage is a common independent risk factor for both CRE and CR-NF colonization, which underscores the importance of antibiotic stewardship programs.

ESPID-0187
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

LACTOCOCCUS LACTIS SPP LACTIS INFECTION IN INFANTS WITH CHRONIC DIARRHEA: REPORT OF THREE CASES

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Lactococcus lactis is a gram-positive, facultative anaerobic coccus which is nonpathogenic in immunocompetant humans, however number of cases of infection with *L. lactis* have been reported in recent years.

In this report, we present three infants who had chronic diarrhea and developed bacteremia and catheter related blood stream infection due to *L. lactis* spp *lactis*.

Cases: The first case is a one-year-old boy with Down syndrome and Hirschprung diseases who developed catheter-related bloodstream infection. He had been hospitalized in the pediatric surgical care unit since birth and ileostomy was carried out on his 30th day of life. The second case is five-month-old boy who underwent volvulus and ileostomy operation on his first day of life, later developed bacteremia. The third case is a six-month-old girl with chronic diarrhea developed catheter-related bloodstream infection. She had been hospitalized since sixteenth day of her life because of chronic diarrhea. All of the infections due to *L. lactis* spp *lactis* were successfully treated with intravenous vancomycin for 10 days.

Conclusion: Although *Lactococcus* species is generally known as nonpathogenic and occasionally colonize human mucocutaneous surfaces including intestine, it may invade blood stream once the mucosal barriers are damaged as in chronic diarrhea, it should be kept in mind as a potential pathogen.

ESPID-0203
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

HEALTHCARE-ASSOCIATED INFECTIONS IN NEWLY OPENED UNIVERSITY HOSPITAL IN TURKEY: RESULTS OF FOUR-YEAR SURVEILLANCE IN NEONATAL INTENSIVE CARE UNIT

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Introduction: Advances in neonatal intensive care have improved the survival of preterm infants. But these patients are at high risk of Healthcare-associated infections (HAIs). The aim of the study was to assess the rate, distribution of HAIs types and pathogens in newly opened neonatal intensive care unit (NICU). **Material and methods:** The Infection Control Team detected and recorded HAIs cases according to the Centers for Disease Control and Prevention's criteria in the NICU of Marmara University Pendik Training and Research Hospital over a four-year period following the opening. Laboratory-based HAIs surveillance was performed prospectively from 1st January 2011 to 31st November 2014. **Results:** During the study period 1301 patients hospitalized in NICU and 378 HAIs were identified. The overall HAIs rate was 29.05% and the incidence density 21.76 per 1000 patient-days. The highest infection rates and incidence density of HAIs were <750 gram and 751-1000 gram groups by birth weight in neonates. The most commonly observed HAIs types were bloodstream infection (BSI 33.1%), pneumonia (24.4%) and urinary tract infection (UTI 12.7%) and the most common 3 HAIs pathogens were *Klebsiella spp.* (27.8%), *Staphylococcus spp.* (26.2%), *Acinetobacter baumanii* (5.8%) and *Escherichia Coli* (5.8%). **Conclusions:** The incidence of HAIs in NICUs is high compared with other wards.The risk of HAIs was found to be higher neonates with a birth weight <1000 gram than the other groups by birth weight.

ESPID-0204
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

HEALTHCARE-ASSOCIATED INFECTIONS IN NEWLY OPENED UNIVERSITY HOSPITAL IN TURKEY: RESULTS OF FOUR-YEAR SURVEILLANCE IN PAEDIATRIC INTENSIVE CARE UNIT

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Introduction: Healthcare-associated infections (HAIs) are an important cause of morbidity and mortality, especially in critically ill patients in intensive care units. The aim of the study was to assess the rate, distribution of HAIs types and pathogens in newly opened 14-bed paediatric intensive care unit (PICU). **Material and methods:** The Infection Control Team detected and recorded HAIs cases according to the Centers for Disease Control and Prevention's criteria in the PICU of Marmara University Pendik Training and Research Hospital over a four-year period following the opening. Laboratory-based HAIs surveillance was performed prospectively from 1st January 2011 to 31st November 2014. **Results:** During the study period 1007 patients hospitalized in PICU and 224 HAIs were identified. The overall HAIs rate was 22.24% and the incidence density 20.71 per 1000 patient-days. The most commonly observed HAIs types were bloodstream infection (BSI 35,7%), pneumonia (21,4%) and urinary tract infection (UTI 20,5%) and the most common 3 HAIs pathogens were *Klebsiella spp.* (19.4%), *Pseudomonas aeruginosa* (13.8%) and *Acinetobacter baumanii* (12%).**Conclusions:** Our local incidence of HAIs was found to be higher than the mean rates reported in PICU studies from the developed countries. Active surveillance studies of HAIs is an essential component of infection control which may contribute to improve preventive strategies in developing countries such as Turkey.

ESPID-0205
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

HEALTHCARE-ASSOCIATED INFECTIONS IN NEWLY OPENED UNIVERSITY HOSPITAL IN TURKEY: RESULTS OF FOUR-YEAR SURVEILLANCE IN PAEDIATRIC SURGERY INTENSIVE CARE UNIT

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Introduction: Healthcare-associated infections (HAIs) are an important cause of morbidity and mortality in critically ill surgical pediatric patients. The aim of the study was to assess the rate, distribution of HAIs types and pathogens in newly opened 8-bed paediatric surgery intensive care unit (PSICU).

Material and methods: The Infection Control Team detected and recorded HAIs cases according to the Centers for Disease Control and Prevention's criteria in the PSICU of Marmara University Pendik Training and Research Hospital over a four-year period following the opening. Laboratory-based HAIs surveillance was performed prospectively from 1st January 2011 to 31st November 2014.

Results: During the study period 599 patients hospitalized in PICU and 90 HAIs were identified. The overall HAIs rate was 15.02% and the incidence density 14.76 per 1000 patient-days. The most commonly observed HAIs types were bloodstream infection (BSI 40%), pneumonia (23,4%) and urinary tract infection (UTI 17,8%) and the most common 3 HAIs pathogens were *Klebsiella spp.* (27.8%), *Acinetobacter baumanii* (13.9%), *Staphylococcus spp.* (13.9%) and *Candida spp.* (13.9%).

Conclusions: Surveillance of HAIs play a substantial role in infection control in the surgical care unit. Effective infection control programmes, such as surveillance and well organized surgical care can reduce the HAIs rates in PSICU.

ESPID-0432
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

EVALUATION OF VENTRICULOPERITONEAL SHUNT INFECTIONS IN CHILDREN

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BACKGROUND: Ventriculoperitoneal (VP) shunt is a device which is mostly used for hidrocephalus. However, infection is a common and serious complication of VP shunt that is responsible for increased mortality and morbidity.

METHODS: A retrospective study of 207 patients with VP shunt infection was performed at pediatric infectious diseases and neurosurgery department in 3 tertiary medical center in Turkey between January 2011 and September 2014.

RESULTS: A total of 207 VP shunts infections were detected during the study period. There were 118 (57%) females and 89 (43%) males with a median age of 11 months (range;1month to 204 months). At least one pathogen was identified in 112 of 207 shunt infections (54%). The most common isolated pathogen was coagulase-negative staphylococci (CoNS) in 47 cases (23%) following *Pseudomonas aeruginosa* in 17 cases (8%) and *Klebsiella pneumoniae* in 9 cases (4%). 91% of CoNS strains were methicillin-resistant. Perioperative prophylaxis with vancomycin was given to all patients. VP shunt infection occurred at a median of 32 days (range, 3 days to 48 months) after insertion of the device. 157 (76%) cases underwent shunt removal. The median duration of antibiotic therapy was 24 days (range 4 to 132 days). All the patients were successfully treated without any complication.

CONCLUSION: However the most common causative agent in VP shunt infections is methicillin-resistant staphylococci and vancomycin is considered as the preoperative prophylaxis, VP shunt infection is stil an important clinical problem in children with VP shunt.

ESPID-0462
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

STUDY OF INFECTION RISKS ASSOCIATED WITH WARD RELOCATION FOR COMPROMISED CHILDREN

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Back ground and Objective
In our hospital (Kurume university hospital), the pediatric ward removed to new building on April 2012. And old building was destructed on June 2014. Almost all of children in our ward are immunocompromised hosts. Some studies suggested that environmental infections increased after ward relocating or building destruction. So we did some strategies like sealing all windows against fungi and soilborne microbe to prevent environmental infection. But we have some patients of invasive fungal infection in 2012. The aim of this study is revealed the effect of ward relocating and building destruction to immunocompromised children at the points of environmental infection.

Methods
Between 2011 and 2013, we retrospectively investigated the number of positive blood culture samples and detected microbes on pediatric ward in Kurume university hospital to evaluate the effects of environmental change before and after the ward relocation for immunocompromised children.

Results
Total blood culture samples are 1747 (2011:546, 2012:564 and 2013:637). And positive samples are 112 (2011:43, 2012:47 and 2013:22). Comparing 2011 to 2012, there is no significance at the rate of positive blood culture. On the other hands comparing 2012 to 2013, the rate of positive blood culture has decreased ($p<0.05$).

Conclusion
Relocating to new building decrease environmental infection. On the other hand, ward relocating and hospital destruction make candida sp infection increase.

ESPID-0320
HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CLINICAL CHARACTERISTICS, MICROBIOLOGY, AND ANTIMICROBIAL TREATMENT OF CEREBROSPINAL FLUID (CSF) SHUNT INFECTIONS IN COSTA RICAN CHILDREN

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BACKGROUND AND AIMS: There have been few publications about CSF shunt infections in Latin American children, and none from Central America. Our main objective was to describe the clinical characteristics, microbiology, and treatment of children with CSF shunt infections admitted at the only pediatric tertiary referral hospital of Costa Rica.

METHODS: Retrospective descriptive study of children <13 years of age discharged with a diagnosis of CSF shunt infection, period January-1-2006 to December-31-2011.

RESULTS: 94 episodes of CSF shunt infections in 84 patients were analyzed. Median age was 32.4 (0-148.5) months, 64% were male. The three most common underlying conditions were congenital hydrocephalus (54.3%), myelomeningocele (31%), and prematurity (24.5%). 47% of children developed their infection after the initial CSF shunt insertion. The most commonly prescribed intravenous antibiotics at admission were vancomycin (86.2%) cefotaxime (60.6%), and ceftazidime (29.8%), and mean length of therapy was 3 weeks. Intraventricular antibiotics were required in 10.6%. CSF cultures were positive in 77%, predominantly by: *S.epidermidis* (35.1%), *S.aureus* (19.1%; 44% MRSA), *P.aeruginosa* (4.3%), *S.marcescens* (3.2%), *K.pneumoniae* (2.1%), and *E.cloacae* (2.1%). Among the most common associated complications, nosocomial infections were documented in 33%, of which 35.5% were respiratory, 32.3% were in CNS (EVD-associated), and 22.6% in bloodstream (CVL-associated predominantly). No deaths occurred.

CONCLUSIONS: In our experience, empirical combined antibiotic therapy for children with presumed CSF shunt infections should be vancomycin plus ceftazidime or cefotaxime, until cultures define modifications to treatment. CSF shunt infections are associated with prolonged lengths of hospitalizations, antibiotic use, and high rates of nosocomial infections.

ESPID-0671
HIV/AIDS

SAFETY OF ZIDOVUDINE/LAMIVUDINE SCORED TABLETS IN CHILDREN WITH HIV INFECTION IN EUROPE AND THAILAND

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Background and aim

Zidovudine (ZDV)/lamivudine (3TC) is a first-line NRTI backbone option for children with HIV infection, available as a fixed-dose combination scored tablet of 300mg ZDV/150mg 3TC for weight ≥14kg. This pharmacovigilance study assessed long-term safety of the tablets.

Methods

Fourteen cohorts (ethics approved) provided data on patients <18 years who took scored tablets in 2008-2012. Rates of Division of AIDS (DAIDS) grade ≥3 adverse events were estimated for hepatobiliary and haematological disorders. Clinical adverse events and discontinuation reasons were described.

Results

Of 541 patients, 38% (203) were from Thailand, 18% (96) from UK/Ireland and 17% (90) from Russia. Median age was 10 years [IQR 7.2-13] at drug start, 46% were male, 21% were ART-naïve and 60% had previously taken ZDV and 3TC; median CD4 count was 660 cells/mm^3 [416-972]. 90% (350/388) with weight and dose were on a licensed dose (Table). Median duration on scored tablets was 30 months [17-56].

In general, DAIDS grade ≥3 hepatobiliary and haematological events were uncommon (Table). Adverse events considered causally related to the tablets were reported for 5 patients aged <10 years on licensed doses (all haematological; one serious but resolved) and 5 with missing weight/dose (all non-serious). Overall 43% (233) discontinued the tablets by last follow-up, most commonly due to treatment simplification (31%) or treatment failure (18%).

Conclusions

Scored ZDV/3TC tablets, both licensed and off-label, appeared to be well tolerated with few side effects in HIV-infected children in Europe and Thailand.

Table: Number and rate of first DAIDS grade ≥3 events by dosing group for children taking scored tablets of ZDV/3TC

	Age <10 years and weight ≥14kg on licensed dose (n=161)	Age ≥10 years and weight ≥14kg on licensed dose (n=189)	Weight ≥14kg on unlicensed dose (n=30)	Weight <14kg (n=8)	Missing weight or dose (n=153)
	n with grade ≥3 result / n with result available (rate per 100 person years (95% CI) – not given if no events or if ≤20 patients with test results available)				
ANC	5/143 (1 (0,3))	6/162 (2 (1,3))	4/20 (-)	0/6 (-)	1/95 (0 (0,2))
ALT	2/143 (0 (0,2))	2/164 (0 (0,2))	0/22 (-)	0/7 (-)	11/93 (4 (2,6))
AST	1/122 (0 (0,2))	0/122 (-)	0/15 (-)	0/6 (-)	1/88 (0 (0,2))
BIL	5/138 (1 (0,3))	5/154 (1 (0,3))	1/20 (-)	1/6 (-)	0/85 (-)
HB	5/140 (1 (0,3))	4/161 (1 (0,3))	0/19 (-)	0/6 (-)	0/67 (-)
PLT	2/132 (1 (0,2))	2/151 (1 (0,2))	0/17 (-)	0/6 (-)	1/87 (0 (0,2))
WBC	0/140 (-)	1/161 (1 (0,1))	0/19 (-)	0/6 (-)	0/90 (-)

ANC – absolute neutrophil count; ALT – alanine aminotransferase; AST – aspartate aminotransferase; BIL – bilirubin; HB – haemoglobin; PLT – platelet count; WBC – white blood cell count

ESPID-1042
HIV/AIDS

THERAPEUTIC CAMPS IN HIV INFECTED ADOLESCENTS

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Background and Aim: Human Immunodeficiency Virus (VIH) infection in adolescence is a challenging chronic disorder, and as any disease in this age faces obstacles like the acceptance of the disease, adherence to therapy and society integration. The search for adequate interventions is constant, and the therapeutic camps emerge as a promising field. The authors describe the methodology of a therapeutic camp for HIV infected adolescents, along with the results of the evaluation performed by the adolescents.

Material and Methods: Therapeutic camps were performed once a year, in 2013 and 2014 with HIV infected adolescents.

Results: Two camps were performed for a period of three days, organized by a multidisciplinary team (physicians, nurses, psychologists, kindergarten teachers, social workers and volunteers). Eighteen and 19 adolescents participated, in 2013 and 2014 respectively, ages ranged from 12 to 18 years. In the camps, workshops are performed on issues related to HIV infection (adherence to therapy, legal issues, sexuality and affectivity) with encouragement of interaction and sharing experiences. In addition outdoor and recreational activities are performed to encourage relationships between peers. The camps were evaluated in a strongly positive manner by adolescents, and the main positive were the possibility of new friendships and learning more about HIV infection.

Conclusions: Previous studies demonstrated that therapeutic camps are effective interventions in adolescents with HIV infection, with improvement in autonomy, acceptance and responsibility when facing the disease.

ESPID-1049
HIV/AIDS

PERINATAL EXPOSURE TO ANTIRETROVIRAL THERAPY IN HIV UNINFECTED CHILDREN

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Background: Mother-to-child HIV transmission hugely decreased in the last 20 years, with an increase in the number of uninfected children perinatally exposed to antiretrovirals(ARV). Although some adverse effects are well described, the long term effects of exposure remain unknown. The aim of this study was to evaluate the adverse effects of perinatal exposure to ARV therapy in uninfected children.**Methods:** Prospective reevaluation of HIV uninfected children exposed to ARV therapy in our unit, between 2001 and 2011.**Results:** One-hundred thirty five children were identified and follow-up was possible in 30 (22%), 67% of which male. Ages ranged from three to 13 years (mean of 6,8 years). Mean maternal age at birth was 29,1 years, 29 infected with HIV type 1. The pregnancy was monitored in 82%, and 53% initiated antiretrovirals in the first trimester, 7% in the second trimester, 10% in the third trimester and in 30% the timing of initiation was unknown. At birth three had cardiac defects and one a single kidney. Four had low intelligence quotient(IQ) and seven children were diagnosed with ADHD. Nine performed MRI(normal in eigth, one with groove enlargement). One child had anemia and measurement of lactate was normal in 15. **Conclusions:**As mentioned in other studies contact and reevaluation of the HIV uninfected children exposed to antiretrovirals was difficult. In the evaluation performed no significant alterations were found so far. Low IQ and ADHD appeared to be more prevalent than in general population.Long-term follow-up of these children is important for a better knowledge of ARV safety.

ESPID-1027
HIV/AIDS

ANTIFUNGAL RESISTANCE OF CANDIDA SPECIES ISOLATED FROM ORAL CAVITY OF HIV+ MEXICAN CHILDREN AND TEENAGERS.

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Background. HIV+ children undergoing highly active antiretroviral therapy show increases in oral colonization by non-albicans candida species. If HIV+ teenagers show this same circumstance is unknown. Objective. To assess species of Candida colonizing oral cavity of HIV+ teenagers and HIV+ children, and establish the degree of resistance to antifungal drugs in both groups. Method: 25 HIV+ patients (≤18 years old) undergoing HAART, referred from General Hospital of Tijuana, Baja California, Mexico were included. Two study groups was formed: children group (≤10 years), composed of 16 patients (8 girls; 8 boys); and teenager group (> 10 years) consisting of 9 patients (6 girls; 3 boys). Previous informed consent a sample of oral mucousa was taken in all patients and seeding in Sabouraud dextrose/chloramphenicol agar. The specie was confirmed by biochemical methods (Microscan, Siemens Panel). The antifungal susceptibility was stablished using the ATB Gallery fungus 3 (bioMérieux).Research protocol was approved by ethics committees of participating institutions Results: In the children group were identified: *C. albicans*, *C. glabrata*, *C. krusei*, *C. lypolitica* and *Candida sp*. 71.4% of these strains showed resistance to Amphotericin B. In the teenager group were identified: *C. albicans*, *C. Krusei*, *C. tropicalis* and *Candida sp*. 75% of strains showed resistance to fluconazole and 63.3% were to Amphotericin B. Conclusions: non-albicans species of candida are most prevalent in oral cavity of HIV+ Mexican children and teenagers. Candida species isolated from oral cavity of HIV+ Mexican children and teenagers showed a surprisingly high resistance to amphotericin B.

ESPID-0089
HIV/AIDS

FOCAL LESIONS OF THE SPLEEN IN HIV POSITIVE CHILDREN

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Background and aim:

The number of splenic focal lesions which were defined during ultrasound examination of HIV –positive children in our clinic increased recently. 2 groups of lesions considered in this retrospective analysis: hypoechoic and milliary hyperechoic focuses (calcification). Tuberculosis infection is one of the main causes of these lesions.

Among 253 HIV positive children who were examined in our hospital during February 2013 - November 2014 4% had focal lesion of spleen.

Material and methods:

Cases of 11 HIV – positive patients with focal lesions of spleen who were treated in our clinic presenting during the period February 2013 - November 2014. All focal lesions of spleen were found during ultrasound examination.

Results:

Among 11 patients 6 were female and 5 male, average ages was 7 years (rank 0-16 yy.)

Splenic lesions were presented: hyperechoic focuses in 73% and multiple hypoechoic- in 27 %

Among HIV-positive children with hypoechoic lesions all 3 patients had a pulmonary TB: one of these patients had a Hodgkin's Lymphoma in co-morbidity. Among children with calcification 88 % had a TB infection.

Discussion:

Focal lesions of spleen could be manifestation of extrapulmonary TB or evidence of TB in the past, but procedures such as ultrasound-guided fine-needle aspiration (FNA) or splenic biopsy might be helpful for verification of diagnosis.

On the other hand abdominal ultrasound is the less costly and noninvasive investigation for a definition of lesions in spleen and could be widely using for screening and management of treatment TB, especially for HIV-positive patients.

ESPID-1056
HIV/AIDS

INFANT COMBINED ANTIRETROVIRAL PROPHYLAXIS TO REDUCE PERINATAL HIV TRANSMISSION: A NATIONAL SURVEY

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Background: Post-exposure antiretroviral prophylaxis for infants born to HIV-infected women is an important component in the prevention of mother-to-child transmission (MTCT) of HIV. Combination prophylaxis in neonates (CNP) is recommended in high-risk situations.
Aim: To investigate the factors associated with the use of CNP and with MTCT in a non-breastfeeding population.
Methods: A national population-based observational study of infants born to HIV-infected women between 2011 and 2013 that received CNP.
Results: Among 704 mother-infant pairs, any neonatal prophylaxis was administered to 697 (99%) infants; 104 (14,9%) received CNP. Eighty received triple-drug (zidovudine+lamivudine+nevirapine) and 24 two-drugs (13 zidovudine+lamivudine; 9 zidovudine+nevirapine; 2 zidovudine+lopinavir). In CNP group, 13 (12,5%) mothers had no antenatal or intrapartum antiretroviral prophylaxis, 16 (15,4%) had only intrapartum prophylaxis, 58 (84%) with antiretrovirals in pregnancy were viraemic near delivery, 12 (16,7%) with CD4 <200 cells/ml, 64 (62,1%) delivered by nonelective caesarean/ vaginal delivery. We had 4 infected infants. Of them, 3 with inappropriate maternal vigilance; 2 had perinatal positive DNA polymerase-chain-reaction (PCR) and in the others, mothers had a late diagnosis in pregnancy and high viral load near delivery, with absence/ <4 weeks of antiretroviral therapy.
Conclusions: In our sample, most common high-risk factor to CNP was lack of mother vigilance. A high viraemia in treated mothers focus the importance of adherence reinforcement. We cannot speculate about the inefficacy of the CNP. Two infected infants must have acquired HIV infection in utero. In the others, CNP can have induced a false negative perinatal PCR, albeit prenatal transmission.

ESPID-1053
HIV/AIDS

HIV VERTICAL TRANSMISSION AT UNIVERSITY HOSPITAL OF SALAMANCA

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INTRODUCTION:

Vertical transmission is the main way of infection of human immunodeficiency virus (HIV) in children in developed countries. It has markedly reduced since 1994, due to the successive introduction of preventive measures in mother and child.

PATIENTS - METHODS:

We performed a retrospective study of all HIV-1 mother-infant pairs born between January 1999 to December 2014 in Complejo Asistencial Universitario de Salamanca. They have been compared with historical cohort of infected patients since 1988.

RESULTS:

A total of 46 mothers and children were included, 98% of the children were uninfected. 7% of the mothers had an older son with vertical transmission infection. 13% of pregnancies were not controlled. 15% did not receive antiretroviral therapy during the gestational period, 13% zidovudine monotherapy or combination therapy with two reverse transcriptase inhibitors and 54% with Highly Active Antiretroviral Therapy (HAART). In 65% planned caesarean section was performed. 63% received chemoprophylaxis and in all neonates with available data prophylactic treatment was performed with zidovudine. 100% of infants received artificial feeding.

From 1988 to 2014 there were 9 HIV patients infected. One mother was diagnosed before pregnancy and didn't receive therapy during pregnancy. The rest of the children were diagnosed after one year old; 22% presented suggested symptoms in a study 33% after direct familiar diagnosis.

COMMENTS:

VIH vertical transmission rate has been reduced from 0.06% to 0% since 1988 untill 2000. It is possible to reduce the HIV vertical transmission in a control population to zero. This proves the efficacy of prevent measures.

ESPID-0332
HIV/AIDS

SEROCONVERSION AND ACCEPTABILITY OF ONE-DOSE IMMUNIZATION WITH NEISSERIA MENINGITIDIS C CONJUGATED VACCINE AMONG HIV-EXPOSED AND UNEXPOSED UNINFECTED CHILDREN, IN RIO DE JANEIRO, BRAZIL

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Background –HIV-exposed but uninfected children (HEU) have a higher mortality rate than HIV-unexposed and uninfected children (HUU). There is some evidence that HEU children have aninferior immune response to vaccines when compared to HUU; however, other reports contradict this finding. The aim of this study is to compare the seroconversion rate for *Neisseria meningitidis* C conjugate vaccine (Novartis; C Polysaccharide/CRM_{197}) (MenC) between HEU and HUU children.

Methods – HIV-uninfected patients, aged 2-18 years oldwere enrolled. Seroconversion was defined as increase of 2 dilutions in serum bactericidal assay (with human complement) titer, as compared to preimmunization titer. Patients were evaluated for adverse events during the immunization, at 20 minutes, and after 3 days and 7 days.

Results - 50 children were enrolled: 24 HEU and 26 HUU. Mean age was 10 years. 29 were male. Mean body mass index (BMI) was 17.7. A total of 8 (16%) children had minor adverse reactions (local pain): 3 among HEU and 5 among HUU, p=0.74In all but one volunteer, the pain faded 7 days after the immunization. No major adverse event was observed. The seroconversion was observed in 76% of the volunteers: 83% among HEU and 69% among HUU, p=0.24.

Conclusion – The MenC seroconversion was higher among HEU, although this was not statistically significant. The vaccine was well tolerated. In this study, there was no evidence for an inferior immune response to MenC among HEU children.

ESPID-1031
HIV/AIDS

PROMOTING ADHERENCE TO ANTIRETROVIRAL THERAPY (ARVT) REMAINS AN ESSENTIAL AND CHALLENGING ELEMENT OF MODERN HUMAN IMMUNODEFICIENCY VIRUS/ACQUIRED IMMUNE DEFICIENCY SYNDROME (HIV/AIDS) CARE

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Introduction: Good adherence to ARVT is necessary to achieve the best virologic response, lower the risk of drug resistance and reduce morbidity and mortality.
Case report: Adolescent 15-years old, HIV infected (vertical transmission), did chemoprophylaxis with Zidovudine (AZT), began ARVT with Lamivudine (3TC), Stavudine (D4T) and Nelfinavir by 3-months old. Therapy was suspended at 13-months old, because of virologic failure. The ARVT was re-introduced at 3-years old associating Nevirapine and Lopinavir/Ritonavir to DT4 and 3CT, because of elevated viral replication and low CD4 count, and it was maintained untill 7-years old. At this age, because of poor compliance and drug resistances, she iniciated Tenofovir, Enfuvirtide and AZT associated to 3TC and Lopinavir/Ritonavir, apparently well tolerated but showing an abcense of virologic and immunologic response after 12 weeks. At 8-years old Darunavir and Etravirine *off label* were also iniciated and a gastrostomy was performed and maintained for 2-years. Then she went on a program of directly observed therapy. She is illegible for therapeutic with Maraviroc. At 12-years old Etravirine was suspended because of resistence and she maintained the previous therapy untill now (20636 copies/ml and CD4 258/mm3). She has participated in summer camps to draw attention to the importance of therapy, with apparently improvement.
Conclusion: Before switching ARVT it's essential improve adherence, by raising awareness of teenagers about their disease and give them social and structural support. In this case, next step could be starting integrase inhibitors, however it's necessary to be careful due to poor compliance and few therapeutic options.

ESPID-1017
HIV/AIDS

FIRST ANTIRETROVIRAL TREATMENT FAILURE

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Introduction

Antiretroviral treatment (ART) is a long term therapy for HIV infection with a high risk of resistance emergency leading to treatment failure. Durability of sustained viral suppression is an important goal for ART.

Methods

Retrospective cohort study of HIV-infected children, who took first-line ART for at least six months with three or more fully effective drugs. Exclusion criteria: use of unboosted protease-inhibitor or three nucleoside-reverse-transcriptase-inhibitors. CDC definition for virological failure (VF) was adopted. Data was analysed using Excel 2013®

Results

Data of 80 HIV-infected children under treatment were analysed. Thirty-one met the eligibility criteria with a median age of 10-years; 15 males. Median age at diagnostic was 2,5 years and 77% were infected through mother-to-child transmission.

Group-1, with VF (n=12): median time to VF 10-months (6-40 months); median age at ART initiation 18-months; poor/irregular adherence to treatment in all.

Group-2, with no VF (n=19): median age at ART initiation 84-months; median time of follow-up 46-months.

All caregivers were biological parents or family members except for one case in Group-2. Both groups had similar baseline viral load (log 5) and immunological status.

Ten out of 16 children on lopinavir-ritonavir and 2/9 on efavirenz based ART had poor adherence/VF.

Conclusion

All patients with good adherence achieved indectable VL with first-line combined ART. Those with poor adherence/VF started ART at a younger age and were predominantly treated with lopinavir – perhaps due the poor palability of the oral solution. Actively intervening in adherence related issues is actually the crucial limitation factor of ART success.

ESPID-0867
HIV/AIDS

EARLY INFANT DIAGNOSIS: SCALING-UP THE PROGRAM TO PREVENT MOTHER-TO-CHILD TRANSMISSION (PMTCT) OF HIV IN EQUATORIAL GUINEA (GQ).

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Background: In the last years great efforts have conducted to implement the PMTCT program in GQ and early infant diagnosis (EID) is considered one of the most priority interventions needed. The aim of this study was to evaluate the rates of mother-to-child HIV transmission based on an EID pilot program.

Methods: A prospective observational study was performed in Hospital of Bata, Bata, GQ. Clinical characteristics of HIV-1-infected mothers and exposed infants were recorded. Dried blood spots (DBS) for EID were collected from November 2012 to December 2013. HIV-1 genome was detected using Siemens VERSANT-HIV-1-RNA 1.0 kPCR assay (kPCR). Infants were considered as HIV-1 infected after a first positive result confirmed with a second analysis in new specimen.

Results: Sixty-nine infants were included, all born by vaginal deliveries. Median age of the mothers at delivery was 22 years (IQR 19-35). Fifty-four women (79.5%) had WHO clinical stage 1 and sixteen (24%) did not receive any antiretroviral treatment (ART) during pregnancy. The median age at the time ofDBS test was 2.3 months (IQR 1.2-4.5). Thirty infants (43.5%) had received postnatal antiretroviral prophylaxis. HIV-1 infection was confirmed by kPCR in 2 infants, with a mean viraemia of 18,840 HIV-1-RNA copies/ml. Thus, the rate of HIV transmission was 2,9%. The two infants infected started HAART before any symptoms were observed.

Conclusions: The rate of perinatal HIV transmission was low in concordance with the moderate rate of women receiving ART. The pilot program leads to early identification of HIV-infected infants before any disease progression.

ESPID-0874
HIV/AIDS

VIROLOGICAL OUTCOMES IN HIV-INFECTED CHILDREN ON ANTIRETROVIRAL TREATMENT (ART) IN GUAYAQUIL, ECUADOR

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Background: Long-term virological suppression (LTVS) in children is required to assure immunological recovery and to prevent disease progression. However LTVS is problematic given the limited availability of drugs, toxicities, difficulties with adherence and risk of drug-resistant virus selection. The aim of this study was to evaluate long-term virological outcomes in a cohort of HIV-infected children.

Methods: Retrospective cohort analysis of HIV-infected children enrolled in care (1998-2014) in *"Hospital del Niño Francisco Ycaza-Bustamante"*, Guayaquil, Ecuador. Epidemiological and clinical characteristics of patients and virological outcomes according to type of ART were assessed.

Results: A total of 477 children were included, with a median age of 10, IQR 6.8-12.5 years. Forty hundred and sixty-five children started HAART (median age of 2.6, IQR1.2-5.2 years): 249 (53.5%) with two nucleoside reverse transcriptase inhibitors (NRTI) plus non nucleoside reverse transcriptase inhibitor (NNRTI) and 202 (43.4%) with 2 NRTIs plus an protease inhibitor (PI). CD4 count/percentage increased from first assessment (median 567/mm^3 [279-910]; 13.8% [8-20]) to the last visit (median CD4 839/ mm^3 [598-1184]). Median follow-up: 6.4 [2.8–9.0] years. Among 278 patients in first treatment schedule, 193 (74.8%) had HIV RNA < 50 copies/ml in last visit; 127 (26.6%) required second and 62 (13%) third line treatments (56.7% and 51,6% with HIV RNA < 50 copies/ml in last visit, respectively). No ART regimen was associated with an increased risk of antiretroviral switch.

Conclusions: Long-term virological suppression is challenging in children. The experience of this cohort may raise concerns faced by other children in Latin-America.

ESPID-0801
HOST-PATHOGEN INTERACTIONS

CHARACTERIZATION OF YEASTS ISOLATES FROM INFANT FECES ON THEIR POSITIVE AND NEGATIVE TRAITS

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The human digestive tract harbors a complex collection of microorganisms which is known as gut microbiota (bacteria, yeasts, fungi…). This microbiota is now considered as an entire organ because of its activity and the very important roles it plays since the beginning of its establishment, immediately at birth. Twenty yeast isolates were recovered from infant feces and identified using API 32C identification system and sequencing the D1 domain of the 26S rDNA. Nineteen isolates were assigned to the genus *Candida* and one isolate to the species *Saccharomyces cerevisiae.* When checked for their antibacterial activity against three pathogenic bacterial strains, only *C. parapsilosis* p48l1 and *C. albicans* p51l1 wre positive. Among all the isolates, only *C. parapsilosis* p48l1 has demonstrated α- hemolytic activity after 24 h incubation. The adhesion assay to Caco-2 cells has demonstrated that the most adherent strain was *S. cerevisiae* p9l1 with 6.56 % adherent level. The two *Candida* strains were cytotoxic. Nevertheless, *C. parapsilosis* p48l1 was more cytotoxic than *C. albicans* p51l1. For *S. cerevisiae* p9l1, no significant difference was noted compared to the control (non infected Caco-2 cells). All the strains were resistant to acidity and to bile salts. The auto-aggregation rate of *S. cerevisiae* was 22 % and 45 % after 2 and 4 h of incubation respectively. This strain showed also a co-aggregation potential with two pathogenic bacteria. The co-aggregation was stronger and faster with *E. coli* (38 %) than with *S. aureus* (23 %) after 2 h of incubation.

ESPID-0608
HOST-PATHOGEN INTERACTIONS

CLINICAL AND GENETIC CHARACTERISTICS OF ENTEROVIRUS INFECTIONS IN CHILDREN: A SINGLE CENTER ANALYSIS IN KOREA

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Background and aims

Enteroviruses (EVs) can cause a wide spectrum of illnesses ranging from a summer cold to myocarditis and meningitis. This study was aimed to investigate the clinical significance of various genotypes of EV infections in children during recent year.

Methods

We collected the stool samples from the pediatric patients with suspected EV infections Inha University Hospital from March 2014 to January 2015. EV detection and genotype identification were performed by real-time RT-PCR and semi-nested RT-PCR at Incheon Research Institute of Public Health and Environment. Phylogenetic trees were constructed by neighbor joining method.

Results

A total of 322 samples were collected during study period. 88 patients (27.32%) were diagnosed with EV infections, 56 genetic sequences of EVs were identified and 32 samples were untypeable. The median age of patient was 3.18 years (0.1-16). Nonspecific febrile illness (34, 38.64%) was the most common clinical manifestation; herpangina (23, 26.14%); hand-foot-mouth disease (21, 23.86%) and meningitis (10, 11.36%). 12 genotypes of EV were identified; coxsackievirus B5 (16, 18.18%), coxsackievirus A16 (11, 12.50%), coxsackievirus A2 (8, 10.00%), enterovirus 71 (6, 6.82%) and coxsackievirus A14 (2, 2.27%). There was no complicated case caused by enterovirus 71. Phylogenetic relationship tree revealed 6 distinct genogroups among 56 EVs.

Conclusions

Diverse EV genotypes circulated among symptomatic children during the study period. These data will provide the scientific evidence for the diagnostic approach of EV infection.

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ESPID-0826
HOST-PATHOGEN INTERACTIONS

COMPARISON IN RISK FACTORS OF ACUTE PYELONEPHRITIS WITH VIRULENCE FACTORS OF ESCHERICHIA COLI IN PEDIATRIC URINARY TRACT INFECTION

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Background: *Escherichia Coli* (*E. coli*)is the most predominant pathogen of urinary tract infection (UTI) in children. The characteristics of phylogenetic groups and virulence factors of *E. coli* were not evaluated clearly in the children with UTI.

Methods: The urinary *E, coli* strains were isolated from the 33 pediatric patients of UTI and analysed by multiplex polymerase chain reaction method. The phylogenetic distribution and virulence factor genes of *E. coli* of UTI groups were compared with that of non-UTI groups. And the contributing risk factors of UTI were evaluated clinically.

Results: The male to female ratio of 33 patients was 1.6:1. Most Uropathogeic E.coli strains were belong to phylogenetic group B2. Type 1 fimbriae and S family fimbriae were present in all of the strains. Although the frequency of P family fimbriae was higher in non-vesicoureteral refulx(VUR) group, there were no significant differences between two groups. On the ^{99m}TC-dimercaptosuccinic acid scan, the renal cortical defect were observed in 79.0 % and VUR in 30.4 % of all patients.

Conclusions: The risk factors, such as male sex, VUR and the virulence genes of *E. coli,* were seemed to play a critical roles in children with UTI. But they were not statistically significant. Further studies should be accomplished to evaluate the multiple risk factor interaction more.

ESPID-0161
HOST-PATHOGEN INTERACTIONS

ORAL CYCLOSPORIN TREATMENT FOR SEVERE ATOPIC DERMATITIS ASSOCIATED WITH KAWASAKI DISEASE IN A COSTA RICAN GIRL

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BACKGROUND AND AIMS: There are very few publications in the literature about the development or worsening of atopic dermatitis (AD) and other allergic diseases in children after suffering Kawasaki disease (KD), and none have come from Latin American countries.

METHODS: We report a girl that required cyclosporin for treating her KD-associated severe AD.

CASE: A 5-yr-old girl was admitted to our only national tertiary referral children's hospital with a classic KD. She was treated with IVIG (2 g/kg) and aspirin (100 mg/kg/day) that was then switched to 5 mg/kg/day for 14 weeks. Admission echocardiogram (ECHO) was normal and she went home on day 3. Two weeks after, a repeat ECHO was normal; however, a 3rd ECHO at 8 weeks evidenced a right coronary artery dilatation that disappeared on repeat ECHO's. Five months after her KD, she developed difficult-to treat AD, with lesions predominantly in face, thorax, abdomen and extremities. Oral loratadine and hydroxyzine, plus topic betamethasone, fucidic acid, and astringent solution were started. Multiple AD relapses and episodes of secondary skin bacterial infections occurred and were treated with different cycles of oral and intravenous antibiotics. As no clinical response was seen, oral cyclosporin was started for her severe AD. Over the next months, she improved clinically and required cyclosporin for 2 years and then was stopped.

CONCLUSIONS: This is the first report from Central America of KD-associated severe AD requiring cyclosporine treatment. Studies are needed to determine the incidence of AD in Latin American children after suffering KD.

ESPID-0267
HOST-PATHOGEN INTERACTIONS

CLINICAL CHARACTERISTICS, ETIOLOGY, AND MANAGEMENT OF STEVENS-JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN) IN COSTA RICAN CHILDREN

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BACKGROUND AND AIMS: In Latin America, pediatric infectious disease specialists usually get involved in the etiologic/differential diagnosis and treatment of children with SJS and TEN. To date, there have been no English-language publications about these diseases in Central American children. Our main objective was to describe the clinical characteristics, etiologies/triggers, and management of children with SJS and TEN who were admitted at the only pediatric tertiary academic referral hospital of Costa Rica.

METHODS: Retrospective descriptive study of children <13 yrs of age with a hospital discharge diagnosis of SJS or TEN, period January-1-1997 to October-31-2013.

RESULTS: 23 patients were analyzed, of which 19(83%) had SJS, 3(13%) NTE, and 1(4%) SJS/TEN overlap. Median age was 5.5 yrs, 52% were girls. Mean hospital length was 13.9 (3-35) days. Among the possible etiologic or triggering factors, medications were identified in 92% (of which 52% were anticonvulsants and 32% antibiotics, predominantly amoxicillin and TMP-SMX), an infectious cause in 4% (*Mycoplasma pneumoniae*), and undetermined in 4%. Intravenous steroids and IVIG were given in 35% and 57%, respectively; 70% of patients required $\geq$1 antibiotic during their hospitalization, being the most commonly used clindamycin, cefotaxime, vancomycin or aminoglycosides. Ocular compromise occurred in 80% of patients. 5 (22%) required PICU admission. Mortality rate was 13%, predominantly due to infectious and metabolic/electrolytic complications.

CONCLUSIONS: SJS and TEN are associated with significant morbidity in Costa Rican children. In this study infectious etiologies were uncommon as causes of SJS and TEN; however, prospective studies are required to establish better their role.

ESPID-0404
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

BACTERIOLOGICAL PROFILE AND RESISTANCE PATTERN OF NEONATAL SEPSIS IN LAST 5 YEARS IN A TERTIARY-CARE CENTRE NICU IN NORTH-EAST INDIA: REDUCING TREND OF MRSA

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Objective: 1.To detect trend of growth of microorganism in Nicu 5- years apart

2.Detect change in resistance pattern of isolated organism

3. Determine incidence of resistant organisms reported by CDC to be of increased threat level.

Design: Retrospective observational study. Study subjects- inborn and outborn babies referred from neighbouring 5 districts and 2 states. Blood-culture drawn according to AAP guidelines for neonatal sepsis. Antibiotic resistance detected by Kirby-Bauer disc diffusion method. Results compared between period A (January to December 2008)and period B (January- December 2013).

Results: Staphyloccus aureus was predominant organism in both periods among inborn (48.61% and 57.6%; p-value .17) and outborn babies (51.85% and 66.67%; p-value .28) followed by Klebsiella sp. **Isolates with methicillin resistance was decreased significantly**(62.27% to 39.47%; p-value .008). For Klebsiella, resistance has increased significantly in last 5 years for Piperacillin-tazobactam (14.3% to 46.16%; p-value .03) and meropenem (0% to 38.47%; p-value 0.002).

Among staphylococcus 53.3% of outborn isolates and 39.47% of inborn isolates were MRSA. **Sixty-five% inborn GNB and 56.25% outborn GNB were ESBL producers. Additionally 12.5 % of inborn GNB and 31.25% outborn GNB were carbapenem resistant.** Fifty-seven% acinetobacter isolates from inborn babies were carbapenem resistant and the rest multidrug resistant. Among outborn isolates all acinetobacter were carbapenem resistant.

Conclusion: There is rise in resistance for antibiotics among Klebsiella isolates with growth of ESBL producing and carbapenem resistant Klebsiella,. Rational antibiotic policy with stewardship both within the institute and peripheral health care centres is necessary to prevent further increase of resistance.

ESPID-0403
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

THE BACTERIOLOGICAL PROFILE OF NEONATAL CONJUNCTIVITIS IN NEONATAL ICU

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Background & aims: Neonatal conjunctivitis is commonly encountered in the neonatal intensive care unit (NICU). However it does not always indicate an infection. Therefore, bacteriological testing is necessary to guide judicious use of antibiotic. The aim of the study is review the types and susceptibility pattern of bacteriological agents isolated and to determine whether there is relationship between the organisms isolated from eye discharge and organisms isolated from rectal swab and/or nasopharyngeal aspirate

Methods: This retrospective study was conducted at the NICU of UKMMC. Results of eye swab sent for culture and sensitivity testing between January 2012 to December 2014 were reviewed. The organisms isolated were compared to the types of organisms isolated from weekly surveillance of rectal swab culture and weekly nasopharyngeal aspirate (NPA) culture among babies on respiratory support.

Results: Organisms were isolated from 29 of 68 (42.6%) specimens reviewed. The organisms were *Coagulase–negative Staphylococcus (CONS)* (24%), *Pseudomonas aeruginosa* (21%) , *Enterobacter sp* (17%) *Klebsiella sp* (10%), *Staphylococcus aureus* (10%), and others (17%). All the causative organisms were susceptible to Chloramphenicol (CMC) except *Pseudomonas aeruginosa* which was only sensitive to Gentamicin. In 93% of cases, the organisms isolated from the eye discharges were the same with that isolated from either the rectal swabs or NPA cultures.

Conclusion: CMC eye drop is a justifiable empirical therapy in neonates with eye discharge. Results of weekly bacteriological surveillance are useful to guide antibiotic treatment in babies who develop eye discharge.

ESPID-0882
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

PREMATURE INFANT WITH LATE-ONSET MULTIDRUG-RESISTANT ACINETOBACTER BAUMANII SEPSIS TREATED WITH VANCOMYCIN-CONTAINING REGIMEN

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Introduction

Acinetobacter baumanii is a common nosocomial pathogen with a tendency to develop antimicrobial resistance which may be a serious problem especially in neonatal intensive care units (NICU). We present a premature infant infected with multidrug-resistant (MDR) *Acinetobacter baumanii*, who responded to combination therapy with vancomycin, meropenem, rifampicin and colistin.

Case

A 27-gestational week-old female infant with a history of 3-week premature rupture of membranes was born by spontaneous vaginal delivery without the need of delivery room resuscitation. After stabilization in NICU, ampicillin and gentamycin treatment was started. On the 8th day of life she started to have apnea episodes and hyperglycemia. Late-onset sepsis was diagnosed and antibiotics were changed to vancomycin and meropenem. Blood culture revealed *Acinetobacter baumanii complex* susceptible to only tigeycline and colistin. Vancomycin was discontinued; colistin was added to treatment. With this treatment *A. baumanii complex* growth continued in blood cultures; patient's clinical and respiratory status deteriorated leading to intubation. Considering in vivo colistin resistance, rifampin was also added with no change in blood cultures. Tigecycline was suggested as an alternative. Failing to have parental consent for tigecycline, vancomycin was restarted on the 17th day of life. Blood culture after 72 hours of this combination treatment, had become sterile. The patient was extubated on the 6th day of vancomycin. Meropenem, rifampicin and colistin were continued for 21 and vancomycin for 14 days.

Conclusion

Treatment of MDR gram-negative bacteremia might be challenging in NICU. Vancomycin may be considered as a complementary drug of choice in complicated cases.

ESPID-0040
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

PREVALENCE OF MRSA AND RISK FACTORS FOR STAPHYLOCOCCUS AUREUS COLONISATION IN CHILDREN ATTENDING A PAEDIATRIC EMERGENCY DEPARTMENT IN IRELAND

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Aims: To determine the prevalence of meticillin-resistant *Staphylococcus aureus* (MRSA), and risk factors for *S. aureus* colonisation in patients attending a paediatric ED.

Methods: Children were enrolled with parental consent at the ED of Temple Street Children's University Hospital between 2008 and 2009. Nasal swabs were taken from the children and the parents/guardians were requested to complete a standardized questionnaire examining 33 risk factors, including age, gender and previous hospital admission. Swabs were inoculated in nutrient broth and subcultured onto selective media. Tube coagulation test, latex agglutination test and multiplex PCR were utilised to confirm the identification of *S. aureus*.

Results: Nasal swabs were taken from 549 children (aged 22 days – 18 years). *S. aureus* was isolated from 173 (34.5%); 166 (96%) were meticillin-sensitive *S. aureus* (MSSA) and 9 (5.2%) were MRSA (2 individuals colonised with both MSSA and MRSA). Statistically significant (p-value<0.05) risk factors for *S. aureus* colonisation were male gender, older age and pet ownership. Previous hospital exposure, extended family in residential care or having a chronic illness were not found to be statistically significant risk factors. Risk factors for MRSA colonisation were not examined due to low rate of MRSA carriage.

Conclusion: This study found a low rate of MRSA colonisation (1.6%) in children attending a paediatric ED and supports a policy of not screening all admissions for MRSA. Larger studies are required to further examine the role of gender, age and pet ownership in *S. aureus* colonisation of children.

ESPID-0840
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

URINARY TRACT INFECTION CAUSED BY EXTENDED-SPECTRUM B-LACTAMASE-PRODUCING BACTERIA IN CHILDREN

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Background: Urinary tract infection (UTI) caused by resistant bacteria is becoming more prevalent, with high UTI recurrence rate, long duration of prophylaxis, hospitalization within the previous 3 months and clean intermittent catheterization as already described risk factors for extended-spectrum β-lactamase (ESBL)-producing bacteria in children..
Objectives: To characterize the population, determine risk factors and identify the causative agents and their antibiotic susceptibility.
Material and Methods: During a 5 year period, children that came to our Emergency Department with the diagnosis of community-onset UTI caused by ESBL-producing bacteria (case) and those with non-ESBL-producing E. coli (control) were identified.
Results: A total of 1506 controls and 33 cases of ESBL-producing bacteria were identified, and prevalence of the UTI by this strains has increased (from 0,7% in 2009 to 2,81% in 2014). Mean of age:44months, median 19M. It was mainly observed in children with urinary malformations(n=6) neurogenic bladder dysfunction(n=3), gastroenteritis/obstipation(n=6). Five were under prophylaxis (Sulfamethoxazole+ trimethoprim). We couldn't identify the infection route in all the cases. Antimicrobial susceptibility test results showed resistance to cephalosporins in all the cases, but big discrepancies existed between the laboratorial results and the actual clinical efficacy (18cases of resistance to cephalosporin in vitro that were treated successfully with a cephalosporin). Six, because of maintained fever, changed the antibiotic to amoxicillin and clavulanate.
Conclusion: The extended-spectrum β-lactamase (ESBL)-producing bacteria are increasing and it's important to determine the risk factors to help establishing new policies in the management of UTI, preventing the risk of having no therapeutic options in the future.

ESPID-0973
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

ANTI-ENTEROPATHOGENIC E. COLI ACTIVITY OF LACTOBACILLUS PARACASEI SUBSP. PARACASEI BMK2005 AND ITS POTENTIAL FOR USE AS AN ANTIDIARRHEAL PROBIOTIC STRAIN

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Abstract

Objective:

- Production of an infantile fermented milk with a lactic acid bacteria presenting an antibacterial activity against enteropathogenic *E. coli* (EPEC)

- Determination of probiotic aptitudes of this bacteria

Methods: The antagonism of *Lactobacillus paracasei* subsp. *paracasei* BMK2005 against EPEC was tested, *in vitro*, using an infantile milk made out by addition of whey to skimmed milk (50/50, v/v). The antagonist effect was determined by wells diffusion agar and co-cultures. Also, some probiotic aptitudes of the strain, as pH effect, gastro-intestinal proteolytic enzymes and biliary salts on the growth of the strain, was determined. An *in vivo* study carried out on rabbits, was realized to confirm the results obtained in the *in vitro* study.

Results The tests showed that the lactobacilli strain presents a good anti-EPEC activity. In the wells diffusion agar method, the strain has shown an important anti-EPEC activity. Therefore, the co-cultures in infantile milk, has demonstrated that the lactobacilli strain caused a significant decrease in EPEC accounts at the end of 8 hours of incubation. The *in vivo* study, has clearly demonstrated a highly significant reduction of the faecal accounts of EPEC in the treated rabbits compared to those untreated where the number of EPEC did not decrease. Furthermore, Lactobacilli strain has presented a good resistance to acidic pH, biliary salts and gastro-enetestinal proteolytic enzymes.

Conclusion This study was demonstrated that *Lactobacillus paracasei* subsp. *paracasei* BMK2005 was endowed with a good anti-EPEC activity in an infantile probiotic formula. This strain has presented good probiotic aptitudes.

ESPID-0792
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

RECENT TRENDS OF ANTIBIORESISTANCE GRAM-POSITIVE BACTERIA ISOLATED FROM CHILDREN IN OUTPATIENTS

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Background and aims
Empirical antibiotic use in outpatients is required when the clinician suspects bacterial infection. The laboratory feedback, knowledge of local antibioresistance and usual practice help us in using the best treatment option for these patients.

Objectives: To investigate antibioresistance pattern of gram-positive pathogen bacteria isolates associated with acute infectious diseases (upper respiratory infections, otitis and conjunctivites).

Methods: The study included children aged up to 5 years; 473 strains of Gram-positive bacteria were isolated from throat, nasal and conjunctival swabs. Patients were treated in outpatient departments in „Dr.V.Babes" Clinic Bucharest, Jan-Dec 2014. The antibiotic susceptibility profiles were analyzed for Streptococcus pneumoniae, Streptococcus pyogenes and Staphylococcus aureus using both Kirby Bauer test procedure and E-test, for erythromycin and beta-lactam antibiotics, fluoroquinolones, glycopeptides, lincosamides (CLSI-2014).

Results: There were 473 bacteria identified in the laboratory over the study time period: Streptococcus pneumoniae 334 (27% carriage), Streptococcus pyogenyes 82, Staphylococcus aureus 57. Staphylococcus aureus was isolated from 57 specimens:19 were methicillin-resistant (MRSA). Streptococcus pneumoniae resistance to erythromycin was 61%, prevalence of penicillin-resistant was 9,8%. Streptococcus pyogenes resistance to erythromycin was 12,4%. Staphylococcus aureus MRSA resistance to erythromycin was 50%, no strain resistant to fluoroquinolones. All isolates were sensitive to vancomycin and linezolid.

Conclusions:
1. A general increase in erythromycin resistance in GAS and Streptococcus

pneumoniae has been observed compared to previous years.
2. Penicillin can be used in patients with susceptible strains because penicillin-resistance of non-meningeal infections was only 9,8%.
3. Staphylococcus aureus MRSA isolates were susceptible to floroquinolones and vancomycin.

ESPID-0578
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

THE DEVELOPMENT OF A QUALITY IMPROVEMENT ANTIBIOTIC STEWARDSHIP PROGRAMME – A SINGLE PAEDIATRIC CENTRE'S EXPERIENCE

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Background and Aims

Increases in multi-drug resistant organism identification and meropenem usage on a paediatric intensive care unit (PICU) identified a need for a paediatric antibiotic stewardship programme (PASP). A quality improvement programme (QIP) was planned to increase awareness, education and feedback of antimicrobial resistance and prescribing practices for all doctors prescribing antimicrobials. The aim of this study was to describe the development process of the QIP PASP.

Methods

In November 2013 a multidisciplinary paediatric antibiotic stewardship group comprised of paediatricians specialising in infectious diseases, microbiologists, pharmacists, infection control and epidemiologists was convened. A number of phased interventions were developed including: a weekly PASP ward round (WR), new prescribing charts, updated empiric antibiotic prescribing guidelines, a paediatric antibiotic prescribing smart phone app, regular teaching sessions for junior doctors, provision of name stamps for all prescribers, screening for carbapenemase-resistant organisms in high risk patients and regular feedback to staff to increase education.

Results

458 antibiotic prescriptions (274 patients) were assessed on the PASP WR from PICU (8 beds) and a general paediatric and surgical ward (22 beds) between February and August 2014. Antimicrobial management was changed in 42% of patients by the PASP WR. The paediatric antibiotic app was downloaded by 279 different users and used over 3500 times in the first 6 months after its introduction.

Conclusion

Development of a paediatric antimicrobial stewardship programme requires close collaboration from a multidisciplinary team and a programme of initiatives but has the potential to optimise antimicrobial prescribing practices.

ESPID-0583
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

INTRODUCTION OF A MULTIDISCIPLINARY PAEDIATRIC ANTIMICROBIAL STEWARDSHIP PROGRAMME TO IMPROVE ANTIMICROBIAL PRESCRIBING

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Background and Aims

A multidisciplinary paediatric antimicrobial stewardship group was established in November 2013 covering a paediatric intensive care unit (PICU) and a general paediatric and surgical ward to improve antimicrobial stewardship practices. This study aimed to assess the impact of initiatives developed by the group on antimicrobial prescribing.

Methods

A multidisciplinary weekly ward round was established. A new paediatric paper drug chart was introduced including a dedicated section for drug indications and stop/review dates, the PICU electronic prescribing system introduced a new field for indications and empiric antibiotic guidelines were updated. Antimicrobial prescribing was evaluated through three prescribing indicators as part of the hospital's quarterly point prevalence survey. The three indicators were % of antimicrobials: 1) in line with policy, 2) with indication documented, and 3) review and stop date recorded. We compared the results of the survey (Jan 2014) prior to the introduction of any of the initiatives to the one after all initiatives were implemented (June 2014) to assess their impact on prescribing practice.

Results

Table 1: Comparison of indicators between the January and June 2014 point prevalence surveys.

	Compliance January 2014		Compliance June 2014	
Indicator	General ward	PICU	General ward	PICU
1) % antimicrobials in line with policy	85%	100%	89%	89%

2) % indication documented on drug chart or in notes	100%	100%	100%	100%
3) % stop/review date documented on drug chart	32%	27%	100%	67%

Conclusion

The introduction of a dedicated paediatric antimicrobial stewardship programme, including a multidisciplinary ward round, improved compliance with the documentation indicators.

ESPID-0070
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

MICROBIOLOGICAL, CHEMICAL AND GEOSPATIAL ASSESSMENT OF MALIR VALLEY WATER SUPPLY AFTER SUPER FLOOD 2012

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ABSTRACT

Introduction:

Malir Valley, in Karachi Pakistan is infact, important for its agricultural land and products.The availability of water is the main issue to the farmers and thus due to water scarcity the quality of water is also another problem faced by the resident population of Malir valley.
Material and Methods: In this study collected about 60 drinking water samples (1 Litre) from various spots of Malir valley. Level of contamination and pollutant concentration has also been examined through interpolation techniques. Microbiologically, all the samples were analyzed by Membrane Filtration Technique (MFT) on different selective and differential microbiological media. Samples tested positive for potential gram-negative and enteric microorganisms including Escherichia. Coli (60%), Enterobacter aerogenes (8%), Proteus vulgaris (10%), Citrobacter freundii 2% Pseudomonas aruginosa(35%), Shigella dysenteriae (25%), Salmonella typhi (30%), Aeromonas hydrpphila (5%) and gram positive include including S. aureus (33%), S. epidermidis (30%), Stept. Pyogenes (12%).All these potential pathogens were identified by conventional and rapid (QTS 10) methods
Results: A very high resistance pattern was observed against a panel of a dozen of antibiotics like Cephalexin (80%), Erythromycin and Tetracycline (48%), Ampicillin(66%), Novobiocin(70%), Doxycycline (99%), Amoxicillin (41%), Ceftrizoxime (95%), Chloramphenicol (40%), Gentamicin (60%), Ofloxacin (30%) and Ciprofloxacin (20%). Minimum Inhibitory Concentration (MIC) was also determined variable ranges against the above mentioned antibiotics.
Conclusion:
Our results suggested the role of unhygienic and contaminated water may result in the spread of infections in villages which also emphasize undertaking proper measures to control possible epidemic especially the diarrhea infections.

ESPID-0993
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

IMPROVING ANTIBIOTIC MANAGEMENT OF PREVALENT ACUTE RESPIRATORY TRACT INFECTIONS (ARTIS) IN A PAEDIATRIC EMERGENCY DEPARTMENT (PED)

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Background/aim:

Antimicrobial stewardship programmes have proved to be an effective tool to improve antibiotic use. An audit of the antibiotic prescribing practice in our tertiary hospital PED for the most prevalent ARTIs was done, after an in-service tutorial programme it was re-audited.

Methods:

Two 15-day-long audits were made: May and September 2014. Electronic clinical data, including prescriptions, of children attending the PED with pharyngitis (PA), acute otitis media (AOM) and community-acquired pneumonia (CAP) were analysed. Between both audits, clinician education based on current guidelines was done.

Results:

Out of a total of 371 patients who were assisted because of ARTIs in May, 219 received antibiotics, as compared to 152/340 in September. There were no differences between both groups regarding epidemiological data or who wrote the prescription (trainee/consultant).

The proportion of antibiotic use in AOMs and CAPs remained similar in both periods, but PA showed a decrease from 52.1% to 38.2% ($p<0.05$). Amoxicillin-clavulanic-acid general use decreased significantly (32.7% to 23.0%, $p<0.05$). The greater reduction in the use of this antibiotic was observed in AOM cases (56.6% to 33.3%, $p<0.05$). Analysing how the individual prescription was written, no significant improvement was found regarding type and dose of antibiotics, in contrast to length, where the adherence to prescribing guidelines rose from 39.5% up to 75.3% ($p<0.05$).

Conclusions:

In our PED, the tutorial programme in ARTIs for clinicians have shown an improvement in antibiotic use criteria and a more accurate use of amoxicillin-clavulanic-acid. Nevertheless, there is still much more effort to be made.

ESPID-0920
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

CURRENT PREVALENCE OF COMMUNITY-ACQUIRED METICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS INFECTIONS IN CHILDREN IN SOUTHERN SPAIN

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BACKGROUNDAND AIMS

Increased prevalence of community-acquiredmethicillin-resistant *Staphylococcusaureus* (CA-MRSA) infections has being reported worldwide.

The aim of this study is to evaluate the percentage ofCA-MRSA infection in children diagnosed in a tertiary-care hospital in theSouthern of Spain.

METHODS

Observational-descriptive study about CA-SAinfections in children <14 year-old assisted in a health-care area, duringthe last 6 years (2009-2013).

SA was considered CA when it was isolated inextrahospitalary patients or in the first 48 hours of admission. Exclusioncriteria: frequent hospital contact because of predisposing factors (cysticfibrosis, chronic skin illness, presence of a percutaneous catheter) orhospital admission during the previous month.

RESULTS

111 CA-SA infections were diagnosed: 37 otitis (33.4%);38 skin infections: 14 superficial (12.6%), 24 deep-seated (21.6%); 7osteoarticular infections (6,3%), 7 scalded skin syndrome (6,3%), 6adenoflegmons (5.4%), 5 pneumonias (4.5%), 5 omphalitis (4.5%), 3 mastitis(2.7%), 1 conjunctivitis (0.9%), 1pansinusitis (0.9%), 1 parotitis (0.9%).

MRSA was isolated in 6 patients (5.4%): adenitis, cellulitisand 4 subcutaneous abscesses. All were natives. Median age was 12.9 month-old(0.75-33). Four patients required admission and five were treated with empiricalresistant antibiotics (4 amoxicillin-clavulanic-acid and 1 cloxacillin). Allinfections drained (3 surgically) with a satisfactory evolution.

No resistance to clindamycin and cotrimoxazole wasdetected, although resistance to macrolides (5), aminoglycosides (2) andquinolones (1) was observed.

CONCLUSIONS

CA-MRSA incidence was low (<10%) in our area.There are not reasons to change empirical treatment in infectious diseases where SA could be involved.

ESPID-0643
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

SPUTUM PATHOGENS AMONG CYSTIC FIBROSIS PATIENTS AFTER 5 AND MORE YEAR THERAPY WITH INHALED TOBI

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Aim:
To assess the diversity of sputum flora among teenaged cystic fibrosis (CF) patients with chronic *Pseudomonas aeruginosa (PA)* colonization treated for 5 years and more with inhaled TOBI.
Material and Methods:
Microbiological investigations (at least twice per year) of sputum flora from 22 CF patients (13 boys and 9 girls) from Sofia cystic fibrosis center, aged 12-18y (mean 15.7y) and receiving 5 and more inhaled TOBI were done. The main blood biochemical parameters for liver (ALAT, ASAT, LDH) and renal function (creatinine, urea, ureic acid), spirometry and audiometric testing also were evaluated.
Results:
PA in sputum was established in 6 patients (27.27%), in two of them in combination with other pathogens; *Candida sp*.- in 3 (13.63%), *Methicillin resistant Staph. aureus* - in 6 (27.27%), *Burkhordelia cepacia* - in one. *Stenotrophomonas maltophilia*, *Acromobacter xylosoxidans*, *Aspergillus sp.* and *Non-tuberculous mycobacteria* were not found. 7 patients (31.81%) were free of sputum pathogens.
FEV1 less than 40% of predicted showed 5 patients (22.73%). In a half of the rest of the patients FEV1 levels were higher than 70%. Out of a slight evaluation of ureic acid level in one, none of the others revealed renal and/or liver dysfunctions, neither were established signs for hearing losses.
Conclusions:
5y and more of inhaled TOBI therapy is safe, shows effective results in about three/fourth of chronically PA infected teenaged patients and leads full sputum pathogen eradication in at least 1/3 of them. New drug inhaled formula are needed for each fourth teenaged CF patients with chronic PA colonization.

ESPID-0594
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

ANTIMICROBIAL STEWARDSHIP IN A SPANISH TERTIARY HOSPITAL: PREVALENCE OF PRESCRIPTION AND PROPER PRESCRIBING AS TOOLS FOR MONITORING AND FUTURE BENCHMARKING

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Background and aims
Antimicrobial stewardship is needed to improve prescribing practices for children. We aim to monitor antibiotic use in our media evaluating prevalence of antimicrobial prescription (PAP) and proper prescribing.

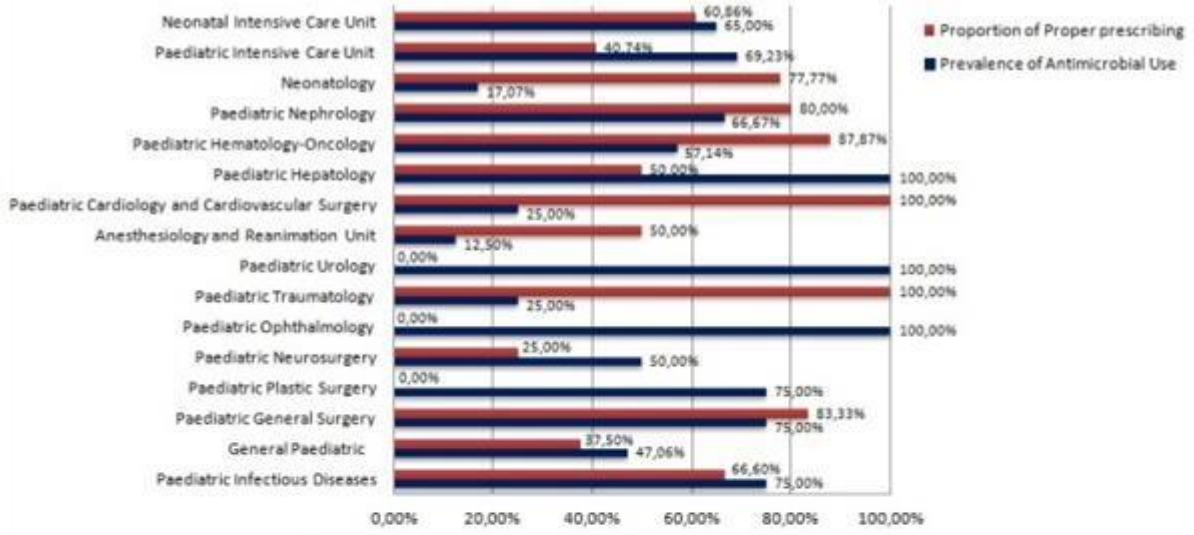
Methods
Cross-sectional point evaluation of PAP and proper prescribing (defined as correct indication plus appropriateness of prescription including correct dose, spectrum and interval) in hospitalized patients was done in different paediatric wards at a single Spanish tertiary hospital. Proper prescribing was evaluated by a paediatric infectious diseases specialist using established antimicrobial guidelines.

Results
Bed occupancy was 171 patients. PAP was 49%. From 113 infectious syndromes described antimicrobial prophylaxis (28.3%) was the most frequent, followed by pneumonia (8.2%) with a low rate of catheter related infections (2.6%). 68.2% patients had risk conditions for developing infection and 60% for multidrug-resistant infection. 161 antimicrobials were prescribed (1.9 antimicrobial per patient): 89 (55.2%) were empiric, 26 (16.1%) were directed and 46 (28.5%) were prophylactic. Amoxicilin-clavulanate (8.7%) and Cotrimoxazole (8.7%) were the most prescribed antimicrobials. Antifungal prescribing (12.4%) and antiviral prescribing (1.8%) were accessed. After evaluation, 98 (60.8%) were properly prescribed. Most common prescribing mistakes were prolonged prescriptions (21.7%) and excessive antimicrobial spectrum (21.1%). There were differences between PAP and proper prescribing proportions between wards in our series (Image1).

Conclusions
Measuring both PAP and proper prescribing could offer valuable information for monitoring appropriate antimicrobial use. More studies are needed to evaluate this

tools adjusted to patient's risks and complexity for future benchmarking.

Image 1. Prevalence of antimicrobial use and proportion of proper prescribing by ward



	Admitted patients	Patients receiving antimicrobials
Paediatric Infectious Diseases	16	12
General Paediatric	17	8
Paediatric General Surgery	4	3
Paediatric Plastic Surgery	4	3
Paediatric Neurosurgery	4	2
Paediatric Ophthalmology	1	1
Paediatric Traumatology	8	2
Paediatric Urology	2	2
Anesthesiology and Reanimation Unit	8	1
Paediatric Cardiology and Cardiovascular Surgery	4	1
Paediatric Hepatology	9	9
Paediatric Hematology-Oncology	14	8
Paediatric Nephrology	6	4
Neonatology	41	7
Paediatric Intensive Care Unit	13	9
Neonatal Intensive Care Unit	20	13

ESPID-0081
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

RISK FACTORS FOR MULTIDRUG-RESISTANT ACINETOBACTER BAUMANNII IN A PEDIATRIC WARD

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Background and Aims

Multidrug-resistant *Acinetobacter baumannii* (MDRA) is an emerging public health threat that is associated with high rates of in-hospital mortality in adults. However, there have been few studies on risk factors for MDRA in children. In response to an outbreak of MDRA (OXA51/ISAba1) in our tertiary care hospital, we conducted PCR-based surveillance. With this background, this study was designed to identify risk factors for MDRA in the pediatric ward compared to those in adult patients in a university hospital.

Methods

The surveillance study was carried out from March 2012 to December 2013. PCR analyses were conducted on samples collected from all children in our pediatric ward and from adult patients in the Emergency and Critical Care Center. A comparison of pediatric and adult MDRA-positive cases was performed to identify specific risk factors for MDRA in children.

Results

Of the 138 cases of *Acinetobacter baumannii* identified during surveillance, 48 were positive for MDRA, including 8 children and 40 adults. Among the MDRA-positive adult cases, most risk factors identified in earlier studies were present in comparison to MDRA-negative cases. In contrast, only two risk factors were identified in pediatric patients: mechanical ventilation ($p<0.001$) and tracheostomy ($p<0.001$). Comparison of MDRA-positive children and adults showed that pediatric patients who had undergone tracheostomy were more likely to have MDRA ($p<0.001$).

Conclusion

Our findings show a particular threat of MDRA in young patients on ventilators and an increased risk of MDRA in pediatric patients after tracheostomy, compared to adult patients.

ESPID-0220
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

SUGGESTIONS OF ANTIMICROBIAL STEWARDSHIP DERIVED FROM A POINT PREVALENCE SURVEY CONDUCTED IN PEDIATRIC INFECTIOUS DISEASES WARD

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Aim: to detect antimicrobials use's features prone to be amended through stewardship interventions

Methods: ECDC's point prevalence survey conducted in pediatric infectious diseases department from 500 beds infectious diseases university clinic from Bucharest, Romania. Electronic charts of patients continuous hospitalized in the selected day were retrieved and demographic and prescribed systemic antimicrobials (ATC J01) information were extracted, entered in an MS Excel© table and analyzed with Epi Info software. An antimicrobial prescription was defined as at least one dose of a systemic antimicrobial written in patient medical form.

Results – the most frequent current diagnoses were: acute enteritis (25%), viral hepatitis A (20%), meningitis (15%), and pneumonia (13.3%).

The top used antimicrobials groups were: third generation cephalosporin (43.1%) (mainly cefuroxime) followed by β-lactamase sensitive penicillin (21.6 %) (mainly benzyl penicillin).

Parenteral route was involved in 81.8 % of cases.

Conclusions – the most striking aspect of above survey was the high prevalence of parenteral route – as a consequence the guided stewardship orientation is currently decreasing the use of this route by switching on oral route as promptly as medical possible.

ESPID-0804
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

PATTERN AND RATES OF ANTIFUNGAL DRUG CONSUMPTION IN NEONATAL AND PEDIATRIC DEPARTMENTS IN A TERTIARY LEVEL HOSPITAL: 2001 TO 2013

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Background: Knowledge of antifungal drug consumption (ADC) is necessary for implementation of antifungal stewardship program. **Objectives**: Assess the pattern and rates of ADC in hospitalized neonates and children. **Methods**: Retrospective study conducted in 2 General-pediatric departments (GPD), a pediatric oncology (PONCO), a PICU and 2 NICUs from 2001 to 2013. ADC data were obtained from the hospital pharmacy and expressed using defined daily doses per 100bed-days (DDD/100BD). **Results**: In PONCO, total ADC (TADC) increased from 5.33 to 15.73 DDD/100BD (p=0.011). Fluconazole and amphotericin B (AMB, all formulations) consumption decreased from 2.45 to 0 DDD/100BD and from 2.88 to 0.17 DDD/100BD (p**Conclusions**: In pediatric and neonatal departments, AMB and azoles had the highest consumption, whereas echinocandins have still limited use. Increasing rates of TADC were documented in PONCO.

ESPID-0834
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

EPIDEMIOLOGY OF CARBAPENEM-RESISTANT GRAM NEGATIVE BACTERIA IN A PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: Patients in pediatric intensive care units (PICU) are at increased risk for colonization and infection by resistant Gram-negative bacteria. Our aim was to study colonization and infection caused by carbapenem-resistant (CR) *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii,* during a 24-month period in a PICU.

Methods: Incidence of new colonization and infection caused by CR bacteria was recorded. The study consisted of 2 periods [1st: January 2013-January 2014, without active surveillance; 2nd: February 2014-December 2014, implementation of an active surveillance program (ASP) and enhanced infection control measures (EICM)]. ASP consisted of weekly taken rectal swabs cultured on MacConkey agar containing 1mg/l meropenem. CR bacteria were phenotypically tested for metallo-beta-lactamase and *K. pneumoniae* carbapenemase (KPC) production.

Results: During 1st period, incidence of infections by CR bacteria was 2.94 infections/1000 bed-days (IBD): 1.26 for *K. pneumoniae* (n=3), 0.42 for *P. aeruginosa* (n=1) and 1.26 for *A. baumannii* (n=3); during 2nd period it was 1.39 IBD: 0.00 for *K. pneumoniae*, 0.93 for *P. aeruginosa* (n=2) and 0.46 for *A. baumannii* (n=1). The percentages of newly colonized patients were 4.7%, 1.5% and 5.5% for *K. pneumoniae, P. aeruginosa* and *A. baumannii*, respectively. During ASP period the rolling average of total incidence of newly colonized patients at a four-week basis ranged between 5% and 15% (p>0.05). Among *K. pneumoniae*, 100% were KPC producers during 1st period and 75% during 2nd period.

Conclusions: A trend in reduction of infections but not colonization with CR bacteria was observed following implementation of ASP and EICM.

ESPID-0972
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

PREVENTION OF NOSOCOMIAL INFECTIONS IN THE PEDIATRIC WARD – OWN EXPERIENCES (1)

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Introduction: Patients of pediatric wards are particularly at risk of nosocomial infections.

Aim: to determine the prevalence, etiology and clinical manifestations of nosocomial infections in hospitalized patients; to evaluate the effectiveness of procedures that aim at preventing hospital rotavirus infections and catheter-related bloodstream infections; to analyse the incidence of flu among staff in two consecutive seasons of the epidemic influenza H1N1 (2009/2010 and 2010/2011); to promote vaccinations of the medical staff.

Material: The study involved 4432 children and 57 members of the medical staff.

Results: Nosocomial infections were diagnosed in 2.2% of hospitalised children, where 96% were acute gastroenteritis; 3% -bloodstream infections associated with the peripheral vascular catheter. The 1% of cases concerned respiratory infections. The hospital gastrointestinal infections were caused by the rotavirus (78%), norovirus (13%) and adenovirus (0.9%). In 1.1% of cases the etiology had not been determined. As a result of implementing prophylactic activities, a statistically significant reduction of the incidence of nosocomial infections by the rotavirus was achieved (7.1-1.5%). The occurrence of catheter-related bloodstream infections was entirely eliminated. Influenza and influenza-like infections were reported in 7-5% of the medical staff. 42% of the medical staff was immunised against the influenza (92% of doctors, 7% nurses, 0% orderlies).

Conclusions: The most common cause of nosocomial infections in the pediatric ward are rotaviruses. Rotavirus infections and catheter-related bloodstream infections are possible to be effectively prevented through regular, proactive preventive measures. Vaccinations of the medical staff against influenza still require implementing measures of a promotional and educational character.
(1) *MCPE grant 501-1-20-19-14*

ESPID-1011
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

SHORT-TERM ANTIBIOTIC TREATMENT OF BONE AND JOINT INFECTIONS IN CHILDREN. RETROSPECTIVE STUDY IN MONTPELLIER UNIVERSITY HOSPITAL FROM 2009 TO 2013

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Introduction:
Osteoarticular infections (OAI) in infants remain a medicosurgical challenge with the potential for significant systemic and musculoskeletal morbidity. Most guidelines recommend the use of prolonged antibiotherapy active against Staphylococcus aureus, Kingella kingae (KK) and streptococci. We aimed to evaluate a short course antibiotic regimen in this context.
Materiel and method:
Short course treatment was based on an initial intravenous (IV) treatment with a revaluation after 48 hours and an early per os (PO) shift in case of favourable clinical course, for a total period of 10 to 15 days. We retrospectively studied this protocol from January 2009 to December 2013 at the University Hospital of Montpellier.
Results:
A total of 191 cases of OAI were included, 121 of them being osteoarthritis and 69 osteomyelitis. A bacteriological diagnosis was possible in 43.5 % of the cases with 37.3% of methicillin-susceptible S. aureus and 26.5% of KK. The mean treatment duration was 5.3 days for IV, and 12.2 days for PO treatment, for a total treatment period of 17.5 days. The secondary surgical revision rate was 4.7% and the sequelae rate was 4.1%.
Conclusion:
The results were equivalent to those found in the literature; they support that a short-term antimicrobial therapy could be considered in OAI in childhood and warrant further multicentric prospective studies.

ESPID-1018
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

EVALUATION OF STEROIDS IN PLEURAL EMPYEMA IN CHILDREN

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Introduction :
Pleural empyema in children remains a subject of medical interest because of it's frequency and the absence of management guidelines.. We focus on the use of steroids in this indication that is controversial. We aim to evaluate the impact of steroids on the duration of fever and the hospitalization for this disease.
Methods:
This is a retrospective study from 2007 to 2009, we include children hospitalized in the CHRU of Montpellier for pleural empyema, We defined three different groups according the absence of steroid therapy (group A), the use of steroids started within the first week of hospitalisation (group B) and the use of steroids started after one week of hospitalization (group C).
Results :
33 children were included, 20 in the group A, 5 in the group B and 8 in the group C. The statistical analysis highlight a shorter duration of hospitalization in the group B compared to the group A (12,6 days vs 17,15 days, p=0,04), without significant decrease of the duration of fever (11,9 days vs 14,8 days, p=0,09). There is also a significant lower duration of intravenous antibiotic treatment in the group B (8,1 days) compare to the groupe C (15,9 days, p=0,003). No difference was found between the group A and C.
Conclusion:
Early corticotherapy can contribute in shortening the period of antibiotherapy and hospitalisation notwithstanding the resevation of the retrospectve nature of this study. A prospective study is needed to confirm these data.

ESPID-1080
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

SURVEILLANCE OF MULTI RESISTENT BACTERIA IN A DEPARTMENT OF NEONATOLOGY

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Background and aims: Infections with multi-drug resistant pathogens (MDR=MRE) are a growing problem in neonatology. The aim of MDR surveillance is to detect colonizations at admission and nosocomial transmissions.

Methods: From April 2013 to December 2014, we evaluated 2,686 surveillance swabs from nose, throat and anus in 2013, and 2,789 in 2014 in the surveillance of multidrug-resistant bacteria in the intensive care unit component of the German nosocomial infections surveillance system (MRE-ITS-KISS).

Results: gram-(MRGN) transmissions: our nosocomial incidence rate [per 1,000 patient days] is in the range of the 75th percentile of all participating intensive care units (mostly for adults) in Germany (2.11 ‰). gram+ (MRSA) transmissions: our nosocomial incidence rate [per 1,000 patient days] is very low (<< P50 of adult reference value).

Conclusions: As about only 20 paediatric intensive care units (PICU) participate in Germanys ITS-KISS, data of MDR-prevalances at admission and of nosocomial transmissions are lacking. Until today no data for neonates are calculated separately in the KISS-system. Because of the long stay of premature babies in NICUs, the numbers of transmissions per 100 patients are higher than in adult intensive care units.

		2013			2014			reference value		
bacteria	**Rate**	**#**	denom.	**rate**	**#**	denom.	**rate**	average	**P50**	**P75**
Σ MRGN	prevalence rate [% pat.]	40	869	4,6	72	984	7,32	2,12	1,3	2,42
Σ MRGN	admission [% pat.]	20	869	2,3	44	984	4,47	1,51	0,75	1,47
Σ MRGN	nosocomial [% pat.]	20	869	2,3	28	984	2,85	0,61	0,4	1
Σ MRGN	nosocomial incidence rate [‰ days]	20	9612	2,08	28	12684	2,21	1,49	0,85	2,11
MRSA	prevalence rate [% pat.]	12	869	1,38	11	984	1,12	1,62	1,26	2,39
MRSA	admission [% pat.]	12	869	1,38	11	984	1,12	1,4	0,73	2
MRSA	nosocomial [% pat.]	0	869	0	0	984	0	0,22	0,11	0,4

ESPID-0799
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

PROLONGED DUAL ANTIBIOTIC COURSES FOR CULTURE POSITIVE NEONATAL SEPSIS IN 3 GREEK NEONATAL UNITS

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Background and Aims

Antimicrobial resistance (AMR) is a major healthcare problem. Antibiotic stewardship programs seek to promote judicious use of antimicrobials. One key element of stewardship interventions is to de-escalate empiric antibiotic therapy following positive culture results.

The aim of this study is to document dual antibiotic therapy in neonates following positive culture results in 3 neonatal units (NNUs) in Greece.

Methods

These are preliminary results of an ongoing prospective antibiotic use surveillance study conducted in 3 NNUs in Athens, Greece. Data collected between March and September 2014 by indication at initiation of antibiotic administration. Cases with only an indication of sepsis were identified and Length of Therapy(LOT), Days of Therapy(DOT) and DOT/LOT were calculated. DOT/LOT ratio was used as a proxy for estimation of antibiotic de-escalation failure.

Results

We documented 39 cases of neonates treated with the diagnosis of “sepsis”. Median LOT was 7(IQR:6-10) days and DOT 14(IQR:12-20)days. Neonates with culture negative sepsis were treated for a median of 7(IQR:5-7)days vs 10(10-15) for those with culture positive sepsis (p=0.0053) (Table-1). 13 neonates(39%) had positive blood cultures. Redundant dual antibiotic therapy was given to 7/13(54%) following culture results, of which 6/7(86%) were gram positive isolates. Table-2 demonstrates antibiotics and isolates from neonates with positive culture results.

Conclusion

We documented prolonged dual antibiotic courses with extensive spectrum in 3 Greek NNUs even in the presence of susceptibility results following positive blood cultures. Narrowing antibiotic regimen is critical especially in neonatal units where broad and prolonged antibiotic courses are often documented.

Table 1 Antibiotic Use in days, Combined and by Culture Result

	Overall	Culture negative	Culture Positive
N	39	26	13
LOT (median-IQR) days	7(6-10)	7(5-7)	10(10-15)
DOT (median-IQR) days	14(12-20)	14(10-16)	19.5(17-22)
DOT/LOT (median-IQR) days	2 (1.6-2)	2(2-3)	1.47(1.27-2)

Length of Therapy (LOT) – the number of days during which at least one dose of any antibiotic was received.
Days of Therapy (DOT) – the aggregate sum of LOT for each antibiotic received

Table 2 Antibiotic Therapy and Isolates of Culture positive cases

	Day 1			Day 4		
Pathogen	**AB1**	**AB2**	**AB3**	**AB1**	**AB2**	**AB3**
klebsiella	Meropenem	Vancomycin		Meropenem	*	
E.coli	Piperacillin/Tazobactam	teicoplanin		Piperacillin/Tazobactam	teicoplanin	
klebsiella	Meropenem	Vancomycin		Meropenem	*	
CONS	Meropenem	Vancomycin		*	Vancomycin	
klebsiella	Meropenem	Vancomycin		Meropenem	*	
Staphylococcus epidermidis	Teicoplanin	Ceftazidime		teicoplanin	Ceftazidime	
CONS	Ampicillin	Vancomycin		Ampicillin	Vancomycin	
Staphylococcus hominis	Vancomycin	Amikacin		Vancomycin	Amikacin	
Staphylococcus haemolyticus	Meropenem	Vancomycin	linezolid	Meropenem	Vancomycin	linezolid
CONS	Meropenem	Vancomycin	Amikacin	Meropenem	Vancomycin	*
Staphylococcus spp	Linezolid			linezolid		
enterococus+CONS(next day)	Meropenem	Vancomycin	Amikacin	Meropenem	Vancomycin	*
Candida	Micafungin			Micafungin		

(*) Discontinued antibiotics on or before Day 4 of Culture draw and initiation of therapy
AB: Antibiotic

ESPID-0896
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

DISTRIBUTION OF COMMUNITY-ACQUIRED GRAM NEGATIVE MICROORGANISMS DETECTED IN URINE SAMPLES OF PEDIATRIC PATIENTS AND 2013 EVALUATION OF ANTIBIOTIC RESISTANCE PATTERNS

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Background and objective: The aim of this study was to determine the distribution of community-acquired microorganisms obtained from urine samples of patients admitted to our clinic in Diyarbakır and their antibiotic susceptibility, as well as detect the ratio of extended spectrum beta-lactamase producing *E.coli* and *Klebsiella* strains in urine samples, and identify the antibiotics that can be used for the empiric treatment by investigating the susceptibility of extended spectrum beta-lactamase positive strains.

Materials methods: Patients admitted to the pediatric polyclinic of our hospital between the dates 1 January-31 December were included in the study. 1167 urine samples sent to Microbiology Laboratory were evaluated. Identifying gram negative strains isolated from the urine cultures and antibiotic susceptibility tests were performed in accordance with Clinical and Laboratory Standards Institute (CLSI) with traditional methods using Biomerium Vitek-2 compact system.

Findings: In this study, 959 *E.coli* from 1167 urine samples and other microorganisms from 26 of 182 *Klebsiella spp.* were isolated. Extended spectrum beta-lactamase production was detected in 445 (46.4%) of *E.coli* strains and in 72 (39.5%) of *Klebsiella* spp.strains. Amicasin resistance was determined as 9.4% in extended spectrum beta-lactamase positive *E.coli* strains, while amicasin resistance was detected as 11% in extended spectrum beta-lactamase positive *Klebsiella spp.* strains. Results: Resistance development against the antibiotics has been observed at higher rates in most of the microorganisms that cause urinary tract infection. We think that this study is significantly important for our hospital, as the antibiotic resistance rates of factors for urinary tract infection vary by centers.

ESPID-0336
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

MULTIDRUG RESISTANT ORGANISMS: AN IMPORATNT PREDICTOR OF MORTALITY IN NEWBORNS WITH BLOOD STREAM INFECTION IN LEVEL III NICU DELHI

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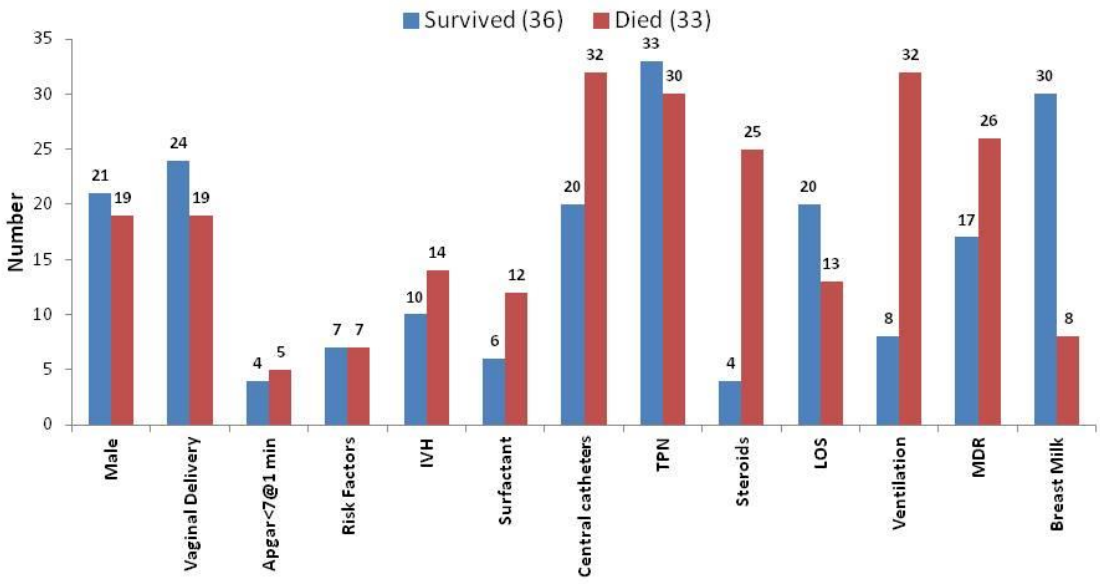
Background and aims: Blood Stream Infection (BSI) contributes significantly to morbidity and mortality among newborns. BSI by multidrug-resistant (MDR) microorganisms increases it further. The aim was to find out the contribution of MDR in mortality due to BSI.

Methods: Medical records of newborns admitted in Neonatal Intensive Care Unit in the period between January 2013 and December 2013 were reviewed. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, ventilator use etc. was retrieved. Multidrug-resistance was defined as per definitions proposed by the joint initiative of ECDC and CDC (2011). Risk factors were evaluated using Univariate and Multivariate Logistic Regression Analysis.

Results: Sixty nine (6.8%) out of total of 1012 blood cultures sent grew organisms. Thirty three babies (47.8%) died. Gender, delivery type, asphyxia, gestation, birth weight, surfactant administration, or presence of risk factors for sepsis did not significantly influence mortality. On univariate analysis factors associated with significantly high mortality were central catheters, steroids, ventilation, ventilation duration, infection with MDR microorganisms and not able to give breast milk. Multivariate logistic regression analysis revealed that steroids (O.R. 28.99, C.I. 1.041-807.242 p 0.047), ventilation (O.R. 57.316, C.I. 4.355-754.292 p 0.02) and infection with MDR (OR 51.442, C.I. 1.801-1469.278 p 0.021) were independent risk factors for mortality.

Conclusions: Multidrug-resistant microorganisms are an important predictor of mortality in neonatal blood stream infections.

Factors Affecting Mortality



Univariate Analysis

Variable	Survived (n=36)	Died (n=33)	O.R.	Confidence interval		p value
Male	21	19	0.969	0.372	2.524	0.949
Vaginal Delivery	24	19	0.679	0.255	1.805	0.437
IVH	10	14	1.916	0.702	5.230	0.204
Duration of Stay (Days)	34.19±18.9	23.61±23.4	0.976	0.953	1.000	**0.047**
Gestation (Weeks)	32.61±4.1	32.03±3.8	0.963	0.854	1.086	0.543
Birth weight (gm)	1491±495	1363±637	1.000	0.999	1.000	0.349
Risk Factors	7	7	1.115	0.345	3.607	0.855
APGAR <7 at 1 min	4	5	1.429	0.349	5.847	0.620
Surfactant	6	12	2.857	0.925	8.823	0.068
Central catheters	20	32	25.60	3.147	208.2	**0.002**
LOS	20	13	0.520	0.199	1.357	0.181
TPN	33	30	0.909	0.170	4.853	0.911
Steroids	4	25	25.000	6.750	92.59	**0.000**
Ventilation	8	32	112.83	13.18	951.8	**0.000**
Ventilation duration	36±2.2	33±9.9	1.098	1.002	1.202	**0.044**
MDR	17	26	4.154	1.437	11.99	**0.009**
Breast Milk	30	8	0.064	0.020	0.209	**0.000**

Multivariate Logistic Regression Analysis

Factors	Odds Ratio	Confidence Interval		P Value
Steroids	28.99	1.041	807.242	**0.047**
Ventilation	57.316	4.355	754.292	**0.002**
MDR	51.442	1.801	1469.278	**0.021**

Multivariate logistic analysis revealed that Steroids , Ventilation and infection with MDR microorganisms were independent risk factors for mortality.

ESPID-0504
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

SHOULD ALL NEONATES WITH BILIOUS VOMITING BE STARTED ON ANTIBIOTICS?

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Background:
Bilious vomiting in a neonate is a presenting sign of intenstinal obstruction. Early onset sepsis (EOS) is a differential diagnosis. Hence, the practise to screen all neonates with bilious voiting for infection and commence antibiotics, pending blood culture and serial C-reactive protein (CRP) results.
Aim:
To review the results of infection screens from neonates with bilious vomiting, in a tertiary neonatal intensive care unit.
Methods:
A retrospective review of the clinical records of neonates with bilious vomiting, admitted between 01/01/2013 and 31/12/2014 (2 years).
Results:
55 neonates with bilious vomiting were admitted. All underwent an infection screen with commencement of benzylpenicillin and gentamicin. All had abdominal radiographs. Additional risk factors for sepsis (NICE CG149 EOS guidelines) were present in 40%. This included all of the 12 neonates with a confirmed infection (positive blood culture or raised CRP) and 9 neonates with no subsequent evidence of infection.
12 neonates had a surgical pathology. However, only one of these neonates had a raised CRP suggestive of infection. This neonate also had additional risk factors for sepsis.
Conclusion:
Bilious vomiting alone was not associated with infection. Neonate with bilious vomiting alone is not an indication for infection screen and starting antibiotics. By applying the NICE EOS guidance, antibiotic pressure could be reduced in babies with bilious vomiting.
Reference:
NICE CG149 guidleine (antibiotics for early onset neonatal infection)

ESPID-0967
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

VENTILATOR-ASSOCIATED PNEUMONIA AND HOW TO HANDLE INFECTION IN A CARDIAC SURGERY CENTRE

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Background and aims:

A retrospective cohort study was conducted in an tertiary cardiac surgery centre to determine the frequency, associated pathogens of ventilator-associated pneumonia (VAP) after pediatric cardiac surgery in Turkey.

Methods:

Infants and children mechanically ventilated for >48 hours after cardiac surgery were assessed with regard to VAP between between January 2011 to December 2013. Data was retrospectively collected according to standard protocols of the National Nosocomial Infections Surveillance System (NosoLINE). VAP rate was reported as number of events per 1,000 ventilator-days.

Results:

In 2011 VAP occurred in 20/306 patients (6.6%). Microbiologic agent was detected in 4/20 patients, in rest VAP was diagnosed clinically and radiologically. The most common isolated microorganism was *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Ventilator utilization ratio was 0,52 with a VAP rate of 9.56 .

In 2012 and 2013 VAP occurred in 49/405 patients (12.1%). Microbiologic agent was detected in 24/ 29 patients in 2012 and 14/28 patients in 2013. *P. aeruginosa, Stenotrophomonas maltophilia* and *Klebsiella pneumoniae* were the most common pathogens. Ventilator utilization ratio was 0,58 with a VAP rate of 18.3 in 2012.

Because of increased VAP rate, education on preventions of VAP and isolation methods was given to all doctors and nurses in pediatric intensive care. Therefore, VAP occurrence decreased to 28/578 (4.8%) in 2013. VAP rate also diminished to 9.3.

Conclusions: It should be kept in mind that reminding all persons in pediatric intensive care about preventions of VAP and isolation methods can be decided VAP occurrence.

ESPID-0602
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

EFFECT OF AN EDUCATION ON PEDIATRIC INFECTIOUS DISEASES ON DIAGNOSING YERSINIA ENTERITIS AND USING APPROPRIATE ANTIBIOTICS TRATMENT FOR BACTERIAL ENTERITIS

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Background and aim

In Japan, *Campylobacter jejuni* and *coli*, and nontyphoidal *Salmonellae*, and Shiga toxin-producing *Escherichia coli* are the major pathogens of bacterial enteritis. Antimicrobial therapy is usually not indicated for immunocompetent patients with bacterial enteritis. Recently, the clinical practice of diagnosing and treating pediatric infectious diseases has changed in our hospital. This was a consequence of an education by infectious disease experts (e.g., the selection of microbiological tests and the use of antibiotics). We have evaluated the effect of this change in clinical practice on the diagnosis and treatment of bacterial enteritis.

Methods

In our study, we investigated immunocompetent patients aged <15 years, who were diagnosed with either *Campylobacter*, nontyphoidal *Salmonellae*, Shiga toxin-producing *Escherichia coli,* or *Yersinia enterocolitica* enteritis, at 2 hospitals in Japan from January 2007 to December 2014.

Results

A total of 161 patients were investigated. Of these, 102, 39, 11, and 9 had enteritis caused by *Campylobacter*, *Salmonellae*, *Escherichia coli,* and *Yersinia*, respectively. Although the number of patients with enteritis decreased since 2013, the number of patients with *Yersinia* enteritis showed an increase since the same time. Almost all *Yersinia* cases were detected by non-routine cultures that were requested by clinicians based on patient's findings. We found a trend for a decline in the proportion of outpatients treated with antibiotics therapy since 2013 (71% [2007], 14% [2013]).

Conclusions

The appropriate education resulted in an improved diagnostic rate of *Yersinia* enteritis. Moreover, the appropriate use of antibiotics in the treatment of bacterial enteritis was markedly diffused.

ESPID-0737
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

NASAL AND INTESTINAL CARRIAGE OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IN NEONATAL INTENSIVE CARE UNIT

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Background and Aims

The current data regardingthe correlation between the methicillin-resistant *Staphylococcusaureus* (MRSA) clones carried in the nasal cavity and digestive tract areinadequate. We aimed at isolating MRSA strains from feces ofthe nasal MRSA carrier to know the risk.

Methods

MRSAstrains were isolated from both the feces and nasal swabs of 21 nasal-MRSA carriers ranging from10 to 104 days of age treated at the neonatal intensive care units of twohospitals. The molecular epidemiological characteristics of the isolates weredetermined: multilocus sequence types, *spa*-types,staphylococcal cassette chromosome *mec* (SCC*mec*) types, carriage of four exotoxin genes, and genescontained in commercially available kit.

Results

The feces of all nasalcarriers contained MRSA at levels ranging from 4.0×10^2 to 2.8×10^8colony forming units/g feces. The MRSA clones isolated from the feces and thenasal swabs of each patient were the same. Four MRSA clones, clonal complex(CC) 8-SCC*mec* IVl, CC8-SCC*mec*IVb, CC1-SCC*mec* IVa and CC5-SCC*mec*IIa were identified from 21 patients. All CC8-SCC*mec*IVl strains and one of three CC5-SCC*mec* IIa strainscarried the toxic shock syndrome toxin gene.

Conclusions

The feces of tested MRSAcarriers contained the same MRSA clones as the nasal isolates in considerableamounts, suggesting that more careful attention should be paid for the handlingof excrement in the case of newborn babies or infants than that of adults.

ESPID-0228
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

ANTIBIOTICRESISTANCE OF DOMINANT OPPORTUNISTIC AGENTS, CAUSING NOSOCOMIAL INFECTION IN CHILDREN WITH BURNS

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The efficacy of antibiotics is important in intensive care of children with infection complications of burn.

Aim. To study the resistance of dominant microorganisns, causing infection in children with hard burn injuries, to antibiotics.

Materials and methods. In 2011–2014 years we isolated 175 clinical strains of opportunistic microorganisms from 108 patients (5-18 years of age) with burn injuries (square 10,0–65,0 %), who nderwent early surgery and complex intensive care, antibiotics. Microbiological diagnostics was used before and after antibiotics' administration. We studied sensitivity to antibiotics, antiseptics (decasan, chlorhexidine).

Results. During first 7 days burn wounds were colonized with *S. aureus* (27,4%)*, S. epidermidis* (9,2%), *P. aeruginosa* (21,2%), *A. bumannii* (32,8%), *E. faecalis* (4,5%), *Proteus spp*. and *E. coli* (both 0,8%) and others.

Isolated *S. aureus* were resistant to oxacillin (69,5%), doxiclin (over 50%), cefalosporins (above 23-34,2%), gentamycin (20-32%), amycacin (20-35%), azithromycin (61%). *A. baumannii* were resistant to cefalosporins (97%), meropenem (61,5%), ciprofloxacin (76,5%), levofloxacin (84%), gatifloxacin (60,5%). As for *P. aeruginosa* we found its high resistance to cefalosporins (90%), gantamycin (72%), tobramycin (70%), meropenem (52%), imipenem (79%), fluoroquilones (82%).

Clinical strains were sensitive to antiseptics. Bactericidal effect of decasan was found on *S. aureus* (1,38±0,81 mkg/ml), *A. baumannii* (50 mkg/ml), *P. aeruginosa* (77,8±6,02 mkg/ml). Chlorhexidine was effective against *S. aureus* (12,47±1,39 mkg/ml), *A. baumannii* (62,5 %), *P. aeruginosa* (107,64±6,79 mkg/ml).

Conclusion. Infectious complications of burn injuries in children are dominantly caused by *S. aureus*, *A. baumannii*, *P. aeruginosa* which are highly resistant to antibiotics and sensitive to antiseptics (decasan, chlorhexidine).

ESPID-0047
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

ANTIBIOTIC CONSUMPTION IN A PAEDIATRICS AND OBSTETRICS/GYNAECOLOGY TERTIARY CARE HOSPITAL IN SINGAPORE: A SEVEN-YEAR TREND ANALYSIS

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Introduction

Surveillance of antibiotic consumption trends is a strategy to understand epidemiological changes in antibiotic prescribing. This study presents the seven-year trend of antibiotic consumption in an 830-bed tertiary care hospital dedicated to Paediatrics and Obstetrics/Gynaecology (OBGYN) services in Singapore from 2006 to 2012.

Methods

Antibiotic consumption data was retrieved retrospectively from pharmacy purchasing records. Total antibiotic weight per 100 patient-days was selected as the surrogate measure to trend consumption. Consumption trends were analysed by linear regression analysis with logarithmic transformations.

Results

Overall antibiotic consumption in Paediatrics remained stable (r^2= -0.016, p=0.669) while there was an increase in OBGYN consumption (r^2= 0.929, p<0.01). Significant increases were observed for both fluoroquinolones (Paediatrics: r^2= 0.752, p<0.01 vs. OBGYN: r^2= 0.635, p<0.01) and extended-spectrum beta-lactams (Paediatrics: r^2= 0.406, p<0.05 vs. OBGYN: r^2= 0.897, p<0.01). In Paediatrics, piperacillin-tazobactam demonstrated a marked three-fold increase (r^2= 0.858, p<0.01). Similar trends were observed in OBGYN with two-fold increases in piperacillin-tazobactam (r^2= 0.639, p<0.01) and amoxicillin-clavulanate (r^2= 0.897, p<0.01) use. In Pediatrics, there was a decline in utilization of macrolides (r^2= 0.657, p<0.01) and aminoglycosides (r^2=0.373, p<0.05) whereas in OBGYN, both macrolides (r^2=0.328, p<0.05) and aminoglycosides consumption increased (r^2=0.837, p<0.01). Utilization of the other antibiotics remained stable.

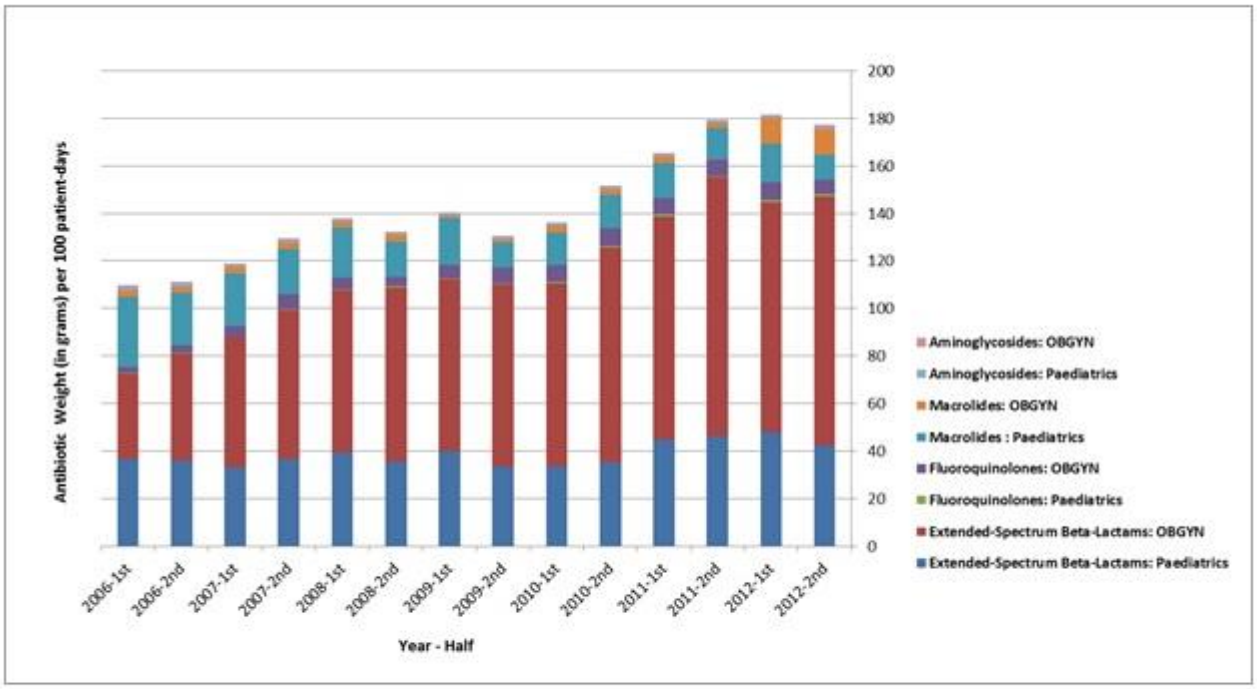

Figure: Trends of Extended-Spectrum Beta-Lactams, Fluoroquinolones, Aminoglycosides and Macrolides consumption in both Paediatrics and OBGYN services from FY 2006 to FY 2012

Conclusion

Increased utilization of broad-spectrum antibiotics like fluoroquinolones and extended-spectrum beta-lactams may be results of existing interventions or greater antimicrobial resistance with suboptimal responses to first-line antimicrobial therapy. Longitudinal surveillance of antibiotic consumption is essential in formulating interventions to advocate for more judicious antibiotic prescribing.

ESPID-0715
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

DETERMINATION OF THE MEASURES TAKEN BY THE NURSES WORKING IN THE PEDIATRIC WARDS FOR PROTECTION AGAINST INFECTION

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Background and aims: Health professionals are under risk of contruction of several infections direct from patients or from the physical enviroment. This study was performed to detect the necessary precautions taken by nurses for protection from contracting infections in pediatric wards.

Methods: The study was carried out in a university hospital. The study included 72 nurses working in pediatric wards. Informed consent and approval of local ethical committee were obtained accordingly. The data were analyzed with number, percentage, and chi-square tests.

Results: 37.8% of the participants washed their hands before the application of any procedure, 97.3% after procedures. 77.0% used the medical gloves in case of the risk of contact with blood or body fluids. 54.1% checked serologic test results and most of the participants were using personal protection materials to protect themselves from HBV and HCV infections. 83.8% of the nurses claimed that they were having boosters routinely for vaccination against HBV, 47.3% tested their serological parameters. 28.4% put extra effort in supporting their immune system, 44.6% took care of their nutrition and 12.2% gave ettention attention to sleeping pattern. 85.1% of the participants claimed that they were given frequent education about infection protection and 58.1% reported that they did not have enough knowledge about this subject.

Conclusions: This study showed that precautions taken for the protection against infection by the nurses working in Pediatric wards were not sufficient, and that continuous updated education and remainder on this subject was needed.

ESPID-1032
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

EVALUATION OF ANTIFUNGAL USE IN A PEDIATRIC HEMATOLOGY/ONCOLOGY UNIT

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Background and aims: Fungal infections cause great morbimortality in children with hemato-oncological diseases, therefore, an appropriate use of antifungal agents (AFA) is vital for their prevention and treatment. However, so far, there are few studies of pediatric antifungal stewardship. The aim of this study was to compare the appropriate use of AFA in hemato-oncological pediatric patients before and after the establishment of a specific protocol (January/2013).

Methods: Medical reports of children <18 years admitted to a hematology-oncology ward receiving AFA from January/2012-December/2013 were evaluated.

Results: 65 episodes of AFA use in 27 patients (40.7% women) were reviewed. Mean age during the episodes was 8.3±5.9 years. Hematological malignancies were the predominant diseases (60%), followed by solid organ malignancies (26.2%). In 44.7% of the episodes the patient had underwent a hematopoietic stem cell transplantation. The AFA was used as prophylaxis in 47.7%, empiric treatment 46.2% and targeted treatment 6.2%. The most common AFA used was mycafungin (35.4%) followed by liposomal amphotericin B (30.8%) and fluconazol (21.5%). Prescription was inadequate in 10.8% of the cases, all of them because the indication of the AFA was not appropriate. No differences in terms of patients' characteristics or AFA use between periods were observed but the inappropriate AFA use decreased in the last period from 18.5% to 5.3% (n.s.).

Conclusions: More than 10% of inadequate prescription of AFA was observed in this study, with a non-significant improvement after the establishment of a protocol. Therefore, specific protocols and antifungal stewardship may improve AFA use in these patients.

ESPID-0793
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

ANTIBIOTIC RESISTANCE PATTERN OF GRAM-NEGATIVE BACTERIA AT 2 TERTIARY HOSPITALS IN SANANDAJ, IRAN

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Background and aims: There is a growing concern about the rapid rise in the resistance of gram negative bacteria to antimicrobial agents. We conducted a study to assess the antibiotic susceptibility patterns of common gram-negative bacteria isolated from infections of normally sterile body sites at two tertiary hospitals in the Sanandaj city, Kurdistan Provenience, Iran.

Methods: From January 2011 to December 2011, all positive cultures from potentially sterile body fluids were gathered from two university hospitals in Sanandaj. The antibiotic susceptibility was determined using the Kirby-Bauer method (disk diffusion technique). The results were interpreted as per Clinical and Laboratory Standards Institute (CLSI) guidelines against a panel of the antimicrobials.

Results: 79 isolates of gram negative bacteria from patients with infections were collected. *Serratia marcescens* was the most frequently isolated organism (38%) followed by *Escherichia coli* (19%), *Klebsiella pneumoniae* (19%), *Acinetobacter baumannii* (6%), *Enterobacter* species (6%), *Serratia odorifera* (4%) and *Pseudomonas* species (5%). The Susceptibility pattern of common isolates i.e. *Serratia marcescens*, *E.coli,* and *K.pneumoniae* were as follows: ampicillin 3.3%, 6.7%, 20%; gentamicin 73.3%, 73.3%, 46.7%; amikacin 76.7, 93.3%, 53.3%; cotrimoxazole 70%, 13.3%, 40%; cephalothin 3.3%, 40%, 33.3%; ceftazidim 80%, 73.3%, 33.3%; piperacillin/tazobactam 90%, 66.7%, 86.7%; cefepim 80%, 86.7%, 46.7%; ciprofloxacin 100%, 73.3%, 86.7%; imipenem 100%, 100%, 100%, respectively.

Conclusions: We found a high resistance rate from bacteria isolated from healthcare associated infections in our hospitals. Different patterns of prevalent bacteria and antibiotic resistances in our county unveil the necessity of continuous surveillance to monitor changing epidemiology of Healthcare associated infection.

ESPID-0577
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

MRSA IN CHILDREN PRESENTING TO HOSPITAL IN CRETE, GREECE

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Background and Aims: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major human pathogen causing both healthcare- and community-associated infections. The aim of the study was to investigate the resistance patterns and molecular characteristics of clinical isolates from children presenting to hospital with invasive and non-invasive MRSA infections over a 6-year period.

Methods/ Results: A total of 37 children (20 boys and 17 girls) aged 3 weeks to 14 years (average 3.7, median 5.0 years) presenting to hospital with community-associated infections between 2008 and 2013 were included. 33 children presented with skin and soft tissue infections and one of each with epidermolysis, pneumonia, osteomyelitis and sepsis related to cellulitis. 35/37 children were hospitalized for 1 to 32 (median 5.0) days. Resistance to erythromycin was observed in 11/37 (29.7%) isolates, all of whom were also resistant to clindamycin. The majority of MRSA isolates were non-susceptible to fusidic acid (30/37, 81.1%) and tetracycline(24/37, 64.9%). All isolates were susceptible to trimethoprim-sulfamethoxazole,rifampin, vancomycin and linezolid. The most commonly identified *spa* type was t044 (28/37, 75.7%) with all of these isolates belonging to sequence type (ST) 80. Genes encoding *mecA* resistance were detected in all isolates, Panton-Valentineleucocidin (PVL) in 30/33 (90.1%) isolates and toxic shock syndrome toxin(TSST-1) in 5/33 isolates (15.2%).

Conclusions: In the study area, community–associated MRSA isolates from children presenting to hospital were commonly PVL producers, resistant to common first-line antistaphylococcal agents and in their majority belonged to the ST80 clone.

ESPID-0517
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

ACTIVE SURVEILLANCE AND GENOTYPING OF HIGHLY RESISTANT MICRO ORGANISMS ON NEONATOLOGY WARDS CAN PREVENT RISKY OUTBREAKS

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Introduction

Hospitals are faced with the increasingly rapid emergence and dissemination of highly resistant micro-organisms (HMRO), Enterobacteriaceae that can exhibit resistance to multiple antibiotics such as extended- spectrum beta-lactamases (ESBL), including carbapenemases, cephalosporins, quinolones and aminoglycosides. Infection is one of the most important reasons for neonatal morbidity and mortality worldwide. Progress in neonatal intensive care has made it possible to decrease mortality among preterm infants with very low birth weights, but these preterm infants are at especially high risk for developing nosocomial infections.

Methods

Active surveillance of neonatology wards was undertaken by weekly screening cultures, and subsequent genotyping of micro-organisms. Cultures were taken by swabs from rectum, grown overnight at 35 ºC, and identified by standard laboratory methods. Genotyping was performed with amplified fragment length polymorphism (AFLP). Genotype banding patterns were analysed using Bionumerics.

Results

Five outbreaks of ESBL positive *Klebsiella pneumoniae* and *Escherichia coli* were identified by clusters of identical genotypes within a timespan of 11 months. The largest outbreak included 6 neonates who were colonized with *E. coli.* Appropriate measurements and precautions were taken for containment of the outbreaks.

Conclusion

Surveillance has proven itself to be an effective method for reducing the frequency of nosocomial infections. Surveillance and genotyping of HMRO at neonatology wards provides an essential tool to identify outbreaks and prevent difficult to treat infections for vulnerable neonates.

ESPID-0497
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

POINT OF CARE TESTING (POCT) AND AUDIT OF CARE PATHWAY FOR PAEDIATRIC RSV PATIENTS

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Background

Annual winter epidemics of Respiratory Synctial Virus (RSV) disease cause significant morbidity and mortality in children. Use of point of care testing (POCT) allows rapid diagnosis and appropriate allocation of patients either to isolation or cohort nursing if admission to hospital is required. Our institution has over 10 years experience of using POCT to manage RSV, and for winter 2013/14 we audited the nurse-led care pathway which had a significant impact on patient management.

Methods

Binax®NOW RSV test was performed on all patients <2years presenting at Emergency Department (ED) or Medical Assessment Unit (MAU) with respiratory symptoms. A 7 day, nurse-led care pathway was established, with 'bed huddles' at 12:00 and 16:00 hours to allocate patients to appropriate management streams. The patient care pathway was audited and results collated at the end of the winter epidemic.

Results

437 POCT tests were performed, of which 202 were positive for RSV (46%).
188 children were admitted and commenced on the patient pathway. Average length of stay was 2.6 days and average age of patient 9.9 months. 92% (160/188) patients were RSV positive.17 patients were commenced on antibiotics, and 10 of these were discontinued at ward round. Nurse discharge was effective in 186/188 (98.9%) cases. Hospital acquired infection (HAI) was a record low of 2.4% for winter 2013/14.

Conclusions

Introduction of the patient care pathway using rapid POCT results allowed patients to be allocated appropriately, reduced antibiotic use, aided bed management and facilitated early implementation of infection control measures.

ESPID-0151
INFECTION CONTROL, ANTIMICROBIAL RESISTANCE, CHEMOPROPHYLAXIS AND ANTIMICROBIAL STEWARDSHIP

EVALUATION OF ANTIBIOTIC SENSITIVITY OF URINARY TRACT PATHOGENS IN CHILDREN IN THE SOUTHEAST OF IRAN

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Background: Urinary tract infections (UTIs) are the most frequent and serious infection in childhood all over the world. E. Coli is the 1st pathogen to be responsible for culture-proven UTI in all age groups. For young children the diagnosis is often uncertain and symptoms and signs may be difficult to interpret. Due to find the appropriate empirical therapy it is very important to investigate the prevalence and the resistance pattern of main responsible bacteria in UTI in southeast of Iran.

Material & Methods: In this cross-sectional study from 2012 to 2014, positive urine samples from 396 patients one to eighteen years old who suspected to have UTI referred to pediatric clinics were assessed. Sex and age of children, kind of isolated bacteria in urine culture, susceptibility and resistance of these bacteria to current antibiotics were studied.

Results: In present study 396 culture-proven children with UTI (girls to boys ratio 4.8:1) were studied. The most common age of urinary tract infection in boys was under 1 year old and in girls was in 1-7 years old. After one year of age the rate of urinary tract infection in females was preceded to males. The most prevalent cause of urinary tract infection in all age groups and both gender was E.coli (77%), afterward was Enterobacter (8.1%) and Klebsiella (7.1%). E. coli spp. were highly sensitive to nitrofurantoin (74.7%), ciprofloxacin (72.5%) and amikacin (64.6%), both highly resistant to cotrimoxazole (74.8%), ampicillin (66.9%) and nalidixic acid (51.1%), and its resistance to ceftriaxone is increasing.

ESPID-0559
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

INITIAL MANAGEMENT OF FEBRILE NEUTROPENIA IN A PAEDIATRIC EMERGENCY DEPARTMENT

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Background: From a pilot project to develop a modified paediatric Sepsis Six pathway for use in an emergency department (ED) setting, we analysed the initial management of febrile neutropenia within the ED of Birmingham Children's Hospital, which has one of the UK's largest paediatric Haematology/Oncology (Haem/Onc) services.

Aim: To assess the performance of the emergency department at managing febrile neutropenia.

Methods: As part of a larger study of sepsis management, we retrospectively audited the management of all patients presenting to the ED with fever and known, or strongly suspected, neutropenia, over a 6 month period. The audit tool was a modified Sepsis Six pathway adapted for use in a paediatric, but not exclusively neutropenic, population.

Results: There were 43 cases of febrile neutropenia treated with IV/IO antibiotics. All patients had appropriate blood cultures taken and were treated with either tazobactam/pipercillin or meropenem. Overall, 28/43 (65.1%) received IV/IO antibiotics within one hour. The mean time to antibiotic administration was 59 minutes.

13/14 (92.8%) patients initially managed by the ED clinicians received IV/IO antibiotics within one hour, with a mean time of 42 minutes. 15/29 patients (51%) referred directly from Triage to the Haem/Onc team received antibiotics within one hour, with a mean time of 67 minutes.

Conclusion: We present evidence that door-to-antibiotic time in paediatric febrile neutropenia was shorter (and more often occurred within one hour) when treatment was initiated by the ED, rather than after referral directly to the tertiary Haem/Onc team.

ESPID-0667
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

A CHRONIC GRANULOMATOUS DISEASE CASE DIAGNOSED WITH SALMONELLA BACTEREMIA

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Patients with altered host defences especially neutrophil dysfunction like chronic granulomatous disease have high risk for development bacteremia with any type of *Salmonella* organisms. Here in, we report a seven years old girl diagnosed as chronic granulomatous disease having *Salmonella enteritidis* bacteremia.

A seven years old patient was admitted to our pediatric intensive care unit with prolonged fever and impaired general condition. The temperature was 38.6^0C. She had impaired mental status with tachycardia (150/min), hypotension (80/40 mmHg) and prolonged capillary refilling time. She was tachypneic with low oxygen saturation (85-90%) and had hepatomegaly. Laboratory analysis revealed leucocytosis (15400/mm^3) with neutrophil predominance**,** thrombocytopenia (75000/ mm^3), high C-reactive protein concentration (19.4 mg/dl) and elevated erythrocyte sedimentation rate (53 mm/h) with impaired liver and renal functions. She was diagnosed as septic shock, encephalopathy and respiratory distress and was intubated for six days. Empirical treatment was started with ceftriaxon, which was later switched to meropenem due to persistant fever. Continuous renal replacement therapy was used for 3 days due to thrombocytopenia and multiorgan failure. *Salmonella enteritis* sensitive to meropenem yielded in 3 blood cultures. She recovered completely at second week.

She was product of non-consanguineous parents with no known diseases. She had history of recurrent pulmonary and urinary system infections. She was vaccinated with live vaccine without event.

On the basis of history of recurrent infections and Salmonella bacteremia immunologic evaluation was performed. Nitroblue tetrazolium test demonstrated the diagnosis of chronic granulomatous disease.

ESPID-0421
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

INTRAVASCULAR CATHETER RELATED BLOODSTREAM INFECTION CAUSED BY DELFTIA ACIDOVORANS IN A PEDIATRIC PATIENT

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Introduction: *Delftia acidovorans*, previously called *Comamonas/Pseudomonas acidovorans* is an aerobic, non-fermentative, gram negative rod. This organism is generally found in soil and water. Although it is assumed as nonpathogen, serious infections like catheter-related-bloodstream infection (CRBSI), endocarditis and ocular infections in immunocompromised individuals have been reported.

Case: An eight year-old boy who had undergone allogenic bone marrow transplantation for aplastic anemia 74 days ago, was admitted due to fever with shiverenig for three day. He was on cyclosporine treatment. His physical examination revealed body temperature, 38.5°C and a tunneled central venous catheter (CVC) with no erythema or induration around it. White blood cell count was 9450/mm^3, absolute neutrophil count was 4500/mm^3, and C-reactive protein was 128 mg/dl. Meropenem (60 mg/kg/d) was started empirically due to epidemologic data. Because of persisting fever, vancomycin (40 mg/kg/d) and amikacin (15 mg/kg/d) were added on the third day. The next day *Delftia acidovorans* grew in catheter blood culture. And after 2 hours, same microorganism grew in peripheral blood culture which was susceptible to carbapenems, and resistant to aminoglycosides. On the 7^{th} day, CVC was removed, and his fever resolved gradually. Meropenem was given for 14 days, amikacin and vancomycin were given for 10 days. Control blood cultures were negative and he was discharged consequently.

Conclusions: Infections due to rare bacterial agents such as *D.acidovorans* should be kept in mind in children presented with immunosuppression and invasive devices like CVC. Catheter removal should be considered at the appropriate time in CRBSI.

ESPID-0789
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

TUBERCULOSIS AND PEDIATRIC END-STAGE RENAL DISEASE

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Background

Tuberculosis(TB) in pediatric renal pre- and post-transplant recipients is a significant cause of morbi-mortality. Diagnosis is challenging due to unspecific symptoms, atypical localization and limited sensitivity of diagnostic methods.

Methods and results

We report one confirmed and two presumed cases of tuberculosis infection in Moroccan children with end-stage renal disease who were successfully treated without impairment of renal function.
A 14-year-old girl was diagnosed of TB infection during a routine renal pretransplant study. She was asymptomatic with normal chest radiograph and positive TST. She received isoniazid and rifampin for 3 months without side effects.
The other two patients were a 7-year-old boy and a 13–year-old boy who had received a renal graft 41 and 24 months earlier, repectively. The former patient had prolonged fever with no source of infection identified after extensive work-up. Anti-TB-Rifampin-sparing treatment was initiated due to presumptive tuberculosis infection based in the epidemiological context and positive PCR for M.complex in urine. TST, IGRA and mycobacterial cultures were negative. Fever abated soon after initiating anti-TB treatment that was then completed. The latter patient had a pleural effusion with lymphocitic predominance and increased ADA levels. TST, PCR and cultures were negative for *M.tuberculosis*. He was successfully treated with a 3-drug-RIF-containing regimen for 1 month followed by 3-drug-RIF-sparing regimen for 11 months.

Conclusions

A high level of suspicion is necessary for the diagnosis of tuberculosis in pediatric patients with end-stage renal disease. Anti-TB treatment should be initiated in presumed or confirmed cases with drug toxicities and interactions monitoring.

ESPID-0751
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

A STUDY OF PAEDIATRIC PATIENTS HOSPITALIZED WITH ELIZABETHKINGIA MENINGOSEPTICA STERILE SITE INFECTIONS

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Background

Elizabethkingia meningoseptica is a multidrug-resistant organism that may affect neonates or immunocompromised hosts, with high morbidity and mortality.

Methods

We conducted a retrospective study of children diagnosed with *E. meningoseptica* sterile site infection in KK Hospital, Singapore (KKH) from 2010-2014. Cases were identified from the hospital's microbiology database. Epidemiology, treatment and outcome data were retrieved from case records.

Results

Ten cases of *E. meningoseptica* sterile site infections were identified, with a median age of 4.3 years (range 11 days to 9 years). Most patients (9/10) were immunocompromised – six had underlying malignancies on chemotherapy, 2 were premature neonates, and 1 had third-degree burns. The remaining patient had a background of haemophilia A. All had bacteraemia. Additionally, the patient with haemophilia had a subdural haematoma with meningitis and possible brain abscess. Most patients (9/10) had central venous catheters upon diagnosis of infection.

Susceptibility to piperacillin/tazobactam, cotrimoxazole, and quinolones was demonstrated in 10/10, 9/10 and 5/5 cases, respectively. One case with persistent bacteraemia eventually showed clearance using a combination of piperacillin/tazobactam, minocycline and moxifloxacin.

Eight cases showed clearance of bacteraemia with documented negative blood cultures. Central lines were removed in 4/9 cases. Two cases of persistent *E. meningoseptica* bacteraemia resulted in mortality. Overall mortality in our study was 40%.

Conclusion

Our study confirms that *E. meningoseptica* is a pathogen that predominantly infects premature neonates and immunocompromised patients. In this study, the majority of isolates were susceptible to piperacillin/tazobactam, cotrimoxazole and quinolones. Mortality in children with *E. meningoseptica* infection was high.

ESPID-0996
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

IMPACT OF EPSTEIN-BARR VIRUS HETEROGENEITY ON THE ADAPTIVE ANTIVIRAL IMMUNE RESPONSE

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Background and aims
Epstein-Barr virus (EBV) is a ubiquitous γ-Herpes virus that is associated with a number of malignancies of epithelial or lymphoid origin. Recently a new EBV strain termed M81 was isolated from an Asian nasopharyngeal carcinoma. M81 differs from the prototype EBV strains B95.8 and Ag876 in cellular tropism and lytic activity. Currently it is not known, whether the different EBV strains differ in immunogenicity and antigenicity. We therefore compared adaptive immune responses against the three EVB strains M81, B95.8, and Ag876.

Methods
DNA-sequences of different EBV strains were compared to identify polymorphisms in viral proteins, respectively known T-cell epitopes. T-cell assays were performed to examine recognition of polymorphic peptides and to assess the role of polymorphic viral proteins in immune evasion. Western blots of viral proteins were performed to analyze cross-reactivity in serum antibodies. T-cell lines were generated by repeated stimulation of PBMC with lymphoblastoid cell lines (LCL) in vitro that were established by infection of B cells with B95.8 or M81 virus and characterized by FACS, cytokine ELISA, and calcein release assay.

Results
Although sequence variations resulted in the loss of several T-cell epitopes in some EBV strains, LCL-stimulated T-cell lines showed protection against target cells infected with different viruses. Furthermore, the rate of T-cell proliferation was increased when LCL established with M81 were used as stimulators.

Conclusions
Our results indicate that established EBV-specific adaptive immunity provides cross-protection against different viral strains. These findings have implications for adoptive T-cell therapy and vaccine design.

ESPID-1034
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

CENTRAL LINE-RELATED BLOODSTREAM INFECTION: COMPARISON OF SAMPLE COLLECTION METHODS IN TOTALLY IMPLANTABLE ACCESS PORTS

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Background and Aims: Long-term venous catheter as totally implantable access ports (TIAPs) has improved patient's quality of life and medical assistance. Central line-related bloodstream infection (CR-BSI) is a major problem once it increases morbidity and mortality. In this study, we compare three microbiological retrieval methods used to identify the causative infection agent with samples from the removed TIAPs.

Methods: This retrospective cross-sectional study was conducted from January to December 2013. Patients from 0 to 18 years old, in treatment at Pediatric Oncology Institute (IOP- GRAACC/UNIFESP-Brazil) who had their TIAPs removed due to CR-BSI were included. After catheter removal, samples were collected through three different methods - 3 ml of physiologic solution flushed through the port, swab of the silicone reservoir and 5 cm of the catheter tip - and sent to microbiology culture. All patients medical records were reviewed and follow chart was completed. Research approved by the scientific commission.

Results: 15 patients had their TIAPs removed due to infection, only 12 of those meet the study criteria. 50% (n=6) of microbiological retrieval were found: 4 yeast, 1 gram positive and 1 gram negative. The cultures were positive in 42%, 42% and 25% for swab, flushed physiologic solution and tip, respectively.

Conclusion: Comparing the three methods of collection, the swab and flushed solution showed higher sensitivity to microbiologic agent retrieval than the tip, the golden standard procedure. Although this is a small study, it suggests that the tip is not the best method to identify CR-BSI.

ESPID-0696
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

NEPHROTOXICITY OF CIDOFOVIR IN PAEDIATRIC HAEMATO-/ONCOLOGIC PATIENTS

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Background and aims

Viral infections are a big issue in immunocompromised children such as haemato-oncologic patients. Cidofovir has broad-spectrum activity against DNA-viruses (e.g. Adenovirus, Herpesviruses). Its use, however, is limited by renal side effects. There is little data on cidofovir treatment in paediatric patients. Our aim was to describe its nephrotoxic effects in a paediatric cohort.

Methods

We retrospectively analysed patients who received cidofovir between 01/2006 and 03/2014 at our department. As supportive precaution, cidofovir was co-administered with probenecid and intravenous saline hydration. We compared creatinine and urea levels obtained before, directly after and after one month of each cidofovir treatment episode using Wilcoxon test/ t-test. One episode is defined as at least one cidofovir administration and ends if for the following 28 days no cidofovir was administered.

Results

We analysed 103 episodes in 72 patients (age: 8 months – 30 years). Per episode, 1-20 (median: 3) cidofovir infusions were administered.
Creatinine levels increase significantly directly after as well as one month after treatment episodes, while urea did not show significant changes.

Conclusions

Although creatinine levels significantly increased with cidofovir treatment, levels remained within a tolerable range. Other nephrotoxic medications might additionally contribute to the observed effects.

	Creatinine, median (min-max)	Urea, median (min-max)
before treatment	0.4(0.1 – 1.2) mg/dl	25(5-83) mg/dl
after treatment	0.4(0.11 – 1.64) mg/dl	23(1-87) mg/dl
change	+2.1%(-57.1% – +250%)	-3.6%(-93.8% – +520%)

	p-value	0.014	n.s.
1 month after treatment		0.4(0.15 – 1.51)	22(8-93) mg/dl
	change	+6%(-79.2% – +229%)	±0%(-480% – +70.2%)
	p-value	0.004	n.s.

ESPID-0569
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

FECAL MICROBIOTA TRANSPLANTATION IN CHILDREN WITH RECURRENT CLOSTRIDIUM DIFFICILE INFECTION

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Background

Clostridium difficile is a ubiquitous bacteria frequently found in the human saprophytic intestinal flora. Rarely, it is involved in the etiology of acute intestinal infections, especially in the circumstances of dysmicrobism or host immunodeficiency.

Material and method

We present two severe recurrent cases of Clostridium difficile colitis in children admitted in The National Institute of Infectious Diseases “Prof. Dr. Matei Bals”. In both cases, diagnosis was established through culture and PCR. Treatment was administered according to standard protocol, with initial favorable evolution but with relapses occurring at increasingly shorter intervals. The first case is a 7 year old girl with 4 relapses over 18 months, and the second case is a 5 year old boy with 6 relapses in 24 months.
In this situation we have opted for fecal transplantation, donors being the mother in the first case and the father in the latter.

Results

Recolonization was achieved through a nasogastric tube inserted up to the proximal segment of the duodenum. The procedures took place without incidents. The first case has not registered any relapses 10 months after transplantation, nor did the second after 2 months.

Conclusions

Fecal microbiota transplantation is a rarely used therapy, this being the first time the procedure was used in a child with recurrent *C. difficile* infection.
We consider that the intestinal recolonization with bacterial flora from a healthy donor was a success, the child being regarded as cured.
These cases are a medical premiere for Romania, worldwide being few cases performed and reported.

ESPID-0933
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

INFLUENZA A (H3N2 SUBTYPE) INFECTION IN A PATIENT WITH COMPLETE INTERFERON GAMMA RECEPTOR 1 DEFICIENCY - FIRST DOCUMENTED CASE

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BACKGROUND:

Infections due to typical or atypical mycobacteria are the most common clinical presentations in patients with autosomal recessive (AR) complete Interferon-gamma Receptor1 (IFN-γR1) deficiency. Clinical cases describing viral infections are very scarce.To date, influenza virus infections have not been reported so far.

CASE REPORT:

A three-year old boy with AR IFN-γR1 (c.523delT/c.652_654delGAA) awaiting matched sibling donor hematopoietic stem cell transplantation (HSCT) presented with low-grade fever (38.2ºC), cough, nausea and vomits. 48 hours earlier his mother showed mild upper respiratory symptoms. Nasopharyngeal swabs were obtained and found positive for influenza A virus using a rapid antigen test. A subsequently performed PCR confirmed the results identifying the H3N2 subtype. Ambulant treatment with oseltamivir (30mg/12 hours during 5 days) resulted in a prompt clinical response, becoming afebril within 24 hours, showing good oral tolerance, whilst upper respiratory symptoms persisted for another 7 days. Virological testing remained positive until 10 days after stopping antiviral treatment. High interferon gamma levels (>200pg/ml, normal<40) warranted to post-pone HSCT for 6 weeks. Transplant was subsequently performed without mayor complications. Currently, 10 months after

transplant, he is in an excellent clinical shape with no signs of GVHD and a stable donor chimerism of >95%.

CONCLUSION:

This is the first documented case of a patient with AR IFN-γR1 deficiency suffering from influenza A virus infection pre HSCT. Although data is lacking regarding vaccine effectiveness in complete IFN-γR1 deficiency, strategies such as family vaccination should be considered in order to prevent potentially severe complications and HSCT delay.

ESPID-0977
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

CYTOMEGALOVIRUS INFECTION IN CHILDREN WHO UNDERWENT HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MALIGNANT AND NON MALIGNANT DISEASES.

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Background : A major potentially fatal complication of allogeneic hematopoietic stem cell transplantation (HSCT) in children is CMV reactivation due to associated impairment of the immune system.
Aim: To determine the frequency of CMV viremia among pediatric HSCT patients and monitor CMV-specific immunity.
Population and methods: A prospective cohort study of 37 pediatric HSCT recipients who underwent weekly virological monitoring (PCR-CMV) at least until +100 day post transplant and immunological monitoring [Quantiferon-CMV assay (Qiagen)] at 30,90,180,270 and 360 days after HSCT. Patients were classified according to underlying disease as non-malignant (n=16) and malignant (n=21) and according to risk of CMV reactivation as high risk [Donor (-)/Recipient(+) (n=12)], intermediate risk [D(+)/R(+) and D(+)/R(-) (n=18)] and low risk [D(-)/R(-) (n=7)].
Results: The incidence of CMV viremia was 51% (19/37) with half of the episodes within the first 30 days post transplant and only 1 patient belonging to the low risk group.CMV disease occurred in 2 patients (5%). Fifteen patients showed CMV-specific immune reconstitution at an average of 82 days. In the non-malignant group viremia occurred in 10 patients (62.5%),most (7/10) classified as intermediate risk. Evidence of CMV- specific immunity within the first 30 days post transplant was found in 31% of the patients in the non-malignant group and in only 19% of those in the malignant group.
Conclusions: Despite monitoring strategies and prophylaxis, CMV infection was a significant problem in this cohort,especially in the high/intermediate groups. Reconstitution of CMV-specific immunity was delayed in the malignant group.

ESPID-0998
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

IFNGAMMA RESPONSES TO LATENT HERPES VIRUSES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND RHEUMATOID ARTHRITIS (RA)

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Reactivations of latent herpes virus infections, such as Cytomegalovirus (CMV) or Varicella-zoster-virus (VZV), pose a high risk in patients with autoimmune arthritis receiving immunosuppressive treatments or biologics. The cellular IFNgamma response may be dysbalanced in autoimmune arthritis due to disease-related factors or immunosuppression.

The study was aimed to analyze the IFNgamma production in T cells from idiopathic juvenile arthritis (JIA) and rheumatoid arthritis (RA) patients compared to healthy, age-matched controls (HC) after CMVpp65- and VZV-specific antigen stimulation and in vitro IL-6- or TNFalpha-blockade using ELISPOT assay and flow cytometry.

JIA and RA patients demonstrated lower unspecific IFNgamma production by peripheral lymphocytes, decreased CD69-mediated activation and lower CD8+ T cell replication, but an increased intracellular IFNgamma production after CMVpp65 stimulation, which was not diminished by TNFalpha or IL-6 blockade. Lower IFNgamma-producing CD4+ T cells after VZV antigen stimulation were found in RA compared to HC, particularly in the presence of anti-IL-6 or anti-TNFalpha in vitro. No impairment of IFNgamma production was demonstrated for T cells of JIA patients stimulated with VZV antigen and treated with TNFalpha or IL-6 blockade in vitro.

Despite poor unspecific intracellular IFNg production, lower CD8+ T cell activation and replication in CMV-seropositive patients, sufficient CMVpp65-specific IFNgamma production suggests an efficient immune response against latent CMV regardless of immunosuppression or in vitro blockade of IL-6 or TNFalpha. Lower cellular IFNgamma responses towards VZV may support the clinical observation of increased zoster rates in RA patients, whereas JIA patients may demonstrate sufficient control of VZV reactivation.

ESPID-1010
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

ANTIBIOTIC LOCK-THERAPY AS ADJUNCTIVE THERAPY FOR CATHETER-RELATED BLOODSTREAM INFECTION (CRBSI) IN PEDIATRIC ONCOLOGY PATIENTS

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Background and aim: Central venous catheters (CVCs) are essential in the management of pediatric oncology patients although associated infections are frequent complications, often requiring catheter removal. CRBSI antibiotic-lock therapy (ALT) associated with systemic antibiotics has been proposed for the management of these infections. The aim of this study was to describe CRBSI cases from our hospital in a 6-years period and to analyze the effectiveness of ALT in these infections.

Methods: Retrospective study of CRBSI episodes from January 2008-November 2014 occurred at a pediatric oncology unit from a Pediatric tertiary hospital in Madrid, Spain. Demographics, CVC history, CRBSI etiology, treatment and CVC outcome were evaluated.

Results: 46 episodes of CRBSI in 38 patients were analyzed; 67.4% males. Median age: 6.4 years (range 0.22-22). Primary diseases were leukemia/lymphoma (52.2%), solid tumor (34,8%) and non-malignant (13%). Etiologies included Gram-positive (61%), Gram-negative bacillii (30%), polimycrobial (7%) and yeast (2%). The most frequent agent was coagulase-negative Staphylococci (CoNS). 73.8% of catheters received ALT. 16 catheter were removed: 7/12(58%) in the group with only systemic antibiotics vs 9/34(26%) in ALT group (p=0,075). Vancomycin and amikacin were the most common agents for ALT. *S. aureus* was associated with catheter removal in 75% of cases. All CoNS episodes cured without catheter removal. No adverse effects of ALT were identified.

Conclusions: Gram-positive cocci were the most common cause of CRBSI in these patients. Systemic antibiotics combined with ALT seemed to be effective as CRBSI treatment (73.5% success in this study), especially when CoNS is involved.

ESPID-0810
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

EFFICACY AND SAFETY OF PRE-EMPTIVE VERSUS EMPIRICAL ANTIFUNGAL THERAPY IN CHILDREN WITH CANCER, FEVER AND NEUTROPENIA

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Background Current recommendations propose to begin empirical antifungal therapy at day five of fever in patients with chemotherapy-associated neutropenia. The aim of this study was to determine efficacy and safety of pre-emptive versus empirical antifungal therapy in children with persistent fever and neutropenia. **Methods**. Prospective, multicenter, randomized study. Children presenting with persistent high risk febrile neutropenia (HRFN) (fever and neutropenia at day 4 of evolution) at five hospitals in Santiago, Chile, were evaluated with a clinical/microbiological/molecular/imaging study and randomized into a current empirical antifungal management (group A) versus pre-emptive antifungal therapy (group B). The pre-emptive group received antifungal therapy only if the persistent fever and neutropenia was accompanied by clinical/microbiological/molecular or imaging predefined criteria. End point were days of fever/ hospitalization/ antifungal use, resolving uneventfully/ developing IFI/need for intensive care unit (ICU) and death. **Results.** A total of 671 FN episodes were evaluated between June 2012 and December 2014. Of them, 470 (70%) were HRFN episodes and 74 (20%) had persistent fever and neutropenia. A total of 53 were randomized, 24 to group A and 29 to group B. Days of antifungal use were 12 *vs* 4, P=0.004, with similar days of fever and hospitalization, similar frequency of resolving uneventfully (89%-87%),developing IFI (10%-9%), need for ICU (24%-12%) and death (10%-8%). **Conclusions.** Pre-emptive antifungal therapy was as safe and effective as empirical antifungal therapy in children with cancer and HRFN. The reduction of antifungal use, based on stringent diagnostic criteria should favor the adoption of evidence-based management strategies in this population.

ESPID-0387
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

COMPARISON OF FEBRILE EPISODES AMONG CHILDREN WITH NEUROBLASTOMA(NB) VS. OTHER SOLID TUMORS AND LYMPHOMA (STL): A PROSPECTIVE MULTICENTER STUDY

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Background: Aggressive protocols for treatment of NB, stressing the potential increased risk for complications in comparison with other STL.

Aims: To characterize and compare clinical course and bacteriology of febrile episodes between children with NB and STL.

Methods: Data from all febrile episodes in children with STL and NB in 5 Israeli hospitals were prospectively collected during 2008-2009, including: demographical, clinical, laboratory , bacteriology, treatment and outcome. A comparison between NB and STL was conducted.

Results: There were 40 episodes among 23 patients with NB, and 415 episodes among 164 patients with STL. Demographic data were similar except younger age in NB vs. STL (mean 38±28 vs. 110±79 months p=0.000). Patients with NB more frequently had Hickman catheters (30% *vs.* 15.5% p=0.02), and intensive chemotherapy (97.5% *vs.* 75.4% p=0.007). No differences were seen in length of neutropenic episodes. Nadir was deeper in STL group (63±108cells/mm³ vs 118±154 p= 0.03). Diagnosis were fever without source 77% in STL , 80% in NB, and CVC associated infection or bacteremia in 9.5% in STL and 7.5 % in NB. Gastrointestinal related infection in 4.3% in STL and 0% in NB, UTI in 3.7% in STL, 7.5% in NB, all were not significant. There were 80 pathogens in the STL group (21% of episodes), 67.5% gram+, 27.5% gram-, 5 % candida. 6 pathogens in NB (15% of episodes) , 83% gram+, 17% gram-. 4 patients with STL died

Conclusions: No significant differences between study groups in terms of type of infections, and bacteriology.

ESPID-0208
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

CYTOMEGALOVIRUS RETINITIS IN THREE CASES WITH ACUTE LYMPHOBLASTIC LEUKEMIA DURING MAINTENANCE PHASE OF CHEMOTHERAPY

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BACKGROUND AND AIMS:

Cytomegalovirus retinitis is usually diagnosed in acquired immunodeficiency syndrome and in allogeneic hematopoietic cell transplant recipients, but rarely may occur in patients with acute lymphoblastic leukemia during maintenance phase who have not received hematopoietic cell transplantation. In order to increase awareness of CMV retinitis in this group herein we describe three cases aged 12, 9 and 3 years who developed cytomegalovirus retinitis suffering from acute lymphoblastic leukemia on maintenance phase of chemotherapy.

RESULTS:

In all our cases ophthalmologic findings revealed active retinitis based on ophtalmological examination. Cytomegalovirus DNA was detected by polymerase chain reaction technique in blood sample of two cases and in the vitreous fluid in one case. For induction therapy of CMV retinitis we used intravenous gancyclovir 10 mg/kg/d for 2-3 weeks, followed by oral valganciclovir prophylaxis. Active lesions of retinitis progressively resolved in all patients.

CONCLUSIONS:

Present cases suggest that CMV retinitis should be kept in mind in patients with ALL in the maintenance phase **for early diagnosis.** The prognosis of CMV retinitis depends on prompt threatment as well as early diagnosis and patient's systemic immunocompetence. In our cases we observed that intravenous gancyclovir treatment with subsequent oral valganciclovir prophylaxis was effective for cytomegalovirus retinitis.

ESPID-0937
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

CLINICAL PRESENTATION AND OUTCOME OF RESPIRATORY INFECTIONS BY RHINOVIRUS IN CHILDREN WITH CANCER, FEVER AND NEUTROPENIA

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Background: There are no data regarding the clinical course and outcomes of infections caused by rhinovirus in episodes of febrile neutropenia(FN) in children with cancer. We determine the clinical presentation and clinical outcome of rhinovirus infections in this population.

Methods: Children with cancer, presenting with FN at three hospitals in Santiago,Chile, were prospectively evaluated (May,2009-October,2014) by clinical examination, blood cultures and nasopharyngeal sample for multiplex-PCR(17 respiratory viruses).Rhinovirus viral loads were measured at day:1,3,7 and 15-30. Clinical and outcome variables were determined.

Results: In 671 episodes of FN, rhinovirus was detected in 145/671(22%) episodes, of which 26/145 were viral co-infections and 43/145 were mixed viral-bacterial infections. 76 episodes with exclusive detection of rhinovirus were analyzed. Median age of children was 7 years, 54% were male. Respiratory symptoms were present in the half of the episodes(nasal congestion:53%;cough:51%).At admission,28% presented abnormal lung sounds and 29% had chest X-ray abnormalities.9/76(12%) episodes required oxygen supplementation and 7/76 were admitted to the PICU.No patient required mechanical ventilation and no mortality was reported.Days of hospitalization were 7 days(IQR 5-9) and days of fever 2 days(IQR 1-3).36/76(47%) episodes were diagnoses as upper respiratory tract infection(RTI) and 23/76(30%) as lower RTI.Rhinovirus median viral loads were 15663 copies/mL at day 1, 1275 at day 3, 687 at day 7 and 0 copies/mL at day 15-30.

Conclusions :To our knowledge this is the first report of clinical outcomes of infections caused by rhinovirus in children with cancer.Our data showed a favorable outcome in all episodes,low viral loads and short viral excretion(FONDECYT-Grant#1130911).

ESPID-0415
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

DE NOVO HEPATITIS B INFECTION AFTER LIVER TRANSPLANTATION - CASE REPORT

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De novo hepatitis B virus (HBV) infection is defined as an infection occurring in HBV surface antigen (HBsAg)-negative patients who become HBsAg positive after organ transplantation. There are several possible routes of transmission: from donors who have antibodies to hepatitis B core antigen (anti-HBc), by reactivation of occult HBV infection in anti-HBc positive recipients, transmission through transfusion of anti-HBc-positive blood products, and transmission from hospital personnel or environment.
The authors present a case of a 6-year-old girl who underwent living donor liver transplantation at 16 months of age because of congenital biliary atresia. She was immunised by two doses of the hexavalent vaccine containing hepatitis B before transplantation, which induced the adequate antiHBs antibody levels. One year after the transplantation the antiHBs levels were negative and remained low after the third and fourth doses of the hepatitis B vaccine. Serologic testing and a high viral load confirmed diagnosis of hepatitis B. Lamivudine was initially administered but a resistance to lamivudine was confirmed after ten months of therapy. Entecavir was then administered instead and showed a good virologic response.
The source of the HBV infection was presumably from the environment (the donor and recipient were antiHBc negative). A failure to complete the immunization before the transplantation and administration of immunosupressive drugs could have led to a failure to prevent the infection.
It is important to closely monitor the antiHBs protective levels, especially when complete immunization cannot be realized in the imunocompromised child because of their age and health status.

ESPID-0898
INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

FATAL CHRONIC CMV INFECTION OF AN INFANT SUFFERING FROM BARE LYMPHOCYTE SYNDROME TYPE 2 DUE TO A NEW RFX5 MUTATION

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Background: Major histocompatibility complex class II (MHC-II) deficiency, also called bare lymphocyte syndrome (BLS) type 2, is a rare primary immunodeficiency. Four genes, *CIITA, RFXANK, RFX5* and *RXFAP* are involved in its pathogenesis. Patients suffer from severe viral, fungal, bacterial and protozoan infections resulting in a markedly reduced life expectancy.

Case: We saw an initially 10-month-old libyan patient suffering from a developmental arrest since the age of 4 months and a spastic tetraparesis. The patient had no endogenous immunoglobulins and no MHC-II molecules detectable on lymphocytes. A new homozygous *RFX5* gene mutation was found. We revealed high cytomegaly virus (CMV) copy numbers in the serum and the cerebrospinal fluid. The patient was treated with ganciclovir until he developed drug resistance. Foscarnet did not have any additional effect. The patient died in CMV septicemia at the age of 14 months.

Discussion: Chronic viral infections play a critical role in the outcome of patients suffering from BLS type 2. Especially CMV is known to increase complications in these patients, mostly in connection with the only curative therapy, the stem cell transplantation. Our patient suffered from a chronic CMV infection with hepatitis and CNS infection. Two transplantation centres declined stem cell transplantation due to the neurological status and the active CMV infection of the patient. After developing ganciclovir resistance there was no effective treatment left. Identifying underlying genetic mutations and genetic counseling will help families to bring affected individuals to stem cell transplantation before chronic infections occur.

ESPID-0461
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

MORGANELLA MORGAGNII INFECTION OF THE FIRST BRANCHIAL CLEFT ANOMALY; A SIGN FOR THE DIAGNOSIS

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Branchial cleft anomaly is the most common congenital causes of a neck mass and arise from the abnormal persistence of branchial apparatus remnants, and account for 17% of all pediatric cervical masses. First branchial cleft anomalies are responsible for fewer than 10% of all branchial cleft defects. Although an ubiquitous gram-negative bacillus, *M. morgagnii is* not a common cause of infections in humans.

Here we describe a case of first branchial cleft anomaly infected with M. morganii in a previously

healthy 10-month-old girl, who presented with a tender mass in the left anterior neck.

The diagnosis of First branchial cleft anomalies is very difficult compared to other cleft anomalies. The patient had been referred to our hospital with a suspicion of mumps infection. Magnetic resonan~~a~~ce imaging demonstrated a cystic benign lesion which was in connection with the left parotid gland suggesting a complicated branchial cyst.

M. morganii are found in the natural environment, normal flora of the gastrointestinal tract of humans, ~~and~~ other mammals and birds and also in healthcare facilities. Despite its widespread distribution, it is considered as a rare pathogen in humans because of its identification difficulties, which could be responsible for the underestimation of the number of infections due to this organism.

This case represents the first report of an infected branchial cleft cyst due to M. morgagnii in an

immunocompetent patient, expanding the spectrum of clinical disease that may be seen with this

organism.

ESPID-0476
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

BRUCELLOSIS WITH VERY HIGH FERRITIN LEVELS: REPORT OF 2 CASES

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Brucellosis a zoonotic diseasecaused by a kind of Brucella bacteria,which commonly appears in humans and rarely causesmortality. In our study, 2 cases who were diagnosed by evaluation of clinicalfindings and serologicaltests, they also had very high ferritin levels, were reported.

CASE 1:A 16-year-old male patient was admittedto a health institution 20 days before due to fever and joint pain. The patient's symptoms did not diminish, and so he applied to ouremergency department. Other findings of patient were normal except pallor and weaknessat his physical examination. Laboratory results were detected asabnormal, as follows: brucella agglutination test: 1/1280, ferritin: 1200ng/ml, lactate dehydrogenase (LDH): 846 U/L and Hb: 11.5 g/dl. Complaints ofthe patient decreased after implementation of binary antibiotic (doxycyclineand rifampin) therapy for 6 weeks and the patient's general condition improved.

CASE 2: A 12-year-old male patient presented toour hospital with complaints of fever, joint pain and cold chills, he had these symptoms for approximately 40 days before he came to thehospital. Upon physical examination, the spleen was palpable 3 cm. Results of laboratory analysis were asfollows: ferritin: 985 ng/ml, LDH: 724 U/L, sedimentation: 48 mm/h, CRP: 96mg/L and brucella tube agglutination test: 1/1280. We started triple antibiotic(doxycycline, rifampicin and streptomycin) therapy. The patient's symptoms andsigns disappeared within 2 weeks after the onset of treatment. Subsequentcontrol investigations were as follows: ferritin: 146 ng/ml, sedimentation: 32mm/h, CRP: 8 mg/L and LDH: 211 U/L.

ESPID-0110
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

USE OF SYNBIOTIC FOR ACUTE WATERY DIARRHEA AMONG CHILDREN IN SOUTH INDIA - A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL

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Objective: To evaluate the use of synbiotic in reducing the frequency and the duration of acute watery diarrhea in children

Methods: This double blinded RCT included 113 children in the age group of 6 months to 12 years with acute diarrhea were randomized into 2 groups- group A and group B. Group A received standard WHO treatment (ORS plus Zinc) and placebo while group B received standard treatment with synbiotic (Bifilac) . The frequency and the duration of acute watery diarrhea in both groups were compared.

Results: The mean stool frequency in synbiotic group was less compared to placebo group after 24 hours (2.84/day Vs 3.59/day) and 48 hours of therapy (1.26 /day Vs 2.46 /day). The mean duration of diarrhea was significantly reduced in the synbiotic group after initiating treatment (3.4 days vs 6.4 days, $p<0.001$).

Conclusion: Use of synbiotic along with standard treatment reduces stool frequency and duration of acute watery diarrhea in children.

ESPID-0592
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

16 YEARS OF VARICELLA-RELATED HOSPITALISATIONS

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Background and aims: Varicella vaccine is available in Portugal since 2004 but is not included the NIP and coverage is low. Our aim is to characterise complications from varicella in the last 16 years.

Methods: Retrospective review of medical records of all children admitted with complications or risk of complications from varicella between 1999-2014, in a tertiary paediatric hospital.

Results: 141 children were hospitalised. Median age was 2Y(11D-15Y), 60% were male, 80% were previously healthy and 24% were the second case in the family. A seasonal distribution was observed, peaking between May and August. The mean number of cases/year was 8.8, with no obvious trends over time. 26.2% were on acyclovir before admission. Only an oncology patient had been vaccinated.

15.6% were admitted because of risk of complications (8 newborns, 14 with underlying disease).

Clinical manifestations began at a median of 3D of illness and the median length of stay was 3D. The most common complication was skin and soft tissue infections (SSTI) (87;61.7%), followed by neurological (15;10.6%), respiratory (13;9.2%) and haematological (4;2.8%) complications. Median age for neurological complications was higher (4Y) compared to SSTI and respiratory (2Y and 1Y respectively).

S. aureus (11) and *S. pyogenes* (7) were isolated in SSTI. All but one (an oncology patient developed chronic varicella) had a favourable outcome.

Conclusions: During this period, complications from varicella accounted for a considerable burden in the healthcare system, requiring care in the ES and hospitalisation. The most common complication was SSTI, which affected younger healthy unvaccinated children.

ESPID-0269
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

IMMUNOPHENOTYPE AND MORPHOLOGY OF PERIPHERAL BLOOD LYMPHOCYTES IN PEDIATRIC. VARIOUS ETIOLOGIES MONONUCLEOSIS-LIKE SYNDROME

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Infectious mononucleosis-like syndrome (IMLS) can be caused by herpesviruses such as Epstein-Barr virus (EBV), cytomegalovirus (CMV) and human herpes virus 6 (HHV6). However, relative occurrence of IMLS of different origin in children and the difference in their immune status is not fully understood. We examined 100 children from 15 months to 16 years old presenting mononucleosis-like clinical symptoms of fever, sore throat, rash and lymphadenopathy. Diagnosis of active herpesvirus infection was carried out by determining IgM and IgG against EBV, CMV and quantitative DNA of EBV, CMV, HHV6 in peripheral blood. The immunophenotype of the peripheral blood mononuclear cells (PBMC) and the percentage of atypical lymphocytes were studied using a microarray of anti-cluster of differentiation (CD) antibodies on a transparent slide with subsequent May-Grunwald-Giemsa staining for morphological examination. 43% of the patients had an active primary EBV infection in 26% EBV-reactivation was detected. Among 31 patients without an active EBV it was determined active HHV6 in 23 children and and in active CMV was found in remaining 5 ones. Active herpesvirus infection was not detected in 5 children.The children with active primary EBV infection had significantly lower CD4/CD8 ratio, higher percentage of CD8+ and HLA-DR+ PBMC and lower percentage of CD19+ PBMC than the patients with EBV reactivation or the patients with latent EBV infection. Atypical lymphocytes were detected in all children (>1% of PBMC), but the percentage is much higher in patients with active primary EBV infection compared to patients with EBV reactivation or to patients without active EBV.

ESPID-0390
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

GIANOTTI-CROSTI SYNDROME ASSOCIATED WITH EPSTEIN-BARR INFECTION AND ACUTE NOROVIRUS DIARRHEA- CASE REPORT

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Background- Gianotti-Crosti syndrome is a distinct infectious exanthem associated with acute anicteric hepatitis.

Methods - The authors describe a case of Gianotti-Crosti syndrome associated with Epstein Barr virus infection, diagnosed retrospectively in the third week of evolution, in the course of hospitalization for a Norovirus diarrhea.

Results - A 3 year old child is hospitalized with watery diarrhea lasting 2 days with acute dehydration. Clinically it detects a maculopapular rash on the face and limbs with a history of 21 days, interpreted as an allergic rash. Biologically is detected a syndrome of hepatic cytolysis. Serology is positive for Epstein Barr virus. Fecal Elisa Ridascreen 3rd generation Norovirus test is positive. History, characteristic topographic rash on the extremities and face, absent on the scalp and trunk, discrete liver damage and serologic confirmation oriented to a Gianotti-Crosti syndrome secondary to Epstein Barr virus infection associated with ongoing noroviral diarrhea.

Conclusions - The presence of a particular acral and facial rash with an evolution for over 10 days and rebellious to antihistaminic therapy should raise the suspicion of Gianotti-Crosti syndrome and initiate the evaluation of the etiology and severity of liver damage. Acrodermatitis can sometimes be the only sign of viral hepatitis and is often underdiagnosed or misinterpreted in the context of skin rashes.

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ESPID-0991
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

A CASE OF KAWASAKI DISEASE ASSOCIATED WITH ACUTE VIRUS CO-INFECTION

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Introduction: Kawasaki disease (KD) is a self-limited vasculitis of unknown cause. The diagnosis is clinical and implies fever lasting more than 5 days combined with 4 or more specific clinical criteria. It is currently the most common cause of acquired heart disease in children.

Case report: A previously healthy 15-month-old boy presented with a 9 day history of fever associated with irritability and difficulty to walk. Physical examination revealed a diffuse rash, confluent in the folds including palms and soles, cheilitis and erythema of the oral cavity, bilateral non-exudative conjunctivitis without uveitis, swelling of the hands and feet as well as cervical lymphadenopathy. The diagnosis of Kawasaki Disease was made and therapy with acetylsalicylic acid (ASA) and intravenous immunoglobulin was initiated promptly. At the end of the second week of illness, clinical improvement with peeling appearance of the fingers was noted.

Initially,slight ecocardiographic changes in the coronary arteries where observed with normalization within 2 weeks.

Analytically anemia, leukocytosis with neutrophilia, thrombocytosis, elevated PCR, hypoalbuminemia, hyponatremia, liver function abnormalities, dyslipidemia and sterile pyuria were detected. Positive results for IgM Epstein Barr virus (EBV) and PCR Parvovirus B19 were obtained.

Conclusions: The etiology of KD, according to literature, may be related to the immune response triggered by infectious agents such as Parvovirus B19 and EBV. Although it is a self-limited disease, the diagnosis is essential for early institution of therapy allowing the reduction of coronary complications and mortality.

ESPID-0918
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

UP TO WHAT AGE SHOULD AMPICILLIN BE USED IN THE INITIAL MANAGEMENT OF THE COMMUNITY-ACQUIRED UTI IN INFANTS?. ROLE OF ENTEROCOCCUS FAECALIS

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Background and aims: Ampicillin plus cephalosporins/aminoglycosides is the empyrical treatment (ET) of community-acquired urinary tract infections (CA-UTI) in patients <3-month-old because of *Enterococcus faecalis* (EF). Current controversial includes treatment in infants 2-3 months of age and the relationship with urinary tract malformations (UTM) of CA-UTI caused by EF.

Methods: Descriptive-retrospective study of patients under 14 years-old with CA-UTI caused by EF treated in a Tertiary Pediatric Hospital (January 2011-December 2014).

Results: 69 patients were included: 72.5% male, median age 2.96 months [p25-p75:1.3-20.5], 74% were younger than 3 months, 24,6% had between 60 and 90-day-old. Median age of children that requiring hospital admission (37, 53.6%) was 1.53 months [p25-p75:0.9-3.43]. 23/37 were admitted because of fever without unknown origin or initial suspicion of UTI, ignoring if they had UTM, with mean age of 1.61 months (±1.13), their characteristics are shown in table 1. Patients older than 90 day-old with acute pyelonephritis (AP) were treated empirically with gentamicin in a case and cefotaxime in another with favorable evolution. All strains were susceptible to ampicillin and vancomycin.

Conclusions: EF shoud be taken into account in infants <3 month-old with UTI and approximately 20% happened in the 60-90 day-age-period. In children without known UTM, it seems safe to use ampicillin plus gentamicin for empirical treatment in infants <3 month-old, as well as the gentamicin use alone in children older than 3 months.

Table 1.		
Age(days)	N(%)	AP/Cystitis(n)
<60	15(65,2%)	6/9
60-90	5(21,8%)	2/3
>90	3(13%)	2/1

ESPID-1063
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

ARDS IN CHILDREN: ETIOLOGY AND EPIDEMIOLOGY

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Background:

The Pequeno Principe Hospital (PPH) is pediatric quartenary hospital, located in South of Brazil, has 360 beds and 32 pediatric specialties. PPH is a Sentinel Unit for investigation of acute respiratory distress syndrome (ARDS), for hospitalized patients. Data obtained over the years has shown that the period of greatest circulation of influenza viruses in this region occurs from May to September. The aim of this study was to determine the ARDS prevalence and their etiology in children attended in a reference pediatric hospital, with respiratory symptoms.

Methods: Between January 2013 to September 2014 we started to investigate ARDS. Lab tests to diagnose the etiology were made in IAL using multiplex RT-PCR. Specimens were collected by oro/nasopharyngeal combined swab .

Results: In this period of surveillance**, 333** cases of ARDS were investigated, 168 cases in 2013 and 164 in 2014. Children under 1 year old were the most frequently affected, 75%(126) in 2013 and 58.78% (97) in 2014.The more prevalent respiratory viruses identified were Rhinovirus 33.33% (56) and Respiratory Syncytial Virus 49.40(83) in 2013.As well Rhinovirus 25.60% (65) and Respiratory Syncytial Virus 39.63% (65) were the most prevalence identified in 2014.

Conclusions: Despite advances in establishing a wide network of information about the circulation of respiratory viruses, there is still little information about the burden of respiratory viruses in children and factors associated.

ESPID-0923
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

FACIAL CELLULITIS AS A COMPLICATION OF DENTAL INFECTION IN CHILDREN, EXPERIENCE IN OUR HOSPITAL

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Background and aims:

Dental infections are relatively common in paediatric patients. Because of its location, odontogenic problems are a potencial source for severe complications: may affect brain, eye or upper respiratory tract. The aim of this report is to describe patients treated in a secondary hospital.

Methods:

We review the cases diagnosed with facial cellulitis of odontogenic origin, and admitted to our hospital during the last 1.5 years. Epidemiological, clinical and evolution features are described.

Results:

Fourteen patients (0.8% total paediatric admissions along the last 1.5 year) presented facial cellulitis as a complication of a dental injury. Eight girls (57%) and 6 boys, from 2.6 to 13.8 years old. The mean lenght of hospitalization was 4.4 days (median 3.5 days).

The most consistent symptoms were swelling and pain (100%), and fever (57%). Admission criteria was mainly the increasing facial oedema (13 cases - 93%).

All cases were admitted with intravenous antibiotic therapy: 13 with amoxicilin-clavulanic acid (A-C), and 1 with cefuroxime. Corticotherapy was associated in most of cases, and 2 patients needed surgical intervention.

Oral A-C was prescribed to all patients after been discharged from hospital, in order to complete at least 10 days of total antibiotic therapy, and dental intervention was recommended.

Conclusions:

Odontogenic infections should be treated early, because of their possible fast evolution to severe diseases. Intravenous antibiotic is necessary in evolved cases, and dental intervention after swelling decreases. Sometimes, surgical treatment is required at acute phase.

ESPID-0458
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

A CASE OF PAEDIATRIC CUTANEOUS MELIOIDOSIS ACQUIRED VIA FRESH WATER EXPOSURE IN SOUTHERN CHINA AND LITERATURE REVIEW

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Background

Melioidosis is a serious infection caused by Burkholderia pseudomallei. It is endemic in Southeast Asia and northern Australia and rarely reported in China. Most cases present as acute serious infection with bacteremia.

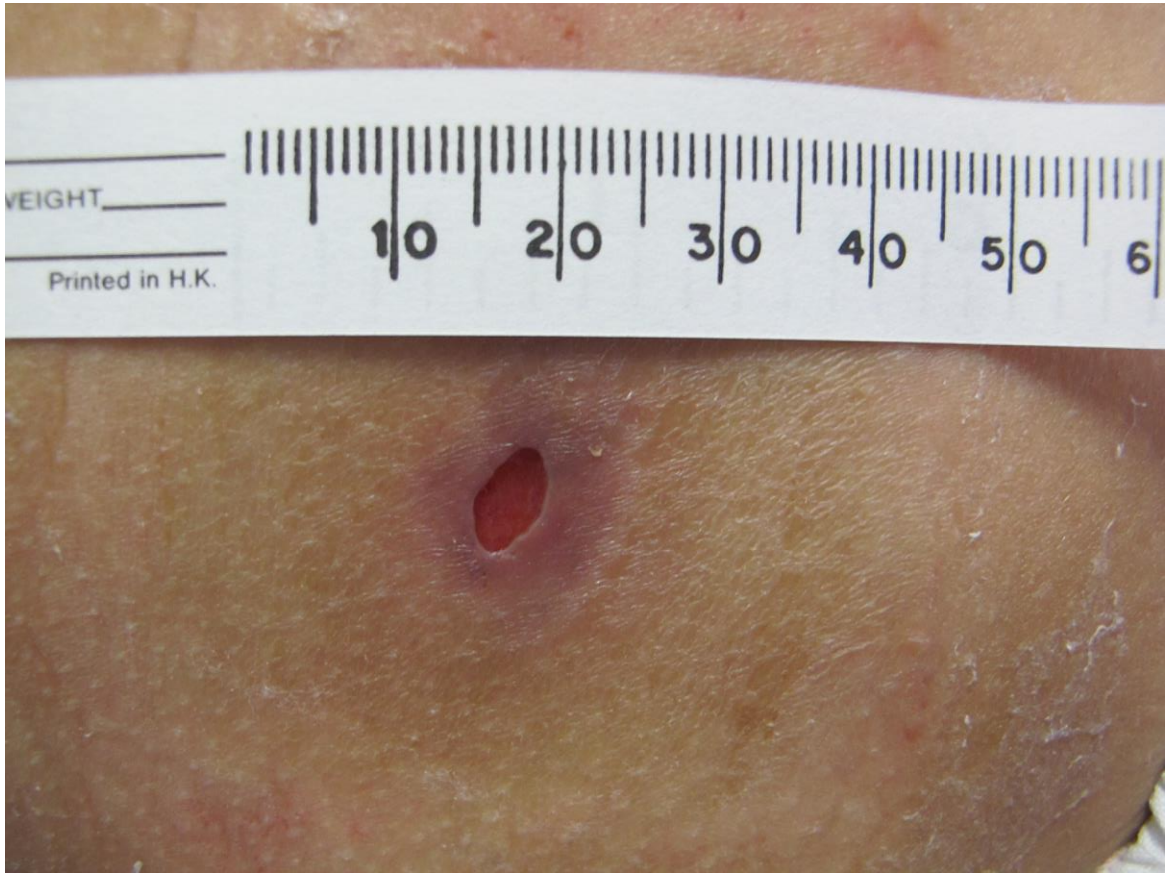
Findings

We described a 8 year-old Chinese girl with non-disseminated melioidosis with unusual presentation. The child enjoyed good past health except eczema. She presented with 1.5 months history of unhealed right abdominal wound. She traveled from China province GuangDong county Huizhou and swam in fresh water from a well 3 weeks before the onset of lesion.

The lesion started as a 2mm tender papule then progress to pustule in a week. There was no preceding wound or skin abrasion. She remained afebrile and systemically well. The pustule erupted 1 week later and became a 8mm wound. The wound swab yielded Burkhoderia pseudomallei. White cell count, inflammatory markers, blood culture, sepsis workup and chest X-ray were all normal. Abdominal ultrasound showed no intra-abdominal collection. Workup for underlying immunodeficiency was unremarkable. Further culture of the fresh water source yielded Burkholderia pseudomallei. She was treated with 2-week course of ceftazidime followed by 4-month course of trimethoprim-sulfamethoxazole. The wound was dried and healed at 3 months post-onset of lesion, 1.5 months post-treatment.

Conclusions

We described a case of localized melioidosis presented with cutaneous wound of prolonged illness course without a clear portal of entry. The source of infection was identified to be the fresh water in Southern China.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ESPID-0788
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

A CASE STUDY QUESTIONING THE CLASSICAL VIEW THAT ACUTE RHEUMATIC FEVER IS CAUSED EXCLUSIVELY BY GROUP A STREPTOCOCCAL PHARYNGITIS

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Rheumatic fever, although now very rare in the Western world, is common in developing countries, with the highest recorded incidences occurring in the indigenous populations of New Zealand, Australia and the Pacific islands. This case study examines the well-established classical view, still widely taught today, that acute rheumatic fever (ARF) is exclusively caused by Group A streptococcal (GAS) pharyngitis, and not GAS skin infections.

A 10-year-old Maori boy presented with a 1 day history of a severely painful and swollen knee. The patient had impetigo 2 weeks previously and no history of sore throat. He was febrile with raised anti-streptolysin and anti-DNAse B titres, raised ESR and aortic regurgitation on echocardiogram, resulting in a diagnosis of ARF. Throat swabs were negative for GAS.

The classical view that ARF is only caused by GAS pharyngitis is based on a large body of laboratory and epidemiological evidence, predominantly from America, in the mid-to-late 20th century. However, this case study suggests the possibility that ARF can be caused by GAS skin infections. This alternative view is supported by studies in Australia, which demonstrated very low GAS throat carriage and incidence of pharyngitis, in contrast to very high incidences of GAS impetigo, in aborigine populations where ARF is hyperendemic.

In conclusion, there is a growing body of evidence complimenting this case study, implicating GAS skin infections in the pathogenesis of ARF. These findings may have global health implications and demonstrate that older studies should not so readily be applied to vastly different populations.

ESPID-0606
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

ROTAVIRUS-ASSOCIATED MILD ENCEPHALOPATHY WITH A REVERSIBLE SPLENIAL LESION (MERS) – THE FIRST CLINICAL CASE REPORT FROM EUROPE

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Introduction

We report the first case to our knowledge of rotavirus-associated Mild Encephalitis/encephalopathy with a Reversible Splenial lesion (MERS) in Europe.

Case description

A previously healthy 4-year-old boy presented with a 2-day history of vomiting, diarrhoea, and fever, complicated by sudden onset of encephalopathy.

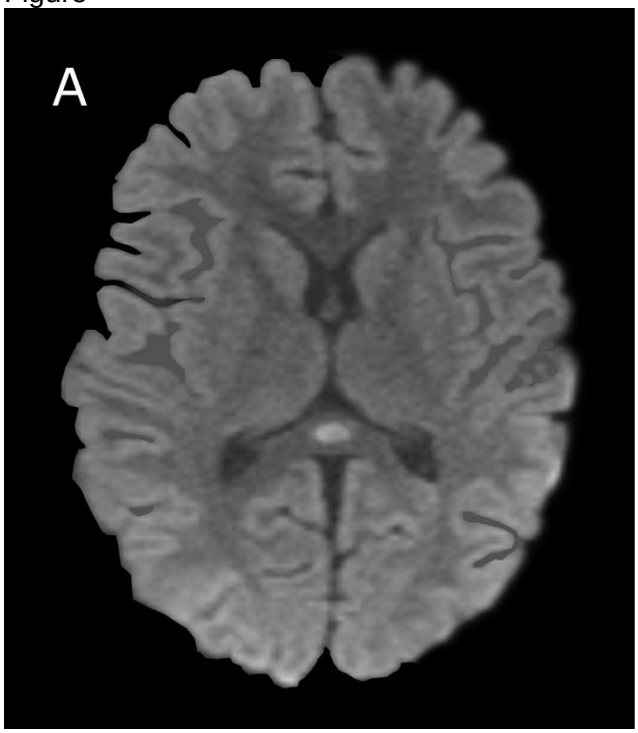
Magnetic resonance imaging of the brain showed a marked hyperintensity in the splenium of the corpus callosum on T2 and diffusion-weighted images (Figure 1). Rotavirus genome was detected by polymerase chain reaction in a stool specimen, but not in CSF. The genotype was identified as G1P8.

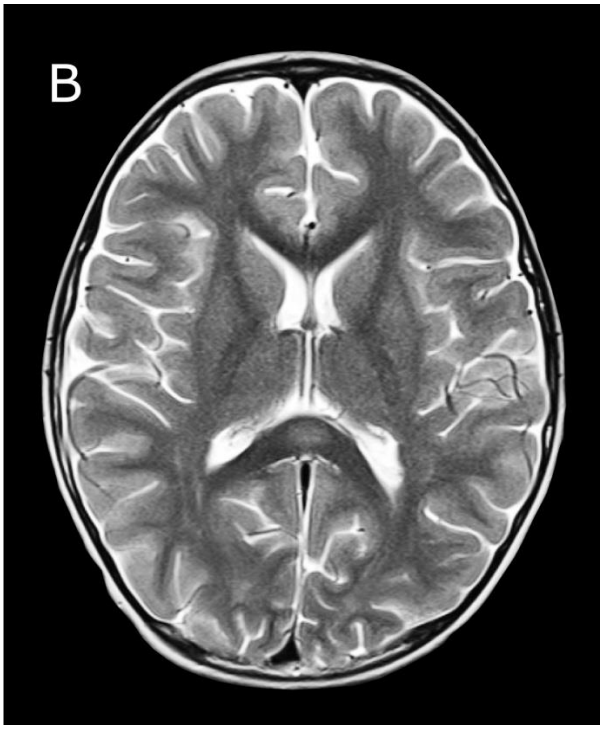
His clinical condition improved with gradual resolution of his symptoms. No neurological complications were evident upon discharge and the patient had no recurring symptoms or significant residual defects when followed up 2 months later.

Discussion

MERS is a novel clinic-radiological syndrome first described in Japan. A transient splenial lesion with reduced diffusion that appears as a high signal intensity in diffusion-weighted MRI is the main diagnostic feature. Rotavirus is one of the most common agents associated with MERS, although to our knowledge previous cases have not been reported from Europe. The majority of patients achieve full recovery following rotavirus-associated MERS, irrespective of treatment. This case, together with other published case reports, supports the hypothesis that rotavirus-associated MERS is unlikely to be the result of direct viral invasion of the CNS. It has been suggested that MERS may be caused by intra-myelinic axonal oedema or local inflammatory cell infiltration. However, the pathogenesis remains incompletely understood.

Figure 1





ESPID-0868
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

NOSOCOMIAL ROTAVIRUS GASTROENTERITIS IN A PEDIATRIC DEPARTMENT: A 5 YEARS RETROSPECTIVE STUDY

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BACKGROUND

Rotavirus is the most common cause of gastroenteritis requiring hospitalization in children. It is a very resistant and contagious virus causing nosocomial infections (NI) In France, the vaccine is available since 2006 and recommended less than six months since February 2014.

Retrospective study's aim was to describe nosocomial rotavirus infections (NRI) and to assess their impact among children hospitalized in the Department of Pédiatrie Générale at the Robert Debré Hospital (Paris) between January 2009 and December 2013.

METHODS

We analyzed demographic characteristics of children and the severity of the NI and assessed whether these children could benefit from vaccination against rotavirus.

RESULTS

136 children presented NRI, with an incidence of 2.5 NI per 1000 days of hospitalization. The incidence of NRI was stable between 2009 and 2013 despite the introduction of specific hygiene measures. The average children age was 7 months (range 0.5-111 months). Most often NRI occurred among children hospitalized for respiratory problems (65% of cases) and requiring prolonged hospitalization (median 18 days). One third of children was born premature (25%). Hydration was oral to 80 patients (59%), intravenous to 18 patients (13%), and intraosseous to a patient. Half of patients was aged less than 5 months and could benefit from the protection afforded by vaccination.

CONCLUSIONS

NRI are common. Rotavirus mass vaccination should have a positive impact on the incidence of NRI by reducing the number of children hospitalized for gastroenteritis, therefore reducing indirectly cross-infections of children with underlying pathologies, too young to be vaccinated.

ESPID-0908
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

HERPES ZOSTER IN CHILDREN

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Background and aims: Herpes zoster (HZ) is rare in healthy children and can occur at any time after varicella or varicella vaccination. Episodes are generally self-limited and antiviral therapy is usually not needed. Our aim was to review the epidemiology and management of HZ in the last 6 years.

Methods: Retrospective review of the medical records of all children with HZ observed from 2009 to 2014 in a tertiary paediatric centre.

Results: 80 children were diagnosed with HZ, 72 observed in the Emergency Service and 8 inpatients. Median age was 8Y (14M-17Y), 56.3% were male. The average patients/year was 13 (8-2009, 19-2011), with no clear trends over time. 52.5% were diagnosed between June and September. 13.8% (n=11) were oncology patients and 2 were under immunosuppressive therapy. When registered (n=16) the median gap between varicella and HZ was 3.5Y (6M–11Y). The most common symptoms were: pruritus (54%), pain (52%) and fever (19%). Rash location was mainly thoracic (62%), facial (16%) and abdominal (12%). 13.8% (n=11) patients were hospitalised (oncology patients-8, on steroid therapy-2). Median length of stay was 7D (2-11). Acyclovir/valacyclovir were prescribed to 52% ambulatory patients and all but one hospitalised children. All had good outcome.

Conclusion: The number of cases of HZ has remained stable during these years. Half of the patients were symptomatic although fewer than described in adults. Despite no intervention being needed in most cases, antiviral treatment was given to more than half of healthy children. Most admitted children had an underlying disease.

ESPID-0713
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

CAUSES OF PROLONGED SUBFEBRILE FEVER IN CHILDREN

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Background and aims. Subfebrile prolonged fever of unknown origin in children is a multicausal syndrome. Some children referred for pediatrician with prolonged fever are actually not having elevated temperatures, others have well-documented fevers associated with clinical, laboratory, or epidemiologic findings that should point to a specific diagnosis. Sometime the reasons of fever remain unknown. This study aimed to analyze the causes of subfebrile fever in children.

Methods. A retrospective analysis of cases of subfebrile prolonged fever in children, consulted in Outpatient Department of Children of Kaunas Clinical Hospital in 2013. Children with daily fever ≤ 38,0°C lasting for ≥14 days were included into the study.

Results. Medical records of 43 patients with subfebrile prolonged fever were analyzed. Patients age ranged from 5 months to17 years (mean 9.35±5.32y); 27 (62.8%, p>0.05) of them were >7 years old; 17 were boys and 26 were girls. Fever mean was 37.42°C and in average lasted for 82.5 days. Final diagnosis was reached in 37 children (86.05%). The most common cause (55.8%) of prolonged subfebrile fever was upper respiratory tract infection (tonsillitis, otitis, etmoiditis, adenoiditis), followed by latent tuberculosis infection (21%), lower respiratory tract infections 4.65% (bronchitis), mononucleosis 4.65%, one case of urinary tract infection and toxocariasis. Some patients had few infections.

Conclusions. 1.The most common cause of prolonged subfebrile fever was upper respiratory tract infection and latent tuberculosis infection. In 13,95% of cases the causes remained unknown. 2. Prolonged subfebrile fever was more common between school age patients.

ESPID-0876
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

GIANOTTI-CROSTI SYNDROME PRECEDED BY VARICELLA-ZOSTER VIRUS INFECTION

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Background – Gianotti-Crosti Syndrome (GCS) is a unique exanthema characterized by papules or papulovesicles symmetrically distributed on the face, buttocks and extremities. It is self-limited and no treatment is required. Although the exact pathogenic mechanism is unknown, GCS seems to be a non-specific cutaneous response to a variety of viral and bacterial infections. The most frequently reported etiologies are hepatitis B virus and Epstein-Barr virus (EBV) infections. Recently, many other microorganisms have been incriminated and occasional cases have been observed after immunization. Herein the authors report a case of GCS preceded by a varicella-zoster virus infection, an occurrence not frequently described in literature.

Case Report – A healthy 2-year-old boy was evaluated for a 5-day history of fever and 3 days of sore throat, anorexia and nonpruritic erythematous papular eruption. Five days prior to these complaints, he presented an itchy vesicular exanthema diagnosed as chickenpox by his General Practitioner. On examination, he was not an ill-appearing child, had tonsillar hyperaemia, multiple bilateral cervical lymphadenopathies, some crust lesions in the trunk (suggestive of chickenpox) and small confluent papules symmetrically distributed over the face, buttocks, forearms, thighs and legs (Figure1). Laboratory studies showed 14.4×10^9/L leukocytes (66% lymphocytes), normal C-reactive protein and normal liver function tests. Serologic tests for hepatitis virus, EBV and cytomegalovirus excluded active infection.

Conclusion – Recent research have associated GCS with several infectious agents. This case report reveals the potential link between GCS and varicella-zoster virus infection.

ESPID-0586
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLOSTRIDIUM DIFFICILE. OUR EXPERIENCE IN THREE DIFFERENT CONTEXTS

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BACKGROUND

Children are recognized as Clostridium Difficile(CD) healthy carriers. Its detection has increased due to improvement of diagnostic techniques, being essential define when determination is indicated.

AIMS

Describe three pediatric patients, in whom CD was isolated

METHODS

- 6 years healthy female. Abdominal pain, vomiting, fever and few loose stools last 48 hours. Leucocytosis, CRP 52mg/L. Admitted for dehydration. 4th day, diarrhoea stopped, but fever persisted with pathological abdomen exam, CRP: 425.2 mg/L and normal ultrasound. CD positive in stools, Metronidazole was started and then switched to Vancomycin because of deterioration. 8th day fever persisted and CT was performed, finding left kidney abscess. Resolution with Amoxicillin Clavulanic (AC).

- 13 years healthy female. Suprapubic pain and fever. AC until 24 hours before for infected wound. Normal ultrasound and laboratory test except CRP 198.6 mg/L. Few hours after admission hypotension, elevated reactants and severe diarrhoea. Normal CT. Cefotaxime and Clindamycin initiated, switched to metronidazole after detection CD in stools. Improvement and completely recovery.

- 6 years female. Feet and abdominal pain, ulcers, fatigue and weight loss. Frequent admissions since 18 months for recurrent fever, aphtas, arthralgias. Anaemia, thrombocytosis and elevated CRP. 2nd day melena and positive CD in stools. Treatment with metronidazole. Diagnosed of Crohn disease by endoscopy.

RESULTS

One patient presented severe diarrhea. Two had classic risk factors. The first one probably corresponded to a carrier.

CONCLUSIONS

Interpretation of CD positive result in stools must be done in context of clinical data, risk factors and age, for avoiding unnecessary treatment in carriers.

ESPID-0769
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

PUO OR POSTSTREPTOCOCCAL SYNDROME

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Acute rheumatic fever and glomerulonephritis are the most recognised non suppurative complications of Group A beta-haemolytic streptococcal infection in children.
We report a case of a 9-year-old boy, who was previously fit and well, and presented with 3 week history of fever and migratory polyarthralgia affecting large joints. He had congested tonsils with no follicles or exudates. Rest of his examination was unremarkable including BP. He had raised inflammatory markers (ESR 164, CRP 88) and ASO tire (1:800) but throat swab was negative. His urine dipstick, ECG and ECHO were normal. A diagnosis of post streptococcal inflammatory syndrome was made as he did not fit in the criteria for acute rheumatic fever. He was treated with benzyl penicillin, followed by prophylaxis and regular Ibuprofen.

He remained symptomatic for further 10 weeks and inflammatory markers, IgG and IgA levels and ASO titres remained high (>1600) despite penicillin and analgesics. He was discussed with immunology, infectious diseases, and rheumatology and oncology teams. Further investigations including serial blood cultures, CSF culture and viral and mycoplasma serology, tuberculosis serology, bone marrow aspirate, bone scan, complements, autoantibodies and immunodeficiency screen, which were all normal.

Once malignancies and infections were ruled out, he was about to be started on oral Prednisolone, before which his symptoms settled over further two weeks. The presentation as unexplained fever and the protracted course of his illness was unique as it did not fit in with any of the classically described post-streptococcal syndromes, including acute rheumatic fever and post streptococcal arthritis.

ESPID-0525
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL ASPECTS OF ACQUIRED CYTOMEGALOVIRUS INFECTION IN IMMUNOCOMPETENT CHILDREN

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Introduction

The clinical aspect of infection with human cytomegalovirus (CMV), a ubiquitous herpesvirus, can range from asymptomatic or mild forms of disease to systemic involvement. The polymorphism of CMV infection can pose difficulties in establishing a correct diagnosis and treatment.

Method

Over a period of 4 years, all cases of CMV infection, admitted in the Pediatric Department of the National Institute of infectious Diseases “Prof. Dr. Matei Bals”, have been studied, and age, sex and clinical form of disease were monitored. Diagnosis was established through serologic tests and confirmed with PCR.

Results

Between January 2011 and December 2014, 39 children were admitted with CMV infection. The clinical forms of disease constituted of: 17 (43.6%) cases of CMV hepatitis, 12 (30.7%) mononucleosis syndromes, 8 (20.5%) rhinopharyngitis with lymphadenopathy and 2 (5%) cases of interstitial pneumonia. 54% of patients were male. Children aged 1 to 3 years were the most affected adding up to 30%, followed closely by infants under 1 year (28.2%). Most cases required several days of hospitalization and surveillance. No deaths were registered.

Conclusions

Because of its ubiquity, the role of CMV in a child’s illness is difficult to distinguish. Most of CMV infections are mild or asymptomatic, but cases that require hospitalization are initially unrecognized, only serologic or molecular tests shedding a light on the illness’s true nature.

ESPID-0308
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

STREPTOCOCCUS PNEUMONIAE NASOPHARYNGEAL COLONISATION IN CHILDREN WITH ACUTE RESPIRATORY INFECTIONS BEFORE INTRODUCTION OF UNIVERSAL CONJUGATED PNEUMOCOCCAL VACCINE IN LITHUANIA

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Background and aims

The study was performed to evaluate the distribution of different *S.pneumoniae* (SP) serotypes in nasopharynx of preschool children and its influence on the course of acute respiratory tract infections (ARTI). The study was performed before universal infant vaccinations with pneumococcal conjugated vaccines (PCV) in Lithuania which started in October, 2014.

Methods

Two seasons before universal vaccination children visiting the Emergency Department of Children's Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos because of ARTI were examined for SP nasopharyngeal colonisation. Children aged 0-6 years, not vaccinated with any PCV previously, were enrolled. Demographic and clinical data were recorded and nasopharyngeal swabs for SP carriage were taken.

Results

A total of 397 children (167 female, 42.1%) were enrolled. SP found in 47%. Serotypes 14, 15, 19F, 23F, 6A, and 6B were found in the majority of cases. The presence of SP during the first days of illness was linked with longer disease duration ($p=0.028$) and more often required treatment with antimicrobials ($p=0.001$). Serotype 14 was associated with the longest disease duration ($p=0.032$). SP colonization was associated with higher frequency of acute otitis media (AOM, $p=0.028$), and mainly serotypes 15, 19F, 23F, 6A, 6B were found.

Conclusions

Accidental SP nasopharyngeal carriage during the first days of ARTI is related to the longer disease duration, more severe forms with the need to use antimicrobials. As the most often find serotypes are included in PCV, therefore further SP surveillance

may show the influence of universal infant vaccination on SP nasopharyngeal carriage.

ESPID-0500
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

INFLUENCE OF RESPIRATORY SYNCYTIAL VIRUS INFECTION ON ACUTE BRONCHIOLITIS IN CHILDREN ADMITTED TO THE VILNIUS UNIVERSITY CHILDREN HOSPITAL IN 2012-2014

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Background and aims. The study was performed to evaluate the aetiological factors of acute bronchiolitis (AB) and duration of hospitalisation.

Methods. Retrospective study was performed in Children Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos during the period of 2012 January – 2014 November. Case histories of 423 children suffering from AB were retrieved for analysis (2012 year – 127 cases, 2013 – 156, 2014 – 140).

Results. Age of the patients ranged from 1 to 24 months; 64.5% were below age of 9 months; 276 (65.2%) of them were males. Most children (53%) were hospitalised during three months – 77 (18.2%) in January, 58 (13.7%) in February and 85 (20.1%) in March. Nasopharyngeal swabs were taken in 296 of cases. In 171 (57.7%) children Respiratory syncytial virus (RSV) infection was confirmed: in 141 cases by detecting of RSV Ag (IF), in 30 by molecular methods (PCR), and in 3 by both the methods. Other viruses were identified by PCR: Bocavirus (19), Rhinovirus (14), Metapneumovirus (3), Coronavirus OC43 (2), Coronavirus 229E (3), Influenzae A (3), Parainfluenzae (3), and Adenovirus (5) among them mixed viruses in 26 patients. Children with laboratory confirmed RSV needed longer hospitalisation: 4.96±2.4 days patients with confirmed RSV 4.21±1.7 with confirmed other aetiology of the disease as compared to 4.3±2 days in patients with negative results of the examination ($p = 0.0097$).

Conclusions. In most cases RSV aetiology of AB was confirmed and this was associated with longer duration of hospitalisation. Viral co-infection was common among investigated patients.

ESPID-0337
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

URINARY INFECTIONS AT CHILDREN IN BITOLA IN THE PERIOD BETWEEN 2011-2013

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Objectives: To show the prevalence of urinary infections at the children aged 0-14 years, from year 2011 to 2013 who were treated at the Children's Department at the Clinical Hospital in Bitola.

Methods: The retrospective, epidemiological study included children aged 0-14 years in the period from year 2011 to 2013 who were diagnosed with urinary infection. It was confirmed by clinical, laboratory, microbiological tests and additional examinations.

Results: During the 3 years long period in Children's Department at the Clinical Hospital were registered a total number of 952 cases, of which 34 (4%) were confirmed with a diagnosis of urinary infection, 11 (32%) male and 23 (68%) female. In relation to age, urinary infections were more common in children from 1 to 4 years and from 7 to 14 years old. From the laboratory and microbiological tests that were done, in more than 50% of the cases, positive urine culture was obtained. Escherichia Coli and rarely Proteus mirabilis were isolated commonly. Identified congenital anomalies were found in 4 children, and renal tubular acidosis in 2 children.

Conclusion: The prevalence of urinary infections at the children younger than 14 years was 4%. More common among girls, aged 1 to 4 and 7 to 14 years. The most common cause is Escherichia coli, and in 12% of them the cause was congenital anomaly.

ESPID-0934
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

COMPARATIVE CHARACTERISTICS OF 2009 PANDEMIC INFLUENZA A (H1N1) VIRUS AND 2010-2011 SEASONAL INFLUENZA IN PEDIATRIC PATIENTS

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Background: In March 2009 a pandemic influenza A (H1N1) strain was identified. At the beginning it seemed that the disease was accompanied by high complications and mortality rate. The main purpose of this study was to identify the burden of pandemic influenza and influence on complicated hospitalization, as compared with seasonal influenza years after the epidemic.

Methods: A retrospective observational study, at the Ruth Rappaport Children's Hospital in Haifa, a tertiary hospital. Data were collected from medical records of all children who were hospitalized, from April 2009-2011, with laboratory-confirmed influenza.

Results: Of 191 patients with influenza, there were 100 with 2009 pandemic influenza, 62 with seasonal influenza, and 29 with influenza virus A (H1N1) in 2010-2011. Patients with 2009 influenza A (H1N1) were characterized by older age, more co-morbidity conditions, more symptoms including fever, cough, rhinitis on admission, but less co-infection with other viral respiratory pathogens. No significant differences were recorded in the outcomes between the groups. Twenty one % of patients hospitalized with pandemic influenza in 2009 had complicated hospitalization, compared with 17.7% of patients hospitalized with seasonal influenza in 2010-2011.

Children with pandemic influenza received more Oseltamivir (Tamiflu) (94% vs. 19.4%, P <0.001), and received more antibiotics than other groups.

Conclusions: There was no effect of the type of the influenza on the outcomes. There was no significant differences between groups in the percentage of in-hospital mortality, hospitalization in intensive care unit, prolonged hospitalization (>9 days), and the development of complications during hospitalization.

ESPID-0172
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

EVALUATION OF OXIDANT-ANTIOXIDANT BALANCE AND TOTAL ANTIOXIDANT CAPACITY OF SERUM IN CHILDREN WITH URINARY TRACT INFECTION

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Background
Urinary Tract Infection (UTI) is the most common bacterial infections in children. The present study was aimed
to investigate the oxidative and antioxidate status of plasma of patient with uri nary tract infection (UTI) and to compare them with those of controls.
Materials and Methods

This case - control study of 50 - 75 children in the given order were performed in 2013 at the pediatric clinic of infectious in Zahedan hospital of Ali Ibn Abi Talib .The antioxidative status of plasma were evaluate by measuring Total ant ioxidant capacity
(TAC) The oxidative status of samples were assessed by measuring The total peroxide and The oxidative stress Index (OSI) Levels.
The means of the parameters were Compared and relationship among them w ere determined.

Data were analyzed by using of SPPS20. Student t-test and Man-Withnny were applied in various situations of our questions 95% CI considered for the level of significant.
Results

The results showed that total oxidant serum status in UTI patients was higher in compared to controls when total antioxidant serum was lower. The balance of oxidant - antioxidant serum was in favor of oxidant serum and this term confirmed by oxidative stress index.
Conclusion

Our results showed that plasma levels of total antioxidant capacity (TAC) in patients with UTI decreased in compared to controls and Oxidant-Antioxidant balance and oxidative stress index caused an increased oxidative stress in patients.

ESPID-0199
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

EPSTEIN-BARR VIRUS ENCEPHALITIS IN A CHILD: SUCCESFULLY TREATED WITH ACYCLOVIR

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Ebstein-Barr Virus (EBV) related neurologic disorders include meningitis, encephalitis, cranial or peripheral neuritis. We describe a 7-years-old boy with EBV encephalitis who was discharged without any sequelae after acyclovir therapy. **Case:** A 7-years-old boy admitted to emergency room with decreased level of consciousness, incoherent speech, hallucination and prolonged fever. His physical examination revealed exudative pharyngitis and neck stiffness. CSF examination revealed a protein level of 59 mg/dL, glucose level of 50 g/dL (simultaneous serum glucose level: 130 g/dL), 80 erythrocyte/mm3 and 20 leukocytes/mm3. Vancomycin, ceftriaxone, and acyclovir therapies were started. Magnetic resonance imaging (MRI) showed contrast enhancement in posterior side of bilateral insular cortex, right hypothalamus and inferior side of left frontal cortex consistent with encephalitis. His level of consciousness worsened in few hours. He was unresponsive to verbal commands. He had resting tremor, rigidity, and hypertonia. EBV DNA was positive in blood and CSF samples by PCR. Serum EBV-VCA IgM was positive as well. The antibiotic therapies were stopped but acyclovir therapy was continued. On the 5th day of admission his level of consciousness was improved. His all symptoms fully recovered and he was discharged without any sequelae. On the second month of his follow-up, cranial MRI showed improvement with obvious decrease in previous contrast enhancements. In conclusion, EBV encephalitis can be seen in immunocompetant children. Acyclovir therapy may be beneficial but further investigations are needed to establish a standard therapeutic approach.

ESPID-0200
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

IS VARICELLA-ZOSTER VIRUS AN ETIOLOGIC FACTOR IN KAWASAKI DISEASE? A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: Kawasaki disease (KD) was first described by Tomisaki Kawasaki in 1967. Further investigation of infectious agents such as varicella-zoster virus could provide a useful clue for the etiology of KD, although the mechanisms of pathogenesis are still unclear. Herein we report a pediatric case with who developed KD. She fulfilled all of the criteria for KD. Chickenpox diagnosis is made by serological and clinical evidence. **Case:** We present a 2-year-old girl with a 5-day history of high fever and a 2-day history of maculopapular eruptions. Phsical exam revealed unilateral cervical lymphadenopathy, dry red lips, a red strawberry tongue, enlarged tonsils with exudates and bilateral bulbar conjunctivitis. Her parents also described vesiculopustuler lesions for possible chickenpox approximately 3-4 weeks ago prior to this presentation. Varicella IgM was found to be positive. She fulfilled all of the criteria for KD, she received a single dose of intravenous immunoglobulin - IVIG (2 gr/kg) and was started on oral acetysalicylic acid at 100 mg/kg/day. She became afebrile after the first dose of IVIG and fever did not show any recurrence. She was discharged on the fifth day of admission. **Conclusion:** Between the years 1998 - 2010, a total of 5 studies were published in the Pubmed database for KD associated with varicella infection. The etiology of KD is still unknown, although an infectious agent is suspected because of the associated symptoms.

ESPID-0206
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

FOUR YEAR RETROSPECTIVE REVIEW OF PRESEPTAL AND ORBITAL CELLULITIS IN HOSPITALIZED CHILDREN

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BACKGROUND AND AIMS: Orbital cellulitis, when left untreated, is a potentially both sight and life-threatening condition. Because a delay in diagnosis and appropriate treatment may result in serious complications we aimed to revisit this ocular emergency condition. ***RESULTS:*** Data were collected by retrospective chart review of all admissions for preseptal and orbital cellulites in department of Pediatrics from January 2011 to January 2015. With chart review, a total of 44 records of children, 23 male and 21 female, with preseptal (PC) or orbital cellulites (OC) were identified. 10 cases had orbital (23%), 34 had preseptal cellulites (77%). The mean ages of patients with OC and PC were 7.5±4 and 5.8±3.4 years, respectively. Eye involvements in 97.6% of cases was unilateral. 60% of OC cases had ophthalmoplegia in addition to hyperemia, tenderness and swelling of periorbital tissues, whereas only 1 case of preseptal cellulitis (3%) showed ophthalmoplegia. Sinusitis was the most common predisposing factor, effected 80% patients with OC and %23.5 patients with PC, and the most common involved sinus was the ethmoid. We used intravenous ampisilin-sulbactam as initial treatment in 41 cases (95.4%). Only 3 cases (4.6%) did not response to antibiotic treatment. Sinus drainage was needed in 4 cases of orbital and 3 cases of PC. No serious complication was observed during follow-up of these patients. ***CONCLUSIONS:*** Early diagnosis and treatment of acute sinusitis may prevent orbital complications

ESPID-0293
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS CAUSED NECROTIZING LYMPHADENITIS IN CHILDREN

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Background: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) had established a worldwide presence over the last decade. Majority of infections involve skin and soft tissue infection. Others are bone and joint infection, severe necrotizing pneumonia and invasive deep tissue infection.

Methods: To demonstrate clinical feature, microbiological characteristic, molecular diagnosis and treatment outcome of CA-MRSA caused necrotizing lymphadenitis in children

Results: Case report of a 7-year-old Japanese boy presented with high fever and right axillary lymphadenitis for 2 weeks. He received many antibiotics without improvement. Physical examination and ultrasonogram revealed inflamed axillary lymphadenitis with central liquefaction. He received ceftriaxone and clindamycin intravenous injection initially with partial response. Core needle biopsy demonstrated necrotizing lymphadenitis without granuloma. Pus culture yielded *S. aureus* with resistance to oxacillin, and susceptibility to clindamycin, erythromycin and vancomycin. Molecular diagnosis characterized ST 834 by multilocus sequence typing. Vancomycin and clindamycin were given for 10 days with good clinical response. Lymphadenitis resolved totally after 2 months of oral clindamycin. Cause of infection was suspected from python exposure with skin infection previously.

Conclusion: CA-MRSA has emerged in pediatric infection with important implication for treatment. Pediatrician should be aware especially in broad antibiotic resistance case.

ESPID-0414
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

VARICELLA: HOSPITALISATIONS AND COMPLICATIONS IN CHILDREN IN KAUNAS CLINICAL HOSPITAL, LITHUANIA, 2014

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Aim of this study was to asses the clinical aspects of hospitalisation and complications of children with varicella.

Method. A retrospective study of hospitalized children varicella cases in Kaunas Clinical Hospital between January and September in 2014.

Results. 69 children were from 1 month to 16 years, 49.3% of them were younger than 3 years (median age 4,2±3,8y), 60.9% - were boys. The mean duration of hospitalisation was 4.91±3.24 days. The most frequent causes of hospitalisation were fever - 94.2% (mean 39.2±0.8ºC, for 4.58±1.7days) and feeding problems with dehydration - 95.6% of cases. Bacterial complications such as otitis were diagnosed in 29% of cases, skin infection - in 23.2%, lower respiratory tract infections - in 15.9%, eye infection – in 8.7% and systemic infections – in 5,8% (sepsis n=3, osteomyelitis n=1) of cases. 17 patients (24,64%) had more than one bacterial complication. 10.1% of patients had one or few neurological varicella-associated symptoms and complications (convulsions – in 4 cases, hallucinations – in 2, ataxia – in 1, meningoencephalitis – in 2 cases). The mean WBC count was 10.5±5.03x10^9/l (range 3.1-30.7x10^9/l); CRP mean was 31.69±39 mg/l (range 0.1-226 mg/l); PLT count ranged from 100 to 483x10^9/l (mean 232,03±83,96x10^9/l). Decreased PLT count (<150x10^9/l) was found in 27 cases (39,13%). Antibacterial treatment was given to 34 (49.3%) patients, acyclovir – to 22 patiets (31.9%).

Conclusions. 1. The mane causes of hospitalisation of children with varicella were fever and feeding problems with dehydration. 2. Thrombocytopenia and bacterial infections were the most frequent complications.

ESPID-0394
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

PROTEIN-LOSING ENTEROPATHY CAUSED BY CYTOMEGALOVIRUS INFECTION IN A TODDLER

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Background: Pediatric Ménétrier disease is a rare condition, of unknown etiology, but has been associated with *Helicobater pylori* and cytomegalovirus (CMV) infection.

Methods: We describe the case of a 3 year-old boy, previously healthy, that presented to emergency department with a 4 day history of progressive abdominal pain and bilateral swelling of the lower limbs. He had no fever, respiratory, urinary or other gastrointestinal symptoms.

On physical exam he presented a maculopapular rash, non-pitting edema of the lower of the limbs and diffuse abdominal tenderness but with no rebound or guarding. The rest of his findings on physical examination were normal.

Results: Laboratory studies revealed hypoalbuminemia (1.6 g/dl) and hypoproteinemia (3.6 g/dl) without proteinuria. It was also detected low serum IgA, IgG and IgM, hypogammagobulinemia and elevated α1/α2. Blood cell count, serum eletrolyte levels, liver and renal function were normal. Serological tests (IgM+/IgG+) and polymerase chain reaction in the blood confirmed CMV infection. Abdominal and renal ultrasound were both normal. Upper gastrointestinal endoscopy was performed and revealed large mucosal fold, as well as ulcers involving the body of the stomach. Histopathological results showed hyperplasia of the gastric pits and superficial epithelium and replacement of normal gastric glands of mucus-secreting cells. CMV DNA was isolated in the gastric tissue by molecular techniques.

He was medicated with esomeprazol (1 mg/kg/day) for 2 weeks and had a complete clinical resolution with no relapse.

Conclusions: This case points out the importance of early recognition of CMV-related gastropathy as a cause of edema and hypoalbuminemia.

ESPID-0218
NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

COMPARISION OF URINE MICROALBUMIN IN CHILDREN WITH WITH URINARY TRACT INFECTIONS WITH HEALTHY CHILDREN

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Background: Microalbuminuria is defined as increased urinary albumin excretion (30-300 mg/day) or microalbumin/creatinine ratio (30-300 mg/g) in a spot urine sample. Although microalbuminuria is a predictor of clinical nephropathy and cardiomyopathy, few studies have investigated microalbuminuria in children with urinary tract infection (UTI). Therefore, we compared the spot urine microalbumin/creatinine ratio in pediatric UTI patients with that of control subjects.

Methods: We investigated the correlation between the ratio in children with UTI and age, weight

Results: We studied 50 patients (6 boys, 44 girls) and 73 healthy children (31 boys, 42 girls). The mean microalbumin/creatinine ratio in UTI patients was statistically significantly increased compared to the control group (195/12±155/66 mg/g vs. 68/96±56/07mg/g, P=0.001).

. Microalbumin/creatinine ratio showed negative correlation to age .

Conclusion: The spot urine microalbumin/creatinine ratio in children with UTI was significantly greater than that in normal children

. This ratio is a potential

prescreening and prognostic marker in UTI patients. Further studies are required to validate the predictability of microalbuminuria in pediatric UTI patients.

ESPID-0878
PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS

NEONATAL AND PAEDIATRIC PENICILLIN POPULATION PHARMACOKINETIC STUDIES: A SYSTEMATIC REVIEW

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Background and aims

Paediatric and neonatal pharmacokinetic/pharmacodynamic (PK/PD) data available for penicillins are limited. Population PK (popPK) statistical modelling now facilitates dose optimization strategies. We aimed to identify paediatric PK studies of selected penicillins that were analysed using population modelling.

Methods

We systematically searched PubMed and EMBASE for neonatal/paediatric popPK studies of amoxicillin, ampicillin, benzylpenicillin, flucloxacillin, and piperacillin.

Results

We identified 11 neonatal/paediatric popPK studies of these penicillins. Both parametric (n=9) and non-parametric modelling approaches (n=2) were used. 9/11 studies focussed on neonates. Table 1 summarises the neonatal studies, including the point estimates for the typical values of clearance (CL) and volume of distribution (Vd). The PK model structures and covariate parameterization varied (data not shown).

Table 1. Summary of neonatal penicillin population PK studies.

Beta-lactam	Study population	Number of subjects	Number of samples for PK modelling	Clearance (CL): population PK parameter point estimate	Volume of Distribution (Vd): population PK parameter point estimate	Elimination half-life ($t_{1/2}$ in hours)	Reference
Amoxicillin	Very low birth weight (VLBW) neonates (<32 weeks, <1500g)	40	214	CL(L/h) = 0.0000805 x weight (g) *or* if on gentamicin then CL(L/h) = 0.0000610 x weight (g)	Vd = 0.678 L	5.2 (without gentamicin) 6.9 (with gentamicin)	J Pharm Sci. 1997;86(11):1288-92.
Amoxicillin	Preterm and term neonates (25-42 weeks GA)	150	674	CL/W = 0.096 L/kg/h (W = weight)	V/W=0.65 L/kg	5.2	Ther Drug Monit. 2006;28(2):226-31.
Amoxicillin	Preterm and term infants (aged 10-52 days)	32	Not stated (mean 5.2 per infant)	CL/W = 0.18 L/kg/h	V/W = 0.66 L/kg	3.0	Ther Drug Monit. 2007;29(3):376-80.
Ampicillin	Preterm and term neonates (24-41 weeks GA)	73	142	CL = 0.078 L/h	Vd = 0.399 L	3.3	Antimicrob Agents Chemother. 2014;58(6):3013-20.
Penicillin G	Preterm neonates (<32 weeks GA)	20	167	CL = 0.103 L/h	Central Vd = 0.359 L	3.9	Antimicrob Agents Chemother. 2007;51(10):3720-5.
Flucloxacillin	Preterm and term neonates (26-42 weeks GA)	55	235	CL = 0.18 L/kg/h	Vd = 0.54 L/kg	2.6	Ther Drug Monit. 2006;28(3):351-8.
Piperacillin	Preterm infants (22-32 weeks GA)	56	211	CL = 0.479 L/h/kg$^{0.75}$	Vd = 2.91 L/kg	6.9	Ther Drug Monit. 2012;34(3):312-9.
Piperacillin	Neonates and young infants (< 2 months)	71	207	CL = 0.133 L/h/kg	Central Vd = 0.742 L	Not stated	Eur J Clin Pharmacol. 2013;69(6):1223-33.
Piperacillin	Premature and term infants (aged <61 days)	32	128	CL = 0.080 L/h/kg	Vd = 0.42 L/kg	3.5	Antimicrob Agents Chemother. 2014;58(5):2856-65.

Conclusions

The literature search identified 11 neonatal/paediatric popPK studies of these 5 penicillins. Only 2 studies included children aged over 2 months. Reporting methods of paediatric popPK studies are heterogeneous, including various model parameterization approaches and different PK parameter units; this impedes pharmacokinetic meta-analysis, without access to original datasets. Since penicillin PK/PD targets relate to the time above the minimum inhibitory concentration within each dosing interval, estimates of CL and Vd at steady state are sufficient to synthesise data from previous studies. However, as popPK studies are now used to make optimal dosing recommendations, standardized reporting methods and open access dataset publication would facilitate data warehousing and future pharmacokinetic meta-analysis.

ESPID-0741
PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS

PAEDIATRIC PHARMACOKINETIC (PK) DATA AVAILABLE FOR ANTIFUNGAL MEDICINES

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BACKGROUND: Dosing of many paediatric medicines is based on studies conducted only on adults. Therefore, safety and information of drug doses for children are often based on expert opinion.

AIMS: To identify, summarise and grade published paediatric PK data available for systemic antifungals published in the *Manual of Childhood Infections.* This work formed part of an ongoing body of work to provide an evidence-base for dosing recommendations of antimicrobials in paediatrics.

MATERIALS AND METHODS: We searched PubMed database using the following keywords: the drug AND "*pharmacokinetic(s)*" OR "*pharmacodynamic(s)*" OR "*pharmacology*" AND "*child*" OR "*infant*" OR "*infant, newborn*" OR "*infant*" OR "*child, preschool"* OR "*adolescent*". We searched the articles for data concerning age, doses, dosing route and tolerability. We determined grading of evidence using the strategy below (Table 1).

RESULTS: A total of 73 studies were idenfied for 14/16 systemic antifungal agents. There were no studies evaluating nystatin or tiabendazole. Most publications were graded as individual PK study with no simulation (Grade 3) (Table 2). The most studied was voriconazole and the least studied were ketokonazole and terbinafine. The most studied age group was 2-11 years and the least studied were neonates (Table 3).

CONCLUSIONS: Most antifungals have undergone paediatric PK studies. While newer agents are better studied, the PK trials are needed for older antifungals and

especially in neonates.

Table 1. PKPD grading described by Barker *et al*[5]

Grade	Type of the study
1a	Meta-analysis of raw PK data
1b	Prospective data warehousing/pooling
2a	Non-systematic/ retrospective data pooling/analysis
2b	External data collection/validation
2c	Recommendation based on simulation or bridging methods
3	Individual PK study with no simulation
4	Case study with PK or TDM described
5	Expert opinion based on first principles, in vitro and animal studies

[5]Barker, CI *et al* Antibiotic dosing in children in Europe: can we grade the evidence from pharmacokinetic/pharmacodynamic studies - and when is enough data enough? Curr Opin Infect Dis. 2012 Jun;25(3):235-42.

Table 2. Distribution of studies depending on grading

Antifungal agent	Total number of publications N = 73	Grade 1 N=0	Grade 2a N = 4	Grade 2c N = 15	Grade 3 N = 36	Grade 4 N = 18
Voriconazole	21	-	1	1	7	12
Micafungin	12	-	-	3	8	1
Amphotericin B	8	-	-	4	4	-
Fluconazole	7	-		2	4	1
Caspofungin	5	-	-	1	3	1
Itraconazole	7	-	-	3	4	-
Flucytosine	4	-	2	1	-	1
Posaconazole	3	-	1	-	2	-
Others (Ketokonazole, Terbinafine, Miconazole)	6	-	-	-	4	2

Table 3. Number of times age groups were included in different studies

Antifungal agent	Neonates N = 21	1 mo to <2 years N = 38	2 to 11 years N = 48	12-18 years N = 33
Voriconazole	4	9	14	11
Micafungin	4	7	7	6
Amphotericin B	2	7	7	6
Fluconazole	5	4	1	1
Caspofungin	1	3	3	2
Itraconazole	1	5	7	4
Flucytosine	2	1	2	-
Posaconazole	-	1	3	2
Others (Ketokonazole, Terbinafine, Miconazole)	2	1	4	1

ESPID-0743
PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS

PAEDIATRIC PHARMACOKINETIC (PK) DATA AVAILABLE FOR ANTIPARASITIC MEDICINES

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BACKGROUND: In paediatrics it is important to take into account the differences of metabolism of a child and an adult. Nevertheless, the doses recommended to children are often based on adult PK studies or expert opinion.

AIMS: (1) To identify and summarise the published paediatric PK data available for systemic anti-parasitics presented in the *Manual of Childhood Infections*; (2) To grade the available evidence for current dosing recommendations.

MATERIALS AND METHODS: PubMed database was searched using the keywords: drug name AND "pharmacokinetic(s)" OR "pharmacodynamic(s)" OR "pharmacology" AND "child" OR "infant" OR "infant, newborn" OR "infant" OR "child, preschool" OR "adolescent". The following data was collected: age, dose, route of administration and tolerability. The grading of the publication was done using the strategy below (Table 1).

RESULTS: Studies were identified for 12/21 of the systemic anti-parasitic medicines (Table 2). No paediatric PK studies were found for diethylcarbamazine, diloxanide, ivermectin, tinidazole, pyrimethamine, mebendazole, levamisole, piperazine or niclosamide. Most of the studies were from small individual PK studies with no simulation (Grade 3) (Table 2). The most studied age group was 2-11 years and the least studied were neonates (Table 3).

CONCLUSIONS: There are limited data supporting the current dosing of anti-parasitics in neonates and children. Studies from well designed PKPD trials utilising methods such as data warehousing, modelling and simulation are needed.

Table 1. PKPD grading described by Barker *et al*[5]

Grade	Type of study
1a	Meta-analysis of raw PK data
1b	Prospective data warehousing/pooling
2a	Non-systematic/ retrospective data pooling/analysis
2b	External data collection/validation
2c	Recommendation based on simulation or bridging methods
3	Individual PK study with no simulation
4	Case study with PK or TDM described
5	Expert opinion based on first principles, in vitro and animal studies

[5]Barker, CI *et al*. Antibiotic dosing in children in Europe: can we grade the evidence from pharmacokinetic/pharmacodynamic studies - and when is enough data enough? Curr Opin Infect Dis. 2012 Jun;25(3):235-42.

Table 2. Distribution of studies depending on grading

Anti-helminth/amoebae/protozoal agent	Total number of publications N= 76	Grade 1 N=0	Grade 2a N=4	Grade 2c N=12	Grade 3 N=59	Grade 4 N=1
Artemether + Lumefantrine	16	-	-	2	14	-
Chloroquine	15	-	1	1	13	-
Sulfadoxine + Pyrimethamine	13	-	1	5	7	-
Mefloquine	10	-	-	-	9	1
Quinine	10	-	1	3	6	-
Sodium Stibogluconate	3	-	-	-	3	-
Atovaquone	2	-	-	-	2	-
Proguanil/ Atovaquone	2	-	-	-	2	-
Others (halofantrine, albendazole, praziquantel, primaquine)	5	-	1	1	3	-

Table 3. Number of times age groups were included in different studies

Anti-helminth/amoebae/protozoal agent	Neonates N=15	1mo to <2 years N=57	2 to 11 years N=72	12-18 years N=26
Artemether + Lumefantrine	8	14	16	9
Chloroquine	-	12	14	5
Sulfadoxine + Pyrimethamine	1	13	11	2
Mefloquine	3	7	9	3
Quinine	1	5	10	1
Sodium Stibogluconate	2	2	3	3
Atovaquone	-	1	2	1
Proguanil/ Atovaquone	-	1	2	1
Others (halofantrine, albendazole, praziquantel, primaquine)	-	2	5	1

ESPID-0154
SEVERE BACTERIAL AND VIRAL INFECTIONS

BURDEN OF MENINGOCOCCAL DISEASE IN UNIVERSITI KEBANGSAAN MALAYSIA MEDICAL CENTRE, KUALA LUMPUR, MALAYSIA FROM 2004 TO 2013

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Background and aims: Global incidence of the disease currently stands at 100 thousand cases a year, with most of the cases occurring as sporadic epidemics in developing countries. Meningococcal disease in Malaysia might be highly under-reported because of its lack of recognition. We conducted this epidemiological study to determine the prevalence of meningococcal disease in Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Malaysia and to identify their plausible risk factors, outcomes and complications

Materials and methods: This is a 10-year retrospective prevalence study of patients admitted to the UKMMC with meningococcal disease. This study will be conducted from the month of April until July 2014. All patients that were admitted with culture-confirmed meningococcal disease within the timeframe of the study. Patients are identified through laboratory records.

Results: During the last 10 years, there were only a total of 5 patients with confirmed meningococcal cases in PPUKM with manifestation of meningitis or septicaemia. Three of the patients fall under the paediatric age group with the youngest at 1 month old to 16 months old. Out of all patients, only there only one mortality. Young children are more susceptible to meningococcal meningitis infection (60%). Household crowding is one of the risk factors of transmission (80%)

Conclusion: Our study showed that there are a small number of meningococcal patients in the span of 10 years in PPUKM. Meningococcal disease is not considered endemic in Malaysia (5 cases in 9 years)

ESPID-0155
SEVERE BACTERIAL AND VIRAL INFECTIONS

NEONATAL NEISSERIA MENINGITIS WITH SEPTICAEMIA COMPLICATED WITH SUBDURAL EFFUSION: A CASE REPORT AND PROGRESS AFTER 2 YEARS

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Objective: To report a full-term newborn infant that developed a sepsis associated to meningitis caused by Neisseria meningitidis serogroup B on the 29th day of life. Case description: The patient was a term male infant, born full term via spontaneous vertex delivery to a 24-year-old mother, with birth weight of 3,390 g. On the 29th day of life, the neonate presented with two days history of high grade fever of 39^{0}C associated with poor oral intake and irritability. Examination showed the neonate was tachycardic, tachypnea with a blood pressure of 105/92 mmHg. Erythematous macular lesions with desquamation were noted over upper chest and neck but there was no purpura. The CSF showed neutrophilic predominance, protein of 3767 mg/dL, and glucose 0.1 mmol/L. Latex agglutination was positive for Neisseria meningitidis serogroup B and was confirmed by the cultures. Ultrasound cranium was done on 2 weeks later due to persistent spiking temperatures and revealed bifrontal subdural effusion however no surgical intervention was warranted. The neonate was hospitalized and received intravenous crystalline penicillin and cefotaxime for 35 days. After hospital discharge, there were no signs of immediate neurological sequels and the infant was able to be breastfed and grow appropriately. Mild hearing loss was noted due the first year of follow up but the patient did not present any delay of developmental milestones. We present the first documented case (to the best of our knowledge) of neonatal meningococcal meningitis in Malaysia.

ESPID-0965
SEVERE BACTERIAL AND VIRAL INFECTIONS

SECONDARY BACTEREMIA DUE TO RAOULTELLA PLANTICOLA COMPLICATING ROTAVIRUS INFECTION

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Rotavirus infection is one of the common causes of severe gastrointestinal disease, primarily in infants and children under 5 years of age. It has a majör global impact on childhood morbidity and mortality (1). Besides its well-known complications, reports including secondary bacteremia following or coinfections with rotavirus infections, were emerging nowadays, although their numbers were limited (2).

Among the other gram negative bacterias; *Raoutella planticola* infection has been rarely reported in humans (3).

We present a case (An 11 month old **immunocompetent** male infant boy) of *R. planticola* bacteriemia following rotavirus infection which was the first case of *R. planticola* bacteriemia in children.
R. **planticola** has rarely been documented as a cause of human infections and only a few cases are reported in the literatüre (1,3) .
Raoutella species can be a causative agent for gram negative bacteremia in children with or without rotavirus gastroenteritis. Thus R.planticola infections should be suspected whenever isolated even in the absence of epidemiologic background.

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ESPID-0572
SEVERE BACTERIAL AND VIRAL INFECTIONS

PAEDIATRIC KINGELLA KINGAE ENDOCARDITIS ASSOCIATED WITH EMBOLIC STROKE: A CASE REPORT OF AN INCREASINGLY REPORTED ASSOCIATION.

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Background and aims:

Kingella kingae endocarditis is a rare, life threatening infection which can require urgent surgical intervention. We report a case complicated by stroke, raising awareness of this association. We discuss inconsistencies in guidelines and limited evidence for empiric antibiotic regimens for paediatric endocarditis.

Methods:

Case report.

Results:

A previously healthy 11-month old boy presented with 3 weeks of fevers and reduced right arm movement. Examination demonstrated reduced power in the right arm and leg and a 2/6 pansystolic murmur, loudest at the apex. Brain MRI showed multiple recent infarcts in left middle cerebral artery (MCA) territory and subacute infarcts in the right MCA territory and left cerebellum, suggestive of central embolic source. Transthoracic and transoesophageal echocadiography showed a large mobile echogenic mitral valve vegetation (12mm x 6mm) with moderate mitral regurgitation. The vegetation was surgically excised and the valve was repaired. Blood cultures were negative. 16S ribosomal PCR on the vegetation detected *K. kingae*. He completed 10 days IV gentamicin (2.5mg/kg TDS) and 5 weeks ceftriaxone (50mg/kg BD then 80mg/kg OD). Repeat echocardiogram showed no regurgitation. He is undergoing rehabilitation with improvement in function.

Conclusions:

K. kingae endocarditis has a relatively high risk of neurological complication. Presentation with stroke and fever should prompt rapid assessment for infective endocarditis. Urgent surgery may be indicated, especially in the setting of both valve destruction and embolism. Bacterial PCR can aid diagnosis and guide antibiotic

therapy. There is limited evidence and inconsistency in guidelines for empiric antibiotic therapy in paediatric endocarditis.

ESPID-0821
SEVERE BACTERIAL AND VIRAL INFECTIONS

ACUTE DISSEMINATED ENCEPHALOMYELITIS ASSOCIATED WITH SALMONELLA JAVA

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Background and aims

Acute disseminated encephalomyelitis (ADEM) is a rare condition in children and can be a parainfectious phenomenon. We present a first report of ADEM associated with *Salmonella java* bacteraemia.

Methods

Case report.

Results

A previously well 7-year old boy presented with seizures and altered sensorium. He had a 5 days history of fever and diarrhoea. He had recently travelled for 4 weeks in Bangladesh. Other family members also had diarrhoea. He became encephalopathic and required intensive care. On examination he had reduced movements on the left side and abnormal right arm movements. MRI showed extensive, multifocal, well demarcated areas of T2 hyperintensity and T1 hypointensity in the left frontal lobe white matter with associated swelling consistent with ADEM.

He was treated for presumed infectious encephalitis until *Salmonella enterica* serovar Paratyphi B variant Java *(S. java)* was identified in blood culture. CSF was normal. He received 2 weeks IV meropenem and was treated for ADEM with pulsed IV methylprednisolone and a weaning course of oral prednisolone. His subsequent blood and stool cultures were negative. He has undergone intensive rehabilitation and has recovered full mobility with signs of residual left hemiparesis. His subsequent neuroimaging showed resolving lesions.

Conclusions

Salmonella spp. infection can result in CNS infections but the association with ADEM has not been previously described. This case adds to the long list of existing infections associated with ADEM. Thorough travel and contact history in this case allowed timely and appropriate empiric antibiotic therapy prior to confirmation of microbiological diagnosis.

ESPID-0028
SEVERE BACTERIAL AND VIRAL INFECTIONS

PEDIATRIC NEUROBRUCELLOSIS ASSOCIATED WITH HYDROCEPHALY

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Brucellosis is an infectiousdisease, frequently encountered in developing countries. It may involvemultiple organ systems of the human body. However, neurobrucellosis is a rarecomplication of brucellosis. The most frequent events of cranial nerveretention are meningitis and meningoencephalitis.

A ten-year old girl was complaints of fever, headache, nausea, vomiting, lethargy,and urinary incontinence. Clinical examinationrevealed a temperature of 38.5^{o}C. Lethargy, nuchal rigidity(++), positiveKernig's and Brudzinski's signs, isochoric pupils, direct and indirect lightreflexes(+) were detected.Romberg (++)and cerebellar tests were competent. Deep tendon reflexes were hypoactive, andpathological reflexes were absent. Grade I papillary edema was observed inophthalmological examination. Cranial computed tomography demonstrated asignificant temporal horn and a communicating hydrocephalus causing dilation ofthe 3rd and lateral ventricles.

Hemoglobin was 9.8mg/dL, erythrocytesedimentation rate was 40mm/h, C-reactive protein was 24mg/L, andwhite blood cell count was 3.700/mm^3.Blood glucose and liver function tests were normal. In lumber puncture (LP),pressure in CSF was increased and a turbidity, pandy test (++) appearance wasobserved. Leukocyte count was 455/mm^3 with 36% of neutrophils and64% of lymphocytes. Protein of CSF was 148 mg/dl. Wright agglutinationtest with a 1:1280 ratio in blood. Gruber-Widal test was(-),and Wright and Rose Bengal test was(+). After the diagnosis ofneurobrucellosis, an external ventricular drainage was performed and thecatheter was removed ten days after the drainage. Rifampicin,doxycycline,gentamicin were applied for 6 weeks as an antibiotic therapy. Dexamethasonewas administered.

ESPID-1055
SEVERE BACTERIAL AND VIRAL INFECTIONS

FEBRILE INFANTS – IS A NEGATIVE URINALYSIS REALLY REASSURING?

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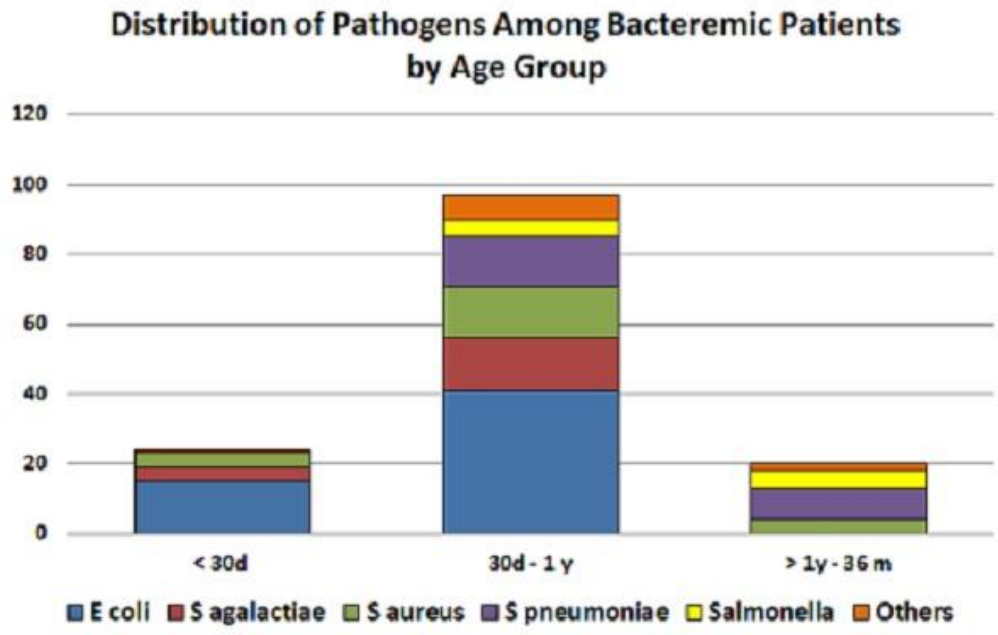
Background and Aims: Evaluation of febrile infants < 36 months (Feb-Inf) has changed; after introduction of conjugate vaccines blood/spinal fluid testing is discouraged in non-toxic subjects presumed to be at very low risk for complications. A urinalysis is recommended to rule-out pyelonephritis, which is the most common serious bacterial infection (SBI). Outpatient management is considered if urinalysis is normal. We propose that Feb-Inf with bacteremia and normal urinalysis are at higher risk of complications including meningitis and death.

Methods: Bacteremic Feb-Inf were identified (7/05-12/13) and their records reviewed. Clinical and demographic information was captured. Bacteremia was defined as complicated if subjects had meningitis, empyema, skeletal infection, deep-organ abscess or died. Abnormal urinalysis was defined as presence of pyuria, leukocyte esterase or nitrite.

Results: *E coli* was the most common isolate (56/141); all in < 1 year olds (Fig 1), 49 with pyelonephritis; only 3 (5.4%) complicated. Overall 35 (24.8%) bacteremic Feb-Inf were complicated (table 1); normal urinalysis was significantly associated (p = 0.002) with complicated bacteremia, particularly in 30 day–1year olds group (OR = 27.3; 95% CI 3.35 – 222.76). *S pneumo* bacteremia had the highest rate of complications.

Conclusions: In the small group of Feb-Inf with SBI, an abnormal urinalysis is suggestive of pyelonephritis, a relatively benign infection. Healthcare providers must be alert that a normal urinalysis may portend serious complications in febrile infants when bacteremic.


Distribution of Pathogens Among Bacteremic Patients by Age Group
120
100
80
60
40
20
0
< 30d
30d - 1 y
> 1y - 36 m
E coli
S agalactiae
S aureus
S pneumoniae
Salmonella
Others

Complication Rate of Bacteremia by Pathogen and Age group								
	2d-29d (n = 24)		30d-1y (n = 97)		> 1y (n = 20)		All (n = 141)	
	Complicated n (%)	Uncomplicated n (%)	Complicated n (%)	Uncomplicated n (%)	Complicated n (%)	Uncomplicated n (%)	Complicated n (%)	Uncomplicated n (%)
E coli	1 (6.7)	14 (94.3)	2 (4.9)	39 (95.1)	0	0	3 (5.4)	53 (94.6)
GBS	1 (25)	3 (75)	3 (20)	12 (80)	0	0	4 (21.1)	15 (78.9)
S aureus	0	4 (100)	5 (33.3)	10 (66.6)	4 (100)	0	9 (39.1)	14 (60.9)
S pneumo	0	0	11 (78.6)	3 (21.4)	5 (35.7)	4 (28.6)	16 (69.6)	7 (30.4)
Salmonella	0	0	1 (20)	4 (80)	1(20)	4(80)	2 (20)	8 (80)
Others	0	1 (100)	0	7 (100)	1 (50)	1(50)	1 (10)	9 (90)
Total	2	22	22	75	11	9	35 (24.8)	106 (75.2)

ESPID-0703
SEVERE BACTERIAL AND VIRAL INFECTIONS

VENTILATOR ASSOCIATED PNEUMONIA IN AN INFANT CAUSED BY CHRYSEOBACTERIUM INDOLOGENES

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Introduction

Chryseobacterium indologenes is an uncommon organism that has been documented to cause a variety of invasive infections mostly in hospitalised patients with severe underlying diseases. In our case *C.indologenes* was isolated from a 3-month-old infant with ventilator-associated pneumonia.

Case

A three-month-old female infant born at term by caesarean section with meningomyelocele and congenital diaphragmatic hernia. She had two surgeries for the repair of meningomyelocele and diaphragmatic hernia on 3 and 14 days of life, respectively. VP shunt had been inserted when she was one month because of hydrocephalus. While on mechanical ventilation on the third month of life, she deteriorated clinically with fever, leukocytosis and increase of acute-phase reactants. Gas exchange condition had became worse. Respiratory secretions, oxygen requirements and ventilator demand had increased. Chest X-ray showed bilateral pulmonary infiltrate. Previous infection episodes including the *Stenotrophomonas maltophilia* had considered and empiric antibiotic therapy with vancomycin, ceftazidime and ciprofloxacin was started. Bacteriological blood, cerebrospinal fluid and urine culture test results were negative. *C.indologenes* was isolated from tracheobronchial secretion sample obtained by endotracheal aspiration. The isolate was susceptible to ciprofloxacin (MIC:0.5 gr/L), levofloxacin, piperasilin-tazobactam, cefepime; it was resistant to meropenem, imipenem, colistin. The treatment was continued with ciprofloxacin. Her fever resolved and gas exchange condition became better after 72 hours of the treatment. The antibiotic treatment was given for a course of 14 days.

Conclusion: C. indologenes may emerge as a potential pathogen in infants with the risk factors as invasive equipment, having underlying diseases and prolonged hospitalization.

ESPID-0405
SEVERE BACTERIAL AND VIRAL INFECTIONS

CRITICAL PERTUSSIS IN CHILDREN: IS HYPERLEUCOCYTOSIS ALONE A RISK FACTOR FOR PULMONARY ARTERIAL HYPERTENSION? A PROSPECTIVE OBSERVATIONAL STUDY.

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Background and Aims

Critical pertussis with hyperleukocytosis is shown to be associated with pulmonary arterial hypertension (PAH), need for ventilation and increased mortality. We aimed to study the incidence of pulmonary arterial hypertension in children with critical pertussis and hyperleucocytosis.

Methods

This prospective study is being conducted since oct-2013 in children aged from 1 month to 12 years admitted to PICU of pediatric hospital in south India. All children with diagnosed critical pertussis and hyperleucocytosis were enrolled consecutively. Details of demographic profile, clinical and laboratory variables were recorded. Need for ventilation was assessed. Chest x-ray and echocardiography were done at admission and subsequently as required.

Results

Twenty patients enrolled with mean age of 12.3±9.8 months. Mean duration of fever was 5±3.5 days, cough; 12±14.6days, and hurried breathing was 3.4±2days. Mean total leucocyte count: 69.86±38.3×10^3cells/mm^3, absolute lymphocyte count; 36.4±17.2, absolute neutrophil count; 28.2±19×10^3cells/mm^3 and platelet count was 8.4±2.5lakhs/mm^3. 75% had no PAH, 15% had mild and only 10% had severe PAH. 40% had hypoxemic respiratory failure and none required ventilation and/or leucoreduction therapy. Mortality rate was 10%. Table 1 illustrates the comparison of patients with severe PAH with no and/or mild PAH.

Conclusions

Though this preliminary data report is inadequate to conclude the association of hyperlecocytosis with PAH, it suggests the hypothesis that other mechanism such as toxin induced acute pulmonary vasoconstriction may have more pathogenic role in PAH and questions the role of leucoreduction therapy in reducing need for ventilation

and increased mortality.

Variable	Severe PAH (n=2)	No or mild PAH (n=18)	P value
Age (months), mean±SD	10.5±10.6	12.5±10	0.079
Heart rate, mean±SD	133±20	130±23	0.859
Respiratory rate, mean±SD	46±14	40±15	0.596
SPO2, mean±SD	98.5	93±8.2	0.399
Total WBC ($\times 10^3$)/mm^3, mean±SD	90.8±12.8	66.4±40	0.412
Absolute lymphocyte count ($\times 10^3$)/mm^3, mean±SD	41±2.6	35.6±18.6	0.693
Absolute neutrophil count ($\times 10^3$)/mm^3, mean±SD	27±8.7	26±19.6	0.944
Platelet count ($\times 10^3$)/mm^3, mean±SD	11.4±4	7.9±2	0.043
Hypoxic respiratory failure, n (%)	2 (100)	6 (33)	0.001
Chest x-ray finding	No infiltrates	No infiltrates	
Encephalopathy, n (%)	0 (0)	4 (22)	0.001
Seizures, n (%)	0 (0)	3 (17)	0.001
Blood transfusion, n (%)	0 (0)	0 (0)	1.000
LOS (ICU) (days), mean±SD	5±4.2	3.75±3.1	0.603
LOS (days), mean±SD	7.5±3.5	6.1±4.9	0.702
Survival, n (%)	2 (100)	16 (89)	0.001

ESPID-0797
SEVERE BACTERIAL AND VIRAL INFECTIONS

ACUTE MYOCARDITIS IN A CHILD: AN ETIOLOGY DIFFICULT TO ASSESS

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We would like to present a case of a suspected HHV-6 related acute myocarditis. Laura is a 10 years-old child, who presented nonspecific thoracic pain and cardiac palpitations episodes with nocturnal awakening over a period of several weeks. In November 2014, due to a severe constipation, she was hospitalised in another centre and developed a sudden cardiac arrest and she was resuscitated by electrical shock and drug therapy. The electrocardiogram showed an ischemic pattern and echocardiogram revealed hypokinesis of left ventricle inferior wall. Hematochemical exams demonstrated alteration in C-reactive protein, B-natriuretic peptide, creatinine kinase and transaminases. The patient was transferred to our centre where was excluded an ischemic damage by CT-scan while a cardiac MRI showed an acute myocarditis. Admission infectious blood investigations (PCR) demonstrated the presence of only 150 copies/ml of HHV-6. Subsequently, she was treated with immunoglobulins and supportive therapy, which progressively improved her clinical conditions. Two weeks later, there was no trace of viral DNA in a blood sample. In addition hair sample was negative as well, confirming the absence of the viral genome integration with the host and thus, supporting the hypothesis of a recent infection. A certain diagnosis however, would have been possible only by endomyocardial biopsy, which was not performed due to the favourable outcome of the treatment. Nonetheless, we believe that the clinical course of Laura's case was positively influenced by the therapy, which was based on the hypothesis of a viral infection.

ESPID-1048
SEVERE BACTERIAL AND VIRAL INFECTIONS

INVASIVE PNEUMOCOCCAL DISEASE: A FIVE-YEAR RETROSPECTIVE REVIEW OF CASES IN A TERTIARY CENTRE

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Background:

The incidence of invasive pneumococcal disease (IPD) has fallen following introduction of pneumococcal conjugate vaccines. IPD remains an important cause of hospitalisation and mortality in children. Immune deficiency has been reported in 10% of children with severe disease[1] however rates in all IPD may be lower. The UK monitors prevalent strains through serotype surveillance of IPD cases. Immune assessment of vaccine failures is recommended, but it is unclear whether all children with IPD should be investigated.

Methods:

Between May 2009 and April 2014 we reviewed all proven IPD cases in our institution, assessing site of infection, outcome, serotype and any immunological assessment undertaken.

Results:

56 children identified: age range 1-153 months. IPD with Streptococcus pneumoniae was confirmed by culture (55 cases - 40 blood, 5 CSF, 5 pleural fluid, 4 joint fluid, 1 peritoneal fluid) or PCR (9 cases - 6 pleural fluid, 2 CSF, 1 blood). 12 children were admitted to intensive care and 3 died.

12 were born before routine pneumococcal vaccination was introduced and 4 presented before two months of age. The infecting serotype was identified in 48 cases.

4 children had features suggesting possible immune deficiency. Case note review showed heterogeneity of investigations undertaken. Overall 12 children had extended immunological assessment.

Following the recorded episode of IPD 7 children presented with further infections, four were oncology patients with episodes of febrile neutropenia.

Conclusion:

Invasive pneumococcal disease continues to be a problem, identifying which children require immunological investigation remains uncertain.

1. Gaschignard J CID 2014

ESPID-0222
SEVERE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGIC AND CLINICAL CHARACTERISTICS OF ENTEROVIRUS AND PARECHOVIRUS INFECTIONS IN PEDIATRIC POPULATION OVER A 4-YEAR PERIOD IN SPAIN

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Introduction. Human enteroviruses (EV) and more recently parechoviruses (HPeV) have been recognized as important viral causes of severe infections in children.

Objectives. To investigate the relative frequencies of specific EV/HPeV types in pediatric infections and their clinical association according to patient age over a 4-y study period (2010-2013) in Spain.

Results. A total of 1251 EV-positive samples from neonates (<28d) (20%), children between 28d and 2y (47%) and children between 2 and 18y (33%) were included in the study. HPeV were detected in 42 specimens, exclusively in infants <8m (62% neonates, $p<0.05$). All but one HPeV were HPeV-3, whereas 32 different EV types were identified. Overall, E-30, E-5 and E-6 were detected most frequently. However, CV-B3, CV-B4, CV-B5 and HPeV-3 were statistically more frequent in neonates than in older patients ($p<0.05$). E-18, E-25, CV-A6, CV-A16 and EV-71 were mainly detected in children 28d-2y ($p<0.05$), whereas E-6, E-21 and E-30 were predominant in children >2y ($p<0.02$).

Clinically, meningitis was more frequent in EV-infected children >2y than in those with HPeV ($p<0.0005$), whereas HPeV-3 infections were associated with encephalitis/ meningoencephalitis in children <2y ($p<0.005$). CV-B types caused 80% of myocarditis in infants <2y and CV-A types were associated with HFMD in children >1m ($p<0.0005$). Neonatal sepsis was no associated with a specific type.

Conclusions. HPeV-3 and CV-B types were prevalent in neonatal and young infant infections in Spain during 2010-2013, while not others that frequently circulated in the same period as E-30 or E-6. Overall, those types presented with greater disease severity.

ESPID-0556
SEVERE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGY OF ACUTE OSTEOARTICULAR INFECTIONS IN CHILDREN IN SPAIN: NATIONAL MULTICENTER STUDY

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Background: Acute osteoarticular infection (AOI) is a potentially severe disease. The aim of this study was to evaluate the epidemiology and etiology of AOI in children in Spain since there are no large studies in our setting.

Methods: Medical records from children [3] in joint fluid were not included.

Results: 641 children were evaluated. 299 cases (46%) were OM (94 confirmed), 232 (36%) SA (111 confirmed), 77 (12%) osteoarthritis, and 33 (5%) spondylodiscitis. 60% were male. Children with OM were older (63 vs 43 months in SA; p*S. aureus* was the most common (155, 63%; 4 MRSA), followed by *K. kingae* (36, 15%) and *S. pyogenes* (22, 9%). *Kingella* was isolated mainly by PCR (only 10% of samples, especially joint fluid). Femur, tibia and foot bones were the most common locations (79%) in OM whereas knee (56%) and hip (26%) in SA.

Conclusions: This is the largest pediatric cohort of AOI in Spain, showing similar results to other epidemiological studies elsewhere. *S. aureus* was the most common isolate although *K. kingae* was recovered in a high proportion of cases. MRSA was not prevalent. Prospective studies are warranted to confirm these findings.

ESPID-0558
SEVERE BACTERIAL AND VIRAL INFECTIONS

DIAGNOSIS OF ACUTE OSTEOARTICULAR INFECTIONS IN CHILDREN: SPANISH NATIONAL MULTICENTER STUDY.

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Background: Acute osteoarticular infections(AOI) are potentially severe diseases. Our aim was to define the diagnostic approach of AOI in Spain.

Methods: Medical records from children [3] in joint fluid were not included.

Results: 641 children were evaluated; 299 cases were OM (94 confirmed), 232 SA (111 confirmed), 77 osteoarthritis, and 33 spondylodiscitis. Median CRP and ESR on admission were 62.3 mgr/l and 53.3 mm, respectively, without differences between OM/SA. Radiological studies are shown in table. MRI and bone scintigraphy had the highest yield for OM diagnosis (94%). 96% of ultrasonographies were compatible with SA. Arthrocentesis was performed in 96% of SA, and joint fluid cultured in 90% (38% positive). Blood culture was obtained in >80% patients (14% positive in AS; 29% in OM). Bacterial PCR was done in 15% of SA (54% positive, mostly *Kingella*).

OM:299 SA:232 OA:77 ED 33 p

R-ray	241(81%)	146(62%)	65(85%)	30(91%)	<0,0001
Ultrasonography	138(46%)	162(70%)	57(74%)	5(15%)	<0,001
Bone scintigraphy	157(54%)	33(14%)	25(33%)	16(48%)	<0,001
MRI	174(58%)	34(15%)	49(64%)	29(88%)	<0,0001

Conclusions: In this Spanish cohort, the yield of synovial fluid culture was low, significantly improving with molecular techniques. MRI and scintigraphy for OM, and ultrasonography for SA were usually done and performed well for the diagnosis. These results will be further compared with the recently published guidelines of the Spanish Pediatric Infectious Disease Society.

ESPID-0074
SEVERE BACTERIAL AND VIRAL INFECTIONS

NEISSERIA MENINGITIDIS AND STREPTOCOCCUS PNEUMONIAE AS LEADING CAUSES OF PEDIATRIC BACTERIAL MENINGITIS IN 9 MEXICAN HOSPITALS FOLLOWING 3 YEARS OF ACTIVE SURVEILLANCE

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BACKGROUND AND AIMS: In Mexico, Meningococcal Meningitis (MM) is considered to be a rare disease however, some studies have shown that is endemic and cause of outbreaks in the northwest. We sought to see whether MM is also present in different areas, and to look which are the predominant bacterial pathogens causing Bacterial Meningitis (BM) in children.

METHODS: Since February/2010 until January/2013, active surveillance for BM in children < 16 years old was implemented in 9 hospitals throughout Mexico. Diagnosis of BM was established by CSF analysis with a positive culture. For all *Neisseria meningitidis* isolates serogroup identification was performed by the Pastorex meningitis kit (Alere, Ltd®, Stockport, UK). For some *Streptococcus pneumoniae* isolates serotype identification was performed using the Quellung reaction (Statens Serum Institute®, Copenhagen,Denmark).

RESULTS: There were 201 cases of meningitis, 72 (36%) considered to be viral, and 129 (64%) presumably bacterial. Culture-confirmed BM was of 73, and isolates were as follows: *N. meningitidis* 24 (33%), *S. pneumoniae* 17 (23.3%), *Enterobacteriaceae* 9 (12%), *S. agalactiae* 6 (8%) and others. MM incidence was much higher in the Northwest (Tijuana, 75%), 41.6% caused by serogroup C. Pneumococcal Meningitis (PM) serotype identification was obtained only in 7 patients, 6 of which were serotype 19A.

CONCLUSIONS: 1. *N. meningitidis* is the leading cause of BM in Mexico, affecting mostly Tijuana, and vaccination should be considered in that region. 2. PM is the second leading cause of BM, 19A is the leading serotype, continuous immunization with the 13-valent pneumococcal conjugated vaccine is mandatory.

ESPID-0318
SEVERE BACTERIAL AND VIRAL INFECTIONS

RESOLVING WITH CONSERVATIVE MANAGEMENT OF MULTIPLE MYCOTIC PULMONARY ARTERY PSEUDOANEURYSMS: AN UNUSUAL COMPLICATION OF STREPTOCOCCUS ANGINOSUS SEPSIS

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Mycotic pulmonary artery pseudoaneurysms (PAPs) are rare but potentially fatal complications of infective disease in childhood. A 14-year-old boy with no specific past history presented with toxic shock syndrome and septic lung due to *Streptococcus anginosus* and subsequent pseudoaneurysms formation of the pulmonary artery while convalescing from sepsis. Contrasted computed tomography (CT) of the pulmonary and bronchial vasculature undertaken for investigation for complication of septic lung revealed multiple large PAPs in both lungs. He did not have hemoptysis or chest pain during a prolonged hospital stay and follow-up. The patient was managed conservatively with prolonged oral as well as intravenous antibiotics. Several multi-slice examinations were performed to follow these aneurysms over a period of 4 months. The PAPs were shown to start regression from the 3 weeks post-development and have been regressed almost completely at 4 months after the diagnosis.

ESPID-0894
SEVERE BACTERIAL AND VIRAL INFECTIONS

OSTEOMYELITIS OF THE SACRUM COMPLICATED BY THROMBOSIS OF THE COMMON ILIAC AND HYPOGASTRIC VEINS – A CASE REPORT

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Background: Venous thrombosis is a relatively rare complication of osteomyelitis. A high index of suspicion and a thorough evaluation is essential to establish the diagnosis.

Case report: A healthy 11-year old girl presented with a 2-day history of abdominal pain in the lower right quadrant, right hip pain, limping and fever, with no history of trauma. On examination, she had pain with hip maneuvers. Inflammatory markers were slightly elevated [C-reactive protein (CRP) 10.8 mg/dL]. Radiography of the pelvis was normal. Ultrassound of the hip did not reveal intra-articular effusion; abdominal ultrassound did not reveal signs of acute abdominal conditions and a bone scintigraphy showed no bone lesions. Two days after admission, the inflammatory markers had worsened (CRP 24.1 mg/dL, sedimentation rate of 120mm/hr). A methicillin-sensitive *Staphylococcus aureus* was isolated in the blood culture. Magnetic resonance imaging revealed osteomyelitis of the right sacral wing and thrombosis of the right common iliac and hipogastric veins. Evaluation for hypercoagulable state revealed no defect. She was started on a regimen of intravenous flucloxacillin and subcutaneous enoxaparin, with progressive improvement of symptoms. She was discharged after seven days of intravenous antibiotic and maintained oral flucloxacillin for six weeks.

Discussion: Osteomyelitis complicated by venous thrombosis is more common in children over eight years old with methicillin-resistant *Staphylococcus aureus* infection and a CRP of >6mg/dL at presentation. The best time for hypercoagulability workup is unknown. A normal bone scintigraphy does not exclude osteomyelitis when there is clinical suspicion.

ESPID-0628
SEVERE BACTERIAL AND VIRAL INFECTIONS

BURDEN OF INVASIVE GROUP B STREPTOCOCCUS DISEASE AND EARLY NEUROLOGICAL SEQUELAE IN SOUTH AFRICAN INFANTS

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Background: GroupB *Streptococcus* (GBS) is a leading cause of neonatal sepsis and meningitis. We aimed to evaluate the burden of invasive early-onset (0-6 days oflife, EOD) and late-onset (7-89 days, LOD) GBS disease in a high HIV prevalence (29.5%) setting.

Methods: A case-control study was undertaken at three hospitals from November 2012 to February 2014 in Johannesburg. Invasive cases in infants <3 months age were identified by daily surveillance of the microbiology laboratories. Neurodevelopmental screening was done in surviving cases and controls at 3 and 6 months of age.

Results: We identified 122 cases of invasive GBS disease over a 12 month period. The incidence (per 1 000 live births) of EOD was similar between HIV-exposed uninfected (HEU) and HIV-unexposed uninfected (HUU) infants (1.13 vs. 1.46; p=0.487), however, there was a 4.67-fold (95%CI:2.24-9.74) greater risk for LOD in HEU than HUU infants (2.27 vs. 0.49;p<0.001). Overall, serotypes Ia, Ib and III constituted 75.8% and 92.5% of EOD and LOD, respectively. The overall case fatality rate among cases was 18.0%. The adjusted odds for neurological sequelae at 6 months of age was13.18-fold (95% CI: 1.44-120.95) greater in cases (13.2%) than controls (0.4%).

Conclusion: The high burden of invasive GBS disease in South Africa, high case fatality rates and significant neurological sequelae among survivors, is partly due to the heightened risk for LOD in HEU infants. An effective trivalent GBS conjugate vaccine targeted at pregnant women could prevent invasive GBS disease in this setting.

ESPID-0106
SEVERE BACTERIAL AND VIRAL INFECTIONS

STAPHYLOCOCCAL EFFUSIVE CONSTRICTIVE PERICARDITIS IN AN IMMUNOCOMPETENT ADOLESCENT: A CASE REPORT.

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INTRODUCTION: Effusive constrictive pericarditis (ECP) is a rare pericardial disease characterized by concurrent constrictive physiology and pericardial effusion. We present a case of ECP in an adolescent that recovered completely after surgical and medical management.

CASE PRESENTATION: A 14 year-old boy was refered to pediatric emergency department with history of fever, breathlessness since 5 days prior to admission. Past medical history was uneventful, with no contact with tuberculosis. Xray chest showed mild cardiomegaly. 2D Echo done revealed a large pericardial effusion with evidence of thickened pericardium with no calcification. He only improved after undergoing pericadiectomy and drainage of purulent material. Work up for malignancy, autoimmune process, tuberculosis was negative. Pericardial pus culture grew staphylococcus aureus and antibiotics were given according to sensitivity. He was discharged after three weeks of hospitalization. Repeat echocardiogram after 4 weeks showed complete resolution of pericardial effusion with normal pressures and ejection fraction.

CONCLUSIONS: Although a rare entity, a high index of suspicion should be maintained for effusive constrictive pericarditis as these group of patients fails to improve by pericardiocentesis alone.

ESPID-0381
SEVERE BACTERIAL AND VIRAL INFECTIONS

BREASTFEEDING AS A CAUSE OF RECURRENT AND LATE ONSET GROUP B STREPTOCOCCAL DISEASE

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Group B Streptococcus (GBS) is the most common cause of bacterial infection in perinatal and neonatal periods. This clinical report discusses the case of a preterm twin with two episodes of late onset GBS sepsis (at nineteen and forty one days old), possibly associated with breast milk transmission. On the second episode, a mother's breast milk culture was obtained and the result was positive for GBS. The approach to this case was providing antibiotics to the mother and patient and withholding breastfeeding since the oropharyngeal and urine cultures of the patient's twin were negative. The breastfeeding was restored for both twins when the mother's milk and the patient's blood cultures where negative. Although in neonatal period GBS infection is more often acquired in utero by ascending route or during the passage on the birth canal, other causes should be investigated when the infection presents after thirty days of life or before recurrent GBS infections.

ESPID-0575
SEVERE BACTERIAL AND VIRAL INFECTIONS

ANTIBIOMICROBIAL RESISTANCE TRENDS FOR PATHOGENS INVOLVED IN URINARY TRACT INFECTION IN A PAEDIATRIC POPULATION IN GREECE (2010 - 2013)

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Background and aims: To evaluate the spectrum of pathogens and the trends in antimicrobial resistance for isolates associated with UTI in Greek children (2010-2013).

Methods: All urine cultures obtained from children (15 days - 14 years), referred to the emergency department or hospitalized in the pediatric wards, were reviewed by using WHONET system, considering only the first isolate per patient. Nosocomial infections were excluded. Identification of the organisms and antimicrobial susceptibility testing were performed by standard methods (disk diffusion method, CLSI guidelines). Antimicrobial resistance mechanisms were researched by phenotypic methods.

Results: A total of 2,893 isolates associated with UTI were recovered. The isolation rates were as follows: *Escherichia coli* (Eco) 63.5%, *Proteus mirabilis* (Pmi) 12.3%, *Klebsiella pneumoniae* (Kpn) 6.8%, *Enterococcus* spp 5.8%, *Pseudomonas aeruginosa* 4.3%, *Enterobacter* spp 2.0%, *Staphylococcus* spp 0.9%, and other bacteria 4.4%. Antimicrobial resistance rates for the three most frequently isolated uropathogens were as follows:

VRE strains were not isolated and all *E. faecalis* isolates were susceptible to ampicillin and nitrofurantoin. Regarding the latter and *E.coli,* resistance rate was

Conclusion: *E. coli* was the most frequent pathogen, as expected. The trend of resistance rates to ampicillin was stable for *E. coli* and downwards for *P. mirabilis*. There was also a downward trend of resistance to cotrimoxazole for all isolates and a worrying upward trend for ciprofloxacin despite its limited use in pediatric population.

Antimicrobial	2010			2011			2012			2013		
	Eco	Pmi	Kpn	Eco	Pmi	Kpn	Eco	Pmi	Kpn	Eco	Pmi	Kpn
	619	101	63	365	75	29	409	78	33	444	104	72
AMPICILLIN	43.5	46.4	-	43.3	34.9	-	44.4	38.7	-	42.9	28.1	-
AMOX/CLAV	11	4.6	17.8	9.4	1.8	14.7	9.1	0.8	9.9	8.2	4.1	4.6
CEFOTAXIME	5.7	2.6	12.2	5.3	0.9	31.1	7.4	0.8	9.8	7.5	0.7	8.1
GENTAMICIN	3.9	5.9	12.2	5.5	2.8	18.0	5.3	2.4	9.8	3.1	6.2	4.7
NETILMICIN	2.1	1.3	11.1	2.0	0.0	16.4	2.1	0.8	13.1	1.1	0.0	4.7
AMIKACIN	1.5	2.7	10.0	1.5	2.8	11.5	2.2	1.6	8.2	1.1	1.4	3.5
CIPROFLOXACIN	5.4	2.7	5.6	3.8	5.6	14.7	6.1	4.0	9.9	7.9	3.4	4.7
COTRIMOXAZOLE	33.7	29.8	25.6	29.2	15.0	26.2	31.5	16.9	19.7	26.1	17.2	14.0

ESPID-0568
SEVERE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGICAL STUDY OF CHILDHOOD BACTERAEMIA DURING A 7-YEAR PERIOD (2007-2013)

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Background and aims: To study the etiology of community-acquired childhood bacteraemia and the antimicrobial resistance of the involved pathogens.

Methods: All episodes of bacteraemia, diagnosed during the first 48 hours of hospitalization from 2007 to 2013, were studied. The Bactec 9240 (BD, USA) system was used (Peds-Plus™/F and Lytic/10-Anaerobic/F vials). Identification and antimicrobial susceptibility testing (CLSI guidelines) was performed with standard methods.

Results: Overall, 337 episodes of bacteremia on equal number of patients (boys 55%, ≤12m 50%) were recorded due to 340 pathogens [171 Gram(-), 169 Gram(+)]: *Escherichia coli* (76, 22.4%), *Streptococcus pneumoniae* (74, 21.8%), *Staphylococcus aureus* (64, 18.8%), *Streptococcus pyogenes* (22, 6.5%), *Salmonella* spp (18, 5.3%), *Neisseria meningitidis* (16, 4.7%), *Streptococcus agalactiae* (13, 3.8%), *Klebsiella* spp (9, 2.6%), *Haemophilus influenzae* type b (7, 2.0%), *Brucella melitensis* (6, 1.8%), other (35, 10.3%). ESBL production was low (*E.coli*; 5, *Klebsiella* spp; 1). Carbapenemases were not detected. MRSA was high (32.8%). Non penicillin susceptible *S.pneumoniae* was 28.4%, only 4% with MIC>1mg/L. No temporal changes were noted, except for a significant decline in *S.pneumoniae* bacteraemia from 2011 and onwards (24.9% vs 11.5%, p=0.012). Most frequent pathogens per age group were: ≤12m, *E.coli*; >12m-5y, *S.pneumoniae*; >5y, *S.aureus*; causing UTI, pneumonia and osteoarticular infections, respectively. The incidence was 1.84/10000 admissions, whereas three patients deceased, due to *S.pneumoniae* and *N.meningitidis*.

Conclusions: As a result of universal childhood immunization against *H.influenzae* type b, *N.meningitidis* and *S.pneumoniae,* bacteraemia due to these pathogens is not as common. Bacteraemia due to *E.coli* and *S.aureus* has now higher relative importance.

ESPID-0681
SEVERE BACTERIAL AND VIRAL INFECTIONS

MICROBIOLOGICAL AND MOLECULAR STUDY OF COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS PNEUMONIA AMONG CHILDREN IN GREECE

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BACKROUND AND AIMS: To evaluate the microbiological and molecular characteristics of community-acquired *S. aureus* (CA-SA) pneumonia in two tertiary paediatric hospitals of Athens (2007-2013).

METHODS: All cases with culture proven CA-SA pneumonia were studied. Identification and antimicrobial susceptibility testing (CLSI guidelines) was performed with standard methods. MICs were determined by Etest®. Molecular investigation was carried out for 25 available *S. aureus* strains: *mec*A, *lukS-lukF*-PV (Panton-Valentine leukocidin, PVL) and *fnba* (fibronectin binding protein A) genes were detected by PCRs. Clones were assigned by *agr* groups, PFGE and MLST.

RESULTS: In total, 41 cases were recorded (boys,61%) with median age of 9m (30d - 11yrs). Cefoxitin-resistant (MRSA) accounted for 31 cases (75.6%). *S. aureus* was isolated from pleural fluid (29 cases), blood (8), pleural fluid and blood (2) and bronchial aspirate (2). All MRSA strains were resistant to fusidic acid, tetracycline and kanamycin. Resistance to clindamycin was 11/41 (26.8%), 1/10 (10%) for MSSA and 10/31 (32.2%) for MRSA (p=0.16), of the inducible resistance phenotype (81.8%). The MIC_{90} of vancomycin was 2mg/l (1-2), teicoplanin 1.5mg/l (0.5-2) and linezolid 1mg/l (0.25-2). Among the 25 available strains, 20 were cefoxitin-resistant and *mecA* - positive (MRSA), carrying also *fnba* gene. Nineteen MRSA strains were PVL(+) belonging to ST80-agr3 clone, whereas, one strain was PVL(-) and ST30-agr1. Five MSSA strains showed polyclonality, three were PVL(+) and three *fnba*(+).

CONCLUSIONS: MRSA and particularly ST80 clone predominate among CA-SA pneumonia in young children. Relatively high MIC_{VA} (≥1 mg/l) and high resistance rate to clindamycin among MRSA strains was observed.

ESPID-0707
SEVERE BACTERIAL AND VIRAL INFECTIONS

LABORATORY-CONFIRMED INVASIVE MENINGOCOCCAL DISEASE IN CHILDREN DURING A 6-YEAR PERIOD IN ATHENS, GREECE

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Background and aims: We studied the epidemiological data of the invasive meningococcal disease (IMD) focusing on the meningococcal phenotypic and genotypic characteristics in children admitted to “P. & A. Kyriakou Children’s Hospital” for the period 2008-2013.

Methods: Laboratory confirmed IMD cases either by culture and/or PCR are included in the study. Culture, identification and serogrouping were carried out by standard methods. Susceptibility to antimicrobials was determined by Etest®. PCR was carried out in all culture negative samples as described previously (Tzanakaki et al, 2005). All isolates or positive biological samples were typed by MLST.

Results: Forty-three IMD cases were recorded (boys 25/43, ranging in age 1m-15y, median 36m). The clinical diagnoses were: meningitis (9), septicemia (6) and meningitis/septicemia (28). Nineteen cases required admission to PICU and one death occurred. The distribution of cases was: 12, 5, 6, 7, 5, 8 per year; 46.5% of cases were solely identified by PCR. Abnormal findings were found in 29/29 tested CSF samples, and positive CSF culture in 12/33 cases. Positive blood culture was found in 15 cases. Serogroup B was predominant (40/43; 93%) and the most frequent clonal complexes were: ST-269 (31.4%), ST-32 (22.8%), ST-162 (17.1%). All isolates were susceptible to cefotaxime, rifampicin and ciprofloxacin, whereas 3/23 showed reduced susceptibility to penicillin (MIC 0.25-0.50mg/L, EUCAST).

Conclusions: Serogroup B is predominant (93%) among the IMD cases over the last years in Greece. PCR was found to be the most sensitive tool for diagnosis. Continuous surveillance is warranted, especially after the introduction of 4CMenB vaccine.

ESPID-1033
SEVERE BACTERIAL AND VIRAL INFECTIONS

PYOMYOSITIS IN CHILDREN: MICROBIOLOGICAL TRENDS AND COHORT REVIEW

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Background/aims:

*S. aureus*is the most common microorganism isolated in pyomyositis, although *S. pyogenes* may have an increasing role. We aimed to describe trends in the microbiological findings and clinical features in our cohort.

Methods:

Medical records of children <14 year-old with pyomyositis assisted at a Tertiary Paediatric Hospital between 2007-2014 were reviewed. Pyomyositis was defined as a primary skeletal muscle infection with microbiological isolation or compatible clinical,analytical and radiological findings.

Results:

Twenty-one cases were included. Mean age was 62.1 months (SD 46.02). The season with the highest rate was summer (8/21). 12/21 presented risk factors(5 varicella). Mean of days with fever previous to admission was 2.81. Clinical presentation: impairment in general condition (9/21) and local swelling (13/21). Median on admission CRP was 160 mg/l, whereas CK-level was normal. Thigh muscles were mainly affected (13/21). 9 (35%) positive cultures were obtained (8 patients): 6 blood and 3 abscess pus. The isolates were 3 (37,5%) *S.aureus*, and 5 (62,5%) *S. pyogenes* (1 varicella case). No temporary changes were found.

Cefotaxime with either cloxacillin (6/21) or clindamycin (6/21) were the most common empiric combination therapy. In 8/12 abscess cases, drainage was performed. Mean treatment length: 29 days (SD 19.27), iv: 18 days (SD 17.16). Three patients

presented complications: venous thrombosis, toxic shock syndrome (both *S.pyogenes)* and septic arthritis due to bacteremia.

Conclusions:

Our cohort showed the significance of *S.pyogenes* as a microorganism involved in pyomiositis, which may indicate changes in the empirical treatment. Our rate of positive cultures remains low.

ESPID-0750
SEVERE BACTERIAL AND VIRAL INFECTIONS

COMORBIDITIES IDENTIFIED IN 616 INFLUENZA CONFIRMED SARI INPATIENT CASES AND 116 DEATHS REPORTED IN SÃO PAULO STATE (SP), BRAZIL, 2014.

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Background: There is limited information about coverage rates in influenza at-risk groups. The aim of this study is to describe the comorbidities identified in influenza confirmed SARI and death cases reported in SP.

Methods: SINAN Influenza Web and Institute Adolfo Lutz data on influenza strains identified in São Paulo in 2014 (EW 1 to 47) were reviewed to identify the most relevant comorbidities identified in SARI inpatient and death cases by type/subtype. Information about immunization was analyzed for deaths and considered valid if the shot had been received at least 14 days before the onset of symptoms.

Results: Information on comorbidity was reported in 577 influenza SARI inpatients; 287 out of 616 (46.6%) presented at least one comorbidity; in 67 out of 116 (57.8%) deaths there were information about comorbidity, and 60 (89.6%) presented at least one comorbidity. The most frequent conditions associated with SARI inpatient and death cases were chronic pulmonary disease, cardiovascular disease and diabetes. The history of immunization was not reported in over 50% of 97 deaths, and only 6 out of 46 (13.0%) patients with fatal outcome had been properly immunized in 2014.

Conclusion: The majority of confirmed influenza SARI and death cases was reported in people with chronic diseases. The reasons for the low influenza vaccine coverage rate in this group should be investigated.

Figure 1 - Distribution of comorbidities identified in 287 influenza confirmed SARI inpatient cases by type/serotype, São Paulo State, 2014.

Comorbidity	A(H1N1)pdm09 N = 59	(%)	A(H3N2) N = 182	(%)	B N = 46	(%)	Total
Cardiovascular disease	19	32.2	37	20.3	13	28.3	**69**
Diabetes mellitus	8	13.6	29	15.9	13	28.3	**50**
Obesity	15	25.4	17	9.3	1	2.2	33
Pulmonary disease	14	23.7	68	37.4	13	28.3	**95**
Immunodeficiency	8	13.6	16	8.8	6	13.0	30
Renal disease	2	3.4	14	7.7	5	10.9	21
Hepatic disease	2	8.5	5	2.7	1	2,.2	8
Neurologic disease	5	1.7	18	9.9	4	8.7	27
Down syndrome	1	0.9	1	0.5	0	0.0	1

*Total = A(H1N1) = 59; A(H3N2) = 182; B = 46.

Source: Sinan Influenza Web/SP/Brazil.

Figure 2 - Distribution of comorbidities identified in 60 influenza confirmed deaths by type and subtype, São Paulo State, 2014.

Comorbidity	A(H1N1)pdm09 N = 26	(%)	A(H3N2) N = 26	(%)	B N = 8	(%)	Total
Cardiovascular disease	10	38.5	7	26.9	3	37.0	**20**
Diabetes mellitus	4	15.4	8	30.8	2	25.0	**14**
Obesity	**9**	**34.6**	2	7.7	0	0.0	11
Pulmonary disease	4	15.4	9	34.6	2	25.0	**15**
Immunodeficiency	2	7.7	3	11.5	0	0.0	5
Renal disease	1	3.8	5	19.2	0	0.0	6
Hepatic disease	0	0.0	3	11.5	1	12.5	3
Neurologic disease	2	7.7	3	11.5	1	12.5	3
Down syndrome	0	0.0	0	0.0	0	0.0	0

** Total = A(H1N1) = 26; A(H3N2) = 26; B = 8.

Source: Sinan Influenza Web/SP/Brazil.

Figure 3 - Distribution of 97 confirmed influenza deaths reported in São Paulo State in 2014, by history of immunization.

Immunization	A(H1N1)pdm09	(%)	A(H3N2)	(%)	B	(%)	Total	(%)
Yes	2	5.0	11 *	26.8	2	12.5	15*	**15.5**
No	20	50.0	16	39.0	4	25.0	40	**41.2**
Unknown	18	45.0	14	34.1	10	62.5	51	**42.3**
Total	**40**	**100.0**	**41**	**100.0**	**16**	**100.0**	**97**	**100.0**

Note: * In 6 deaths the data of immunization was not reported, and in 3 the patient received the shot < 14 days before the onset of symptoms.

Source: Sinan Influenza Web/SP/Brazil.

ESPID-0756
SEVERE BACTERIAL AND VIRAL INFECTIONS

REVIEW OF 3,310 SERIOUS ACUTE RESPIRATORY INFECTIONS (SARI) AND 567 DEATHS CAUSED BY INFLUENZA, SÃO PAULO STATE (SP), BRAZIL, 2013-2014

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Background: Influenza has been associated with large number of serious acute respiratory infection (SARI) and deaths. During the 2009 pandemic, the surveillance for SARI hospitalized cases and deaths caused by influenza were improved in SP with the introduction of RT-PCR technique. The aim of this study is to describe the influenza SRAI cases and deaths confirmed in SP in the last 2 seasons.

Methods: Data recorded in the SINAN Influenza Web from January/2013 until November/2014 (EW 47) were reviewed. A total of 89 SARI and 31 deaths caused by influenza A subtype unknown were not considered. The data describe the influenza strains detected in SARI inpatient and death cases confirmed by strain type/subtype and age groups.

Results: In 2013, Influenza A(H1N1)pdm09 was predominant (72.6%) in influenza SARI inpatient cases, mainly in adults (25-59 years). Influenza B cases in 0-24 years age group represented 57.4%. In 2014, Influenza A(H3N2) was responsible for 65.2% of influenza SARI cases. Among them 43.3% of cases occurred in adults (25-59 years) and 48.8% of deaths occurred in elderly (≥ 60 years).

Conclusions: Both influenza A and B caused substantial morbidity and mortality in all age groups. The majority of confirmed SARI cases and deaths were reported in young adults. In 2013, a disproportional impact of influenza B in individuals < 25 years of age in SARI inpatient cases was observed.

Figure 1 - Confirmed influenza in SARI inpatients cases and deaths reported in São Paulo State broken down by type/subtype and age groups, 2013.

Age group (years)	A (H1N1)pdm09				A (H3N2)				B				Total			
	Cases		Deaths		Cases		Deaths		Cases		Deaths		Cases		Deaths	
	n	%	n	%	n	%	n	%	n	%	n	%	N	%	n	%
02 – 24	488	24.5	40	9.8	33	20.8	1	5.6	341	57.4	13	30.2	862	31.4	54	11.5
25 - 59	1188	59.6	273	67.1	78	49.1	8	44.4	191	32.2	21	48.8	1457	53.0	**302**	**64.5**
>= 60	318	15.9	94	23.1	48	30.2	9	50.0	62	10.4	9	20.9	428	15.6	112	23.9
Total	**1994**	**100**	**407**	**100**	**159**	**100**	**18**	**100**	**594**	**100**	**43**	**100**	**2747**	**100**	**468**	**100**

Source: Sinan Influenza Web/SP/Brazil.

Figure 2 - Confirmed influenza in SARI inpatients cases and deaths reported in São Paulo State broken down by type/subtype and age groups, 2014.

Age group (years)	A (H1N1)pdm09				A (H3N2)				B				Total			
	Cases		Deaths		Cases		Deaths		Cases		Deaths		Cases		Deaths	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
02 – 24	21	19.6	3	7.5	130	35.4	3	7.3	13	14.6	1	6.3	164	29.1	7	7.2
25 - 59	70	65.4	29	72.5	159	43.3	18	43.9	52	58.4	8	50.0	281	49.9	55	56.7
>= 60	16	15.0	8	20.0	78	21.3	20	48.8	24	27.0	7	43.8	118	21.0	35	36.1
Total	**107**	**100**	**40**	**100**	**367**	**100**	**41**	**100**	**89**	**100**	**16**	**100**	**563**	**100**	**97**	**100**

Source: Sinan Influenza Web/SP/Brazil.

ESPID-0584
SEVERE BACTERIAL AND VIRAL INFECTIONS

ENCEPHALITIS BY PARVOVIRUS B19

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Introduction

Parvovirus B19–associated encephalitis is a rare condition in children and adults, which has been increasingly reported in the literature. However, its' physiopathology remains unclear, making it relevant to document emerging cases. Our aim is to report two children with Parvovirus B19-associated encephalitis that were admitted at an insular hospital, in July of 2014, where three contemporaneous cases in adults had already occurred.

Methods

Retrospective consultation of medical archives belonging to both patients.

Cases Report

The first case consists of a 6 year-old boy, with personal history of cognitive impairment and suspected autism, presenting in the ER with fever, seizures and altered mental status. From the investigation made, we highlight the detection of parvovirus B19 DNA in serum and CSF, hypodensity of the white matter in the head CT-scan and anomalies in the right parietal area in the EEG. The second case refers to a two-year-old autistic girl that presented with fever and seven seizures in 24 hours. She had positive detection of parvovirus B19 DNA in serum and CSF, normal head CT-scan and generalized paroxistic activity in the EEG. Both of them were admitted and started empirical intravenous antimicrobial treatment before the definitive diagnosis. They were discharged clinically recovered.

Discussion

The investigation of Parvovirus B19 in these two cases was made in the context of positive epidemiologic criteria, as it is not routinely performed in encephalitis in children. Interestingly, both patients had autistic features, which has not been associated with an increased risk of CNS infection.

ESPID-0832
SEVERE BACTERIAL AND VIRAL INFECTIONS

IS LUMBAR PUNCTURE NECESSARY WHEN EVALUATING WELL-APPEARING NEONATES WITH FEVER WITHOUT SOURCE (FWS) AT LOW RISK FOR SERIOUS BACTERIAL INFECTION?

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Background and aims:
Virtually all guidelines for the management of febrile neonates in the Emergency Department (ED) include routine performance of lumbar puncture (LP). Our aim is to assess the necessity of routine LP in well-appearing febrile newborns (WAFN) meeting low risk criteria (LRC) for invasive bacterial infection (IBI).

Methods:
All newborns with FWS presenting to the ED from January 2009 to June 2014 were retrospectively studied. Routine workup included blood count and urinalysis as well as blood and urine cultures. LP was routinely performed in non-well-appearing newborns and in those meeting any risk criteria (leukocytes >15000cs/mm3, neutrophils >10000cs/mm3, procalcitonin ≥0.5ng/dl, C-reactive protein ≥3mg/dl or abnormal urine dipstick). LP remained elective according to facultative judgment in WAFN with LRC. A nested case-control study was performed among WAFN who met LRC to evaluate clinical outcomes related to LP performance.

Results:
158 newborns with FWS were included; 80 were WAFN meeting LRC; LP was not performed in the ED in 44(55%). LP group was younger (14.2(SD=7.6) vs 18.9(SD=6.4) days p= 0.004), presented higher rate of antibiotic treatment in ED (91.8% vs 6.8%, p=0.0001) and greater length of stay (4.1(SD=2.1) vs 2.4(SD=1.6) days; p=0.001). No case of IBI was found.

Conclusions:
Performance of LP in WAFN who meet LRC for IBI is not necessary in the initial workup of FWS. In addition non performance of LP significantly reduces use of

antibiotics and decreases the length of stay without compromising safety of patients.

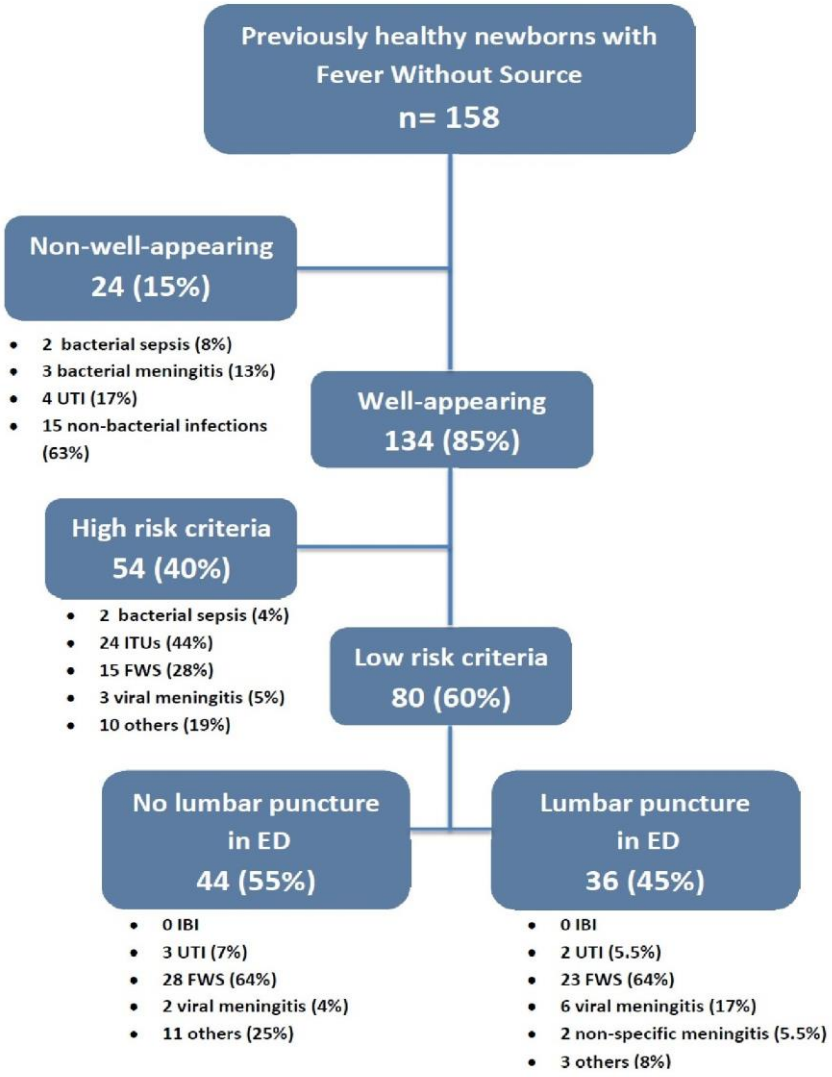

FIGURE 1.- Distribution of febrile newborns presented to the emergency department with Fever Withouth Source and corresponding diagnosis at discharge.

ESPID-0986
SEVERE BACTERIAL AND VIRAL INFECTIONS

NEONATAL STAPHYLOCOCCAL SCALED SKIN SYNDROME

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BACKGROUND & AIMS: Staphylococcal scalded skin syndrome (SSSS) is a toxin-mediated disease rarely seen in neonates, although its incidence seems to be increasing in the last years. The aim of our study was to obtain epidemiological information concerning this disease in neonates due to the lack of these data in our environment.

METHODS: Descriptive study of neonatal (under one month of age) cases of SSSS, from 1997 to 2014 in a tertiary Pediatric Spanish hospital.

RESULTS: Thirty four patients were diagnosed, 6 out of which were neonates (17%). Neonatal cases accounted for 15% of all SSSS episodes in the first nine years of our study (4/26), and for 25% (2/8) in the last ones (p=0.6). Median age at disease onset was 17 days (range 11-25). Male: female ratio was 2:1. All patients presented with erythroderma, bullae, perioral and nasal fissures, and purulent conjunctivitis. None had fever or significant elevation of acute phase reactants. Methillin-sensitive *S. aureus* was isolated in all nasal and conjunctival samples. All blood cultures were sterile but one (methicilin-sensitive *S.aureus*). All patients received intravenous cloxacilin for a mean period of 7 days, and the mean length of hospital stay was 9.3 days. All patients had a favorable outcome and none developed complications.

CONCLUSIONS: Neonatal SSSS is an uncommon condition, although it represents nearly one fifth of the total pediatric cases. Most neonates present with usual mucocutaneous signs and symptoms and no fever, and respond to appropriate antibiotic therapy.

ESPID-1001
SEVERE BACTERIAL AND VIRAL INFECTIONS

POTT'S PUFFY TUMOR: IS SURGICAL TREATMENT NECESSARY?

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BACKGROUND AND AIMS: Pott's puffy tumor (PPT) is a rare complication of frontal sinusitis. Recommended treatment is a combination of antibiotics and surgery. Our objective was to analyze frequency, treatment and outcome of PPT cases.

MATERIAL AND METHODS: Descriptive study of inpatients with complicated frontal sinusitis and final diagnosis of PPT in a tertiary pediatric hospital (2000-2013).

RESULTS: We identified 7 patients with complicated frontal sinusitis, three PPT (42%) and four other different complications (pre/postseptal cellulitis, subperiosteal/epidural abscesses). All patients with PPT presented with painful frontal swelling and prolonged upper respiratory symptoms. However, only one had been previously diagnosed with sinusitis. One patient had fever. Pansinusitis was described in imaging studies (CT and/or MRI) in two cases, whereas the other had fronto-ethmoidal involvement. All imaging studies revealed abscesses or subperiosteal inflammatory changes, with disruption of the sinus wall in two. Blood cultures were negative. Initial antibiotic treatment was meropenem in two patients and cefotaxime plus metronidazole in one. After a median of 3 weeks (range 2-4), treatment was switched to oral route with amoxicillin-clavulanate (2 cases) or levofloxacin (1) to complete 12 weeks. No patients required surgery. All presented favorable clinical course and radiological resolution.

CONCLUSIONS: Complications of frontal sinusitis are rare but PPT accounts for a significant proportion of them. Painful frontal swelling, not necessarily associated with fever, is the most common presentation. Although combined medical and surgical treatment is recommended, all patients presented a favorable outcome with prolonged medical treatment alone.

ESPID-0964
SEVERE BACTERIAL AND VIRAL INFECTIONS

ANTI NMDA RECEPTOR ANTIBODY ENCEPHALITIS COMPLICATING HSV 1 ENCEPHALITIS – A CASE SERIES.

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Background: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a new phenomenon complicating HSV encephalitis (HSE). With many features common to both; dyskinesias including oro-lingual-facial, hemiballismus, choreoathetosis and autonomic dysfunction should prompt consideration of NMDAR encephalitis. We outline three cases describing this entity.

Case 1: 16 month old with proven HSE improving on high-dose acyclovir (HD-ACV) and leviteracetam for seizures unexpectedly developed status epilepticus on D12. Suspecting progression of HSE, IV HD-ACV was increased with escalation of anti-seizure medications improving her seizures. Irritability, hemiballismus and profound encephalopathy subsequently evolved with anti-NMDAR antibodies detected in CSF.After failing to improve with intravenous immunoglobulin (IVIG), high-dose steroids and plasmapheresis she ultimately responded to cyclophosphamide and rituximab.

Case 2: 4½ month old receiving HD-ACV for proven HSE began lip-smacking on D10. Prednisolone was commenced but weaned when repeat CSF for HSV-PCR and anti-NMDAR antibody was negative. On D31 he developed seizures, hemiballismus and oro-motor dysfunction with anti-NMDAR antibodies detected in CSF. Administration of IVIG and prednisolone resulted in resolution of hyperkinesia and improved oro-motor coordination.

Case 3: 15 month old completed 21 days HD-ACV for proven HSE. Discharged on Valaciclovir, she represented on D24 with marked agitation, dyskinesia and oro-motor dysfunction. IV ACV, methylprednisolone and IVIG were commenced for presumed NMDAR encephalitis and CSF confirmed this. Despite high-dose steroids, IVIG and plasmapheresis her choreoathetosis worsened with associated autonomic instability. Slow improvement has been observed after initial dose of Rituximab.

Conclusion: The above identification of anti-NMDAR antibodies highlights the frequency of NMDAR encephalitis as a complication of HSE.

ESPID-0382
SEVERE BACTERIAL AND VIRAL INFECTIONS

ACUTE DISSEMINATED ENCEPHALOMYELITIS – A CASE SERIES

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Background: Acute disseminated encephalomyelitis (ADEM) is a monophasic acute demyelinating disorder of the central nervous system characterized by diffuse neurologic signs and symptoms coupled with multifocal demyelinating lesions on neuroimaging.
Aims: Describe the epidemiologic, clinical, neuroimaging, and laboratory features, treatment, and outcome in a cohort of children with ADEM.
Methods: A 5-year retrospective review of children with the diagnosis of ADEM in Braga Hospital.
Results: Eleven cases were identified with male predominance (n=7) and ages between 8months and 16years. Seven patients (63,6%) presented in winter/spring. Four children (36,4%) had a recent upper respiratory tract illness. Patients presented most often with motor deficits (72,7%), altered consciousness (45,4%), cranial neuropathy (27,3%) and stiff neck (27,3%). Spinal fluid abnormalities occurred in 100%. A definite microbiologic diagnosis was established in two children with Epstein-Barr virus disease and probable/possible diagnoses in two children with previous rotavirus disease or varicella. Brain magnetic resonance imaging (MRI) identified lesions in different regions. All patients were treated with corticosteroids, and two were treated with intravenous immunoglobulin. There was one case with recurrence (after 1year of follow up) and two cases began to have criteria of multiple sclerosis (MS). All patients survived. Two patients (18,2%) had neurologic sequelae. One patient (9,1%) had iatrogenic cushing.
Conclusions: Epidemiologic evidence from our case series suggests an infectious cause for ADEM. MRI was the neuroimaging study of choice for diagnosis and follow-up. Prognosis was excellent. It remains difficult to differentiate the diagnosis of ADEM and MS.

ESPID-0518
SEVERE BACTERIAL AND VIRAL INFECTIONS

POLYCLONAL IGM ENRICHED IMMUNOGLOBULIN IMPROVES OUTCOMES IN EXTREME PRETERMS WITH GRAM NEGATIVE SEPSIS

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Gram negative sepsis is a leading cause of death and morbidity in extreme premature infants in developing nations.Inability to mount a robust IgM response is a major contributing factor.It has been shown in a few studies that IgM-enriched polyclonal immunoglobulin is superior to IVIG in neonatal sepsis. Our goal was to determine if polyclonal immunoglobulin improves outcomes in neonatal sepsis.
We administered IgM - enriched immunoglobulin (Pentaglobin, Biotest at a dose of 5ml/kg/ day for 3 days) to 52 extremely preterm infants (<30 weeks gestational age) with suspected late-onset sepsis (>7 days of age), at the time of initiation of antibiotic therapy, after informed consent. 44 infants with positive blood cultures for gram negative bacilli were included in the study (treatment group) from 2012 -2015. Those who received wrong antibiotics initially (based on sensitivity) were excluded. The control group included 27 infants who did not receive pentaglobin (due to parental decision or non-availability despite consent). The following parameters were compared

	treatment group	control group	p value
average birth weight and gestation	995g, 28.5 weeks	1206g, 29.7 weeks	
need for escalating respiratory support after sepsis	9/ 44	17/27	
need for blood products after sepsis	2/44	15/27	
need for triple inotropes after sepsis	3/44	10/27	
survival	41/44	17/27	<0.05
average cost of hospitalization for 14 days from diagnosis of sepsis	INR 58000	INR 91000	<0.05

Polyclonal IgM-enriched immunoglobulin improves survival, reduces morbidity and cost of hospitalization in extremely premature infants with gram negative sepsis, and needs to be evaluated further .

ESPID-0034
SEVERE BACTERIAL AND VIRAL INFECTIONS

STAPHYLOCOCCAL INFECTION MANAGEMENT USING DAPTOMYCIN IN PREMATURE NEONATES: A SINGLE CENTRE EXPERIENCE

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Background and Aims:

Staphylococcal infection management is complicated as glycopeptide efficacy appears to be reducing when managing invasive infections. In neonates, vancomycin dosing is complicated by changing volumes of distribution. Clinical experience in premature neonates with lipopeptide antibiotics is limited.

Methods:

Data from neonates who received daptomycin at Heart of England Hospital, Birmingham UK between November 2011 and December 2013 was collected. Clinical, demographic and laboratory data was collected. Bacterial isolates were identified by MALDI-TOF MS, vancomycin susceptibility determined by gradient diffusion (E-test). Daptomycin serum levels were measured by high-performance liquid chromatography.

Results:

10 children received daptomycin routinely. Median gestational age at birth was 26 weeks (range 25 - 36). 8 of 10 children were treated for bacteraemias that failed to resolve clinically or microbiologically after vancomycin. Bacteraemia organisms were Staphylococcus aureus (2), MRSA (1), Staphylococcus haemolyticus (1), Staphylococcus epidermidis (3), Staphylocccus warneri (1). The 2 other cases were soft tissue infection due to MRSA. The mean vancomycin MIC was 1.6 mg/L (range 1-4). All patients received 15mg/kg of daptomycin once daily. Average trough levels were 6.5 mg/L (range 1-34.1 mg/L). No significant rise in creatine kinase was recorded. Mean duration of treatment was 7.5 days (range 6-14 days), resulting in microbiological clearance within 72 hours for all cases.

Conclusion:

Premature neonates appear to tolerate daptomycin with no adverse events. Daptomycin could be considered as an alternative agent to vancomycin in cases of severe infection or therapeutic failure. Further studies are warranted to clarify the role of daptomycin in these patients.

ESPID-0863
SEVERE BACTERIAL AND VIRAL INFECTIONS

A FIVE-YEAR RETROSPECTIVE REVIEW OF THE MANAGEMENT OF CHILDHOOD ENCEPHALITIS

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Background

Encephalitis is a serious neurological condition characterised by inflammation of the brain parenchyma. The clinical presentation in children can be non-specific causing delays in diagnosis and treatment. We reviewed the management of children with encephalitis in South East England.

Methods

A retrospective review of patient records was conducted between April 2013 and January 2014 across four hospitals (3 district general and 1 tertiary). Children (0-17 years) with a discharge diagnosis of encephalitis and admitted between 2008 and 2012 were identified through the clinical coding department. Data on clinical features, investigation and treatment were collected.

Findings

Thirty-four children were identified. Clinical features at presentation were fever (67.6%), diarrhoea and vomiting (59%), seizures (44%) and confusion/altered behaviour (18%). A lumbar puncture was performed in 31/34 (91%) cases. A complete CSF order set (defined as CSF white and red cell count, gram stain, paired CSF and serum glucose and CSF protein) was requested in 21/30 (70%) cases. Complete PCR panel (CSF sent for the 3 main viral causes of encephalitis in children: enterovirus, herpes simplex and varicella zoster virus) was performed in 20/30 (67%) cases. The median time to performing brain CT scan was 24 hours (range 23-168) and 48 hours (range 24 -240) for brain MRI scan. The first dose of intravenous aciclovir was administered within 48 hours for 33(97%) cases but the dose was incorrect in 15(44%) cases.

Conclusion

The management of childhood encephalitis is heterogeneous. Guidelines will help standardise practice. Urgent steps are needed to reduce aciclovir prescription errors.

ESPID-0879
SEVERE BACTERIAL AND VIRAL INFECTIONS

PCV10 IMPACT ON STREPTOCOCCUS PNEUMONIAE SEROTYPES DISTRIBUTION: A SEVEN-YEAR HOSPITAL-BASED SURVEILLANCE STUDY IN INVASIVE PNEUMOCOCCAL DISEASE

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Background and aims – PCV10 was introduced in Brazilian National Vaccination Program (PNI) in 2010. Because this vaccine targets only ten of the more than 92 pneumococcal serotypes, concerns that non-vaccine serotypes (NVTs) could increase in prevalence and reduce the benefits of vaccination exist. This ongoing study describes the evolution of the *S. pneumoniae* serotypes causing IPD over the last 6 years in Sao Paulo.

Methods - Santa Casa is a general pediatric hospital with 3500 pediatric annual admissions**.** We conducted a retrospective surveillance study of IPD (defined as isolation of *S. pneumoniae* in blood, cerebrospinal fluid or any other sterile site) in children aged under 16. Serotypes were analyzed in three historical periods, created to evaluate the impact of PCV10 implementation: pre-vaccination period (2007-2009), implementation year (2010), and post-vaccination period (2011-2014).

Results - From 2007 to 2014, 94 IPD episodes in children under 16 were evaluated: 4.7 cases/1.000 admissions during the pre-vaccination period, 3.7 cases/1.000 admissions during the implementation year, and 2.2 cases/1.000 admissions during post-vaccination period (p=0,001). The most prevalent serotypes over the cited periods were 14 (36%), 6B/D (23%), and 14 (9,6%), respectively. There was marked reduction of vaccine serotypes after vaccination (62% vs 35,5%; p=0,001), while there wasn't increase in NVTs (p=0,5).

Conclusion - absolute cases of IPD in children dropped since introduction of PCV10 in PNI. Despite marked reduction in recent prevalence, serotype 14 is still the most prevalent serotype among studied periods. Serotype replacement with previously less usual NVTs occurred in post-vaccination period.

ESPID-0881
SEVERE BACTERIAL AND VIRAL INFECTIONS

ATYPICAL HEMOLYTIC UREMIC SYNDROME ASSOCIATED TO STREPTOCOCCUS PNEUMONIAE: A REPORT OF TWO CASES

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Background and aims - *Streptococcus pneumoniae* has been associated with hemolytic uremic syndrome (SpHUS), which is an unusual but serious disease in childhood. Unlike typical HUS caused by *Escherichia coli* (O157:H7), SpHUS carries a higher risk of mortality and morbidity. We describe two cases of acute hemolytic anemia, thrombocytopenia and acute kidney injury in patients with invasive *S. pneumoniae* infection.

Patient 1 – a previously healthy 8-year-old boy, admitted with cough, fever and dyspnea for 4 days. Pneumonia with pleural effusion was diagnosed. Eight days after onset of respiratory symptoms the patient developed cardiorespiratory distress, septic shock and acute renal insufficiency (BUN=170,39mg/dl; serum creatinine; Cr=2,5mg/dl). Additional anemia (Hb=9,5g/dl), platelets count of 31.000/µl and normal serum C3/C4 levels [DJ1] suggested HUS. Peritoneal dialysis was necessary for 7 days and *S. pneumonia* serotype 3 was latter isolated in blood culture.

Patient 2 – a previously healthy 9-month-old girl was admitted with cough and dyspnea for 2 days. Acute bronchiolitis with secondary pneumonia was diagnosed. Vomiting, diarrhea, oliguria (BUN=110mg/dl; Cr=1,9mg/dl), anemia (Hb=8,5g/dl) and thrombocytopenia (39.000 platelets/µl) developed along following days. Serum C3/C4 levels were[DJ2] normal. Peritoneal dialysis was necessary for at least 8 days, since patient got transferred to another service. *S. pneumonia* serotype 19A was isolated in blood culture. Interval between onset of pneumococcus-related symptoms and development of SpHUS was 3 days.

Conclusion – There were no deaths or sequel until the conclusion of this abstract. Awareness of this rare entity could improve time for diagnosis, adequate therapy, and outcome.

ESPID-0883
SEVERE BACTERIAL AND VIRAL INFECTIONS

PCV10 IMPACT ON STREPTOCOCCUS PNEUMONIAE CLINICAL DIAGNOSIS: A SEVEN-YEAR HOSPITAL-BASED SURVEILLANCE STUDY IN INVASIVE PNEUMOCOCCAL DISEASE

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Background and aims - Pneumococcal conjugate vaccine (PCV10) was introduced in Brazilian National Vaccination Program in 2010. An ongoing study in a quaternary care hospital analyzes the clinical diagnosis, outcomes, and vaccine impact on IPD in Sao Paulo.

Methods - a retrospective surveillance study of IPD (defined as isolation of *S. pneumoniae* in blood, cerebrospinal fluid or any other sterile site) in children under the age of 16 is ongoing. We analyzed clinical diagnosis and outcome among three historical period, created to evaluate the impact of the PCV10 vaccine implementation in 2010: pre-vaccination period (2007-09), implementation year (2010), and post-vaccination period (2011-2014).

Results - From 2007 to 2014, we assessed 94 IPD episodes: fifty events through the pre-vaccination period, 13 events during the transition year, and 31 events throughout post-vaccination period. Pneumonia accounted with 54% of the episodes in pre-vaccination period (9,0 cases/year), followed by bacteremia (24%; 4,0 cases/year), and meningitis (16%; 2,6 cases/year). During transition year, pneumonia was responsible for 46% of the episodes, meningitis 30% and bacteremia 15%. In post-vaccination period pneumonia accounted with 54,8% (4,2 cases/year), followed by bacteremia (25,8%; 2,0 cases/year), and meningitis (12,9%; 1 case/year). Crude mortality was 0,04% and 0,07% during pre and post-vaccination periods, respectively.

Conclusion – annual cases of IPD in children dropped since introduction of PCV10 in Brazilian National Vaccination Program. However, there were no changes in the clinical diagnosis distribution or improvements in mortality when comparing studied periods.

ESPID-0551
SEVERE BACTERIAL AND VIRAL INFECTIONS

NEONATAL SEPSIS AND SEPSIS SHOCK

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BACKROUND AND AIMS:neonatal sepsis and sepsis shock is a great problem in neonatology,that provokes mortality and several complications.METHODS:Ther was cross section research during 2 month.research was agreed with clinical bioethic board.There was studied 118 newborns with symptoms of sepsis,age of 0-5 days.The diagnosis of sepsis was confirmed in 54 newborns with clinical-laboratory studies.Was chosen 2 groups:1st-33 newborns with sepsis,2nd with sepsis shock.We investigated c-reaqtive protein(CRP) in the bload serum by latex-agglutination methods,procalcitonin(PC) by-immune-luminometric method,in 41%cases we obtained the blood culture.We studied thyroxin T4,three-iode-thyronin T3,Thyro-stimulation hormone(TSH).RESULTS:in the 1st group levels of T4 and T3 was decreased,TSH was increasd.b-Endorphin was normal.In the 2nd group levels of T4,T3,TSH was decreased,b-Endorphine was greatly increased.Bacteriological view:Staphiloccus aureus-7,Group B-streptococci-8,Serratia marcesens-5,pseudomonas aeruginosa-9,Klebsiella pneumoniae-11,escherichia coli-3,Acinetobacter-7.CRP and PC was increased in the both group.CONCLUSIONS:1/CRP and PC are reliable diagnostic markers at the early stage of sepsis.2.In the Neonatal sepsis was hipofunction of thyroid gland.3.In sepsis shock was increased b-endorfine due to persistent hypotensioniit is necessary to include Naloxon in the complexs treatment.

ESPID-0088
SEVERE BACTERIAL AND VIRAL INFECTIONS

ACUTE BACTERIAL MENINGITIS IN CHILDHOOD: CLINICAL PRESENTATION AND LABORATORY FINDINGS ON ADMISSION DEPENDING ON AGE, SEX, AND DURATION OF ILLNESS.

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Aim: To review the clinical presentation and laboratory findings of acute bacterial meningitis amongst children age 1 month – 17 years in Västerbotten County 1986 – 2005.

Methods: A population-based study in Västerbotten County based on County councils' data base registers of diseases and the registers of positive bacterial cultures. Medical records were reviewed to extract data and confirm the diagnosis.

Results: 81 cases of acute bacterial meningitis were included. Significant differences in clinical presentation and laboratory findings of acute bacterial meningitis depended on several factors, age being the most important. Younger children were more ill, but also presented with more diffuse symptoms. Furthermore, important differences were found depending on patient's sex, differences that might aid in explaining the higher case-fatality rates for boys compared to girls. Boys had, to a higher extent, indications of a disturbance in the blood brain barrier which is a known negative prognostic factor.

Conclusion: Acute bacterial meningitis is a serious condition and clinical presentation varies. Clinicians must be aware of the fact that children can present with different symptoms and signs depending on age but also on sex and to a lesser extent duration of illness.

ESPID-0454
SEVERE BACTERIAL AND VIRAL INFECTIONS

EFFICACY OF ORAL ANTIBIOTIC THERAPY FOR BACTEREMIA DUE TO STREPTOCOCCUS PNEUMONIA FOLLOWING SHORT COURSE PARENTERAL THERAPY IN CHILDREN

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Background and aims In Japan, Pneumococcal conjugate vaccine has been introduced from February 2010 and the number of pediatric invasive pneumococcus diseases decreased markedly. However, some cases of bacteremia due to non-vaccine serotype *Streptococcus pneumonia* are remaining in children. We assessed the efficacy of oral antibiotic therapy for bacteremia due to *Streptococcus pneumonia* following short course parenteral therapy in children.

Methods Pediatric patients diagnosed bacteremia due to *Streptococcus pneunmoniae* between August 2011 and November 2014 were recruited. For all bacteremia cases, we started empiric therapy with parenteral antibiotics and permitted to switch oral antibiotics if parenteral therapy responded clinically, central nervous system infection was ruled out and susceptibility of *Streptococcus pneunmoniae* was identified.

Results During the observation period, 26 cases of bacteremia caused by *Streptococcus pneumonia* were identified and median age was 12 month-old. All of 26 patients started an empiric therapy with parenteral antibiotics. They were diagnosed with occultbacteremia (n=11),pneumonia (n=10),meningitis (n=2),periorbital cellulitis (n=1),mastoiditis (n=1) and acute otitis media (n=1). Six patients (23%) including 2 meningitis cases were treated with parenteral antibiotics consistently and the average of total therapeutic duration was 16.7 days. Other 20 patients (77%) were changed to oral antibiotics and the average of total therapeutic duration was 10.7 days that included 6.5 days of oral therapy. There was no recurrence case of bacteremia in both groups.

Conclusions Our study suggests that the use of oral therapy for bacteremia due to *Steptococcus pneumonia* for children without central nervous system infection was satisfactory effective.

ESPID-0739
SEVERE BACTERIAL AND VIRAL INFECTIONS

PENICILINE RESISTANT STREPTOCOCCUS PNEUMONIAE MENINGITIS IN A CHILD WITH SENSORINEURAL HEARING LOSS, SPLIT HAND/FOOT MALFORMATION TYPE 1 (SHFM1) AND MONDINI DYSPLASIA.

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Introduction: Mondini dysplasia (MD) is a congenital malformation of the inner ear, commonly associated with hearing impairment, cerebrospinal fluid otorrhea / rhinorrhea and recurrent meningitis. Split-hand / split-foot malformation (SHFM) is a limb malformation involving the central rays of the autopod and presenting with syndactyly, median clefts of the hands and feet, and aplasia and / or hypoplasia of the phalanges, metacarpals, and metatarsals. Some patients with SHFM1 have been found to have mental retardation, ectodermal and craniofacial findings, orofacial clefting and neurosensory hearing loss.

Case: A nine year-old girl presented to our clinic with the complaint of persistant fever and vomiting. MD and sensorianeural hearing loss in the both ears was diagnosed when she was three years old. She had one brother and one sister with SHFM1 and hearing loss. Her sister died because of meningitis at one year of age. She hadn't been vaccinated with pneumococcal vaccine. She had fever, weakness, hearing loss, nuchal rigidity and SHFM1 (Picture). Brudzinski and Kernig signs were both positive. Cerebrospinal fluid (CSF) showed cell count of 1200 leukocytes/mm^3. Penicilline resistant *Streptococcus pneumoniae* was isolated from her CSF culture.

Conclusion: SHFM1 with hearing loss is a rare SHFM variant**.** There are limited number of cases of Mondini dysplasia together with deafness and SHFM1. Additionally, our case had meningitis. In familial cases, often autosomal dominant inheritance is reported. All family members with SHFM1 should be evaluated for MD and they must be immunizied with pneumococcal vaccine because of the risk of recurrent meningitis.

ESPID-0422
SEVERE BACTERIAL AND VIRAL INFECTIONS

A FIRST CASE OF MILD ENCEPHALITIS/ENCEPHALOPATHY WITH A REVERSIBLE SPLENIAL LESION ASSOCIATED WITH HUMAN PARECHOVIRUS TYPE 3 INFECTION

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Introduction:

Human parechoviruses (HPeVs) are members of the family Picornaviridae. HPeV types 3 is associated with severe neonatal infection include neonatal sepsis, neonatal meningoencephalitis and hepatitis-coagulopathy syndrome, but severe forms in child are rare presentations.

Mild encephalopathy with reversible splenial lesion (MERS) is a clinico-radiological syndrome. It is characterised acute mild encephalopathy with change the splenium of the corpus callosum on brain magnetic resonance imaging (MRI). Most common cause of MERS is viral infection, especially Influenza virus infection.

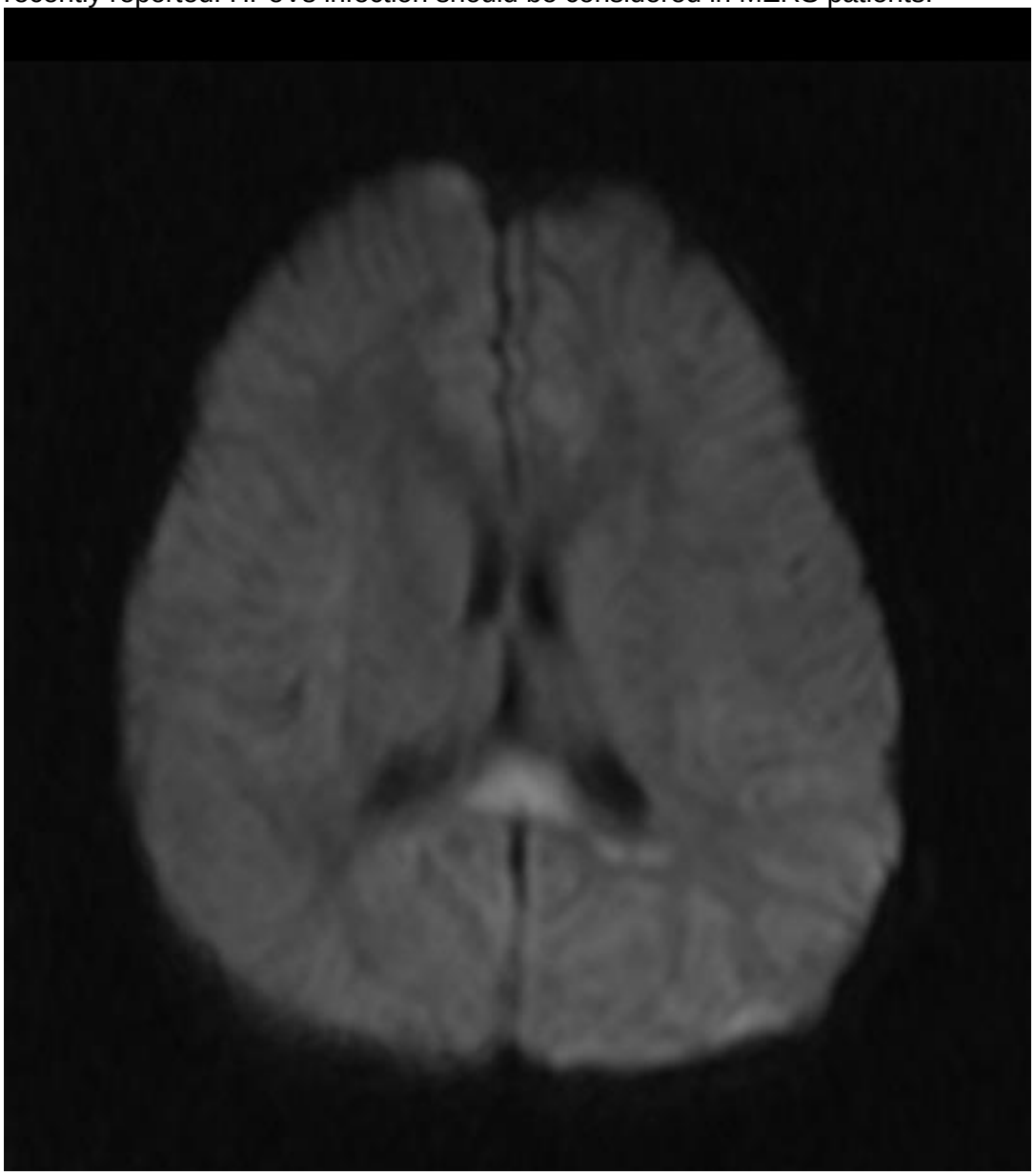
We report a first case of MERS associated with HPeV3 infection in a four-year old girl.

Case presentation:

A previously health four-year old girl came to hospital with four days fever and impaired consciousness. Her six-month old sister also had fever and rash like a hand-foot -mouse disease. We diagnosed status epilepticus, because she appeared generalized tonic seizure. Her seizure was under controlled continuous intravenous midazolam infusion. Emergency brain MRI showed high intensity lesion of the splenial lesion on diffusion weighted image (Image. 1), we diagnosed MERS based specific MRI findings. The diagnosis of HPeV3 infection was made by positive HPeV3 real-time PCR in feces. No other viruses include Influenza virus were detected. Three days after methylprednisolone pulse therapy, her clinical presentations were improved. She was recovered without sequela and discharged on 23th hospital day.

Conclusion:

Although MERS is rare presentation in Europe, european patients of MERS were recently reported. HPeVs infection should be considered in MERS patients.



ESPID-0802
SEVERE BACTERIAL AND VIRAL INFECTIONS

INFECTIVE ENDOCARDITIS CAUSED BY MORGANELLA MORGANII IN A IMMUNOCOMPETENT PATIENT WITH CHRONIC OTITIS MEDIA

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Background and aims: *Morganella morganii* is a gram negative aerobe, found often as intestinal commensal. It is commonly implicated in urinary tract infections and pyogenic infections, but rarely causes bacteremia.

Case: We report herein a case of a 15-year-old boy who presented with recurrent headache, tinnitus and fever for 7 days. Right tympanic membrane perforation was found in his physical examination. Chronic otitis media, acute sinusitis and increased aeration of mastoid bones was identified on temporal bone CT. Meropenem and vancomycin were started. Meanwhile, *Morganella morganii* was isolated from blood culture. Gentamicin was added to meropenem. The transthoracic echocardiogram revealed 10 mm of vegetation on the tricuspid valve. Medical follow-up and close monitoring were suggested by cardiovascular surgery. Drug abuse and suspected sexuel activity were not determined. Primer and secondary immundeficiency were not identified. We investigated for urinary and gastrointestintal truct pathologies. Thus, a ulcerated polypoid lesions where was at the level of 6 to 9 hours were seen in anal canal on colonoscopy. Biopsy of the lesion was consistent with adenomatous polyps. In light of all these results, infective endocarditis caused by *Morganella morganii* was thought to be due to the chronic otitis media. The transthoracic echocardiogram revealed only thickening of the tricuspid valve after a total of 8 weeks of meropenem treatment. The patient was discharged and still being followed up with outpatient follow-up.

Conclusions: To the best of our knowledge, the patient is the first immunocompetent patient suffering from infective endocarditis caused by *Morganella morganii.*

ESPID-0969
SEVERE BACTERIAL AND VIRAL INFECTIONS

CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION CAUSED BY CANDIDA PELLICULOSA: A CASE REPORT

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Background and aims:

Candida pelliculosa is a yeast frequently found in various fruits, tree exudates, soil, vegetables. It has rarel been reported as the causative agent of nosocomial fungemia.

Case: We reported a case of a 7-month-old girl who presented with growth retardation. The baby was diagnosed as truncus arteriosus type-1. Since the patient worsened on the 25th postoperative day, blood cultures were taken. Then *Candida pelliculosa* was isolated in the blood cultures. Because the patient was administered amphotericin B empirically for 7 days, caspofungin was started. Central line was replaced. Vegetation was not found by echocardiography. There was no endophthalmitis on examination of fundus. Abdominal ultrasonography was normal. Candidemia did not repeat. The patient was successfully treated by caspofungin therapy.

Conclusions: Physicians should consider *C. pelliculosa* as one of the possible fungal pathogens causing catheter-related infections.

ESPID-0092
SEVERE BACTERIAL AND VIRAL INFECTIONS

LIVER ABSCESS CAUSED BY CAPNOCYTOPHAGA GINGIVALIS.

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Background: Pyogenic liver abscess is a serious but rare condition in otherwise well immunocompetent patients. Staphylococcus aureus is the most common pathogen.
Aim & methods: We report a case of a Capnocytophaga spp. liver abscess in a previously healthy white Caucasian 15 year old boy. The patient presented with a ten day history of fatigue, low grade fever and generalised abdominal pain. Examination revealed right upper quadrant tenderness and there was systemic iflammation and impaired liver function on laboratory evaluation. Ultrasonography demonstrated multiple communicating abscesses within the right lobe of the liver measuring 12 cm*8 cm.
600 ml of purulent material was drained by US guided puncture and an intrahepatic catheter was placed percutaneously. Therapy with intravenous ampicillin, gentamicin and metronidazole was given. Abscess pus cultures yielded a gram negative rod, identified as Capnocytophaga gingivalis. As the fever subsided and the patient improved subjectively, the catheter was removed after seven days of drainage and antibiotics were switched to oral co-amoxiclav.
However, the patient was re-admitted two days later with fever and right pleural effusion. Ultrasound revealed 6cm*2cm liver ascess, necessitating a second percutaneous drainage and further intravenous antibiotics. In total, the patient received two months of antibiotics (intravenous and oral). Subsequent tests for granulocytic dysfunction and immunodeficiency were all negative.
Conclusion: Capnocytophaga gingivalis, normally part of the normal oral microflora, can cause liver abscesses in previously healthy individuals without underlying immunodeficiency. Although rare, liver abscess should be considered in the differential diagnosis of children presenting with abdominal complaints associated with fevers.

ESPID-0560
SEVERE BACTERIAL AND VIRAL INFECTIONS

MENINGITIS BY NEISSERIA MENINGITIDIS AND ENTEROVIRUS: A CASE REPORT

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Meningitis is an inflammatory disease of the leptomeninges, the tissues surrounding the brain and spinal cord. The simultaneous occurrence of bacterial and viral meningitis was first described in 1962 by Wright *et al*. Only a few cases have since been reported.

We describe a case of a previously healthy 3-year-old boy, admitted to the paediatric ER, in October 2014, with a 7-hour history of vomiting and fever (38,5º C). There was no diarrhoea, headache, cough or sick contacts. On physical examination, he presented a good general condition, pallor, Glasgow coma scale score 15. Neurological examination disclosed mild meningeal irritation without other signs. The patient was kept under observation and after 6 hours of admission he began a severe headache, with fever every 3 hours showing neck rigidity and Brudzinki's sign. A lumbar puncture was performed and cerebrospinal fluid (CSF) findings were: glucose 65.6 mg/dL, proteins 53,3 mg/dl and white blood cells >1000.0 /mm3, with predominance of neutrophils. The blood counts were normal and C-reactive protein 5.57 mg/dL. A diagnosis of acute meningitis was made and he started intravenous ceftriaxone. There was good response on the first 12 hours, with no fever, vomiting or headache. Gram and culture of the CSF were negative. CSF was positive for both *Enterovirus*-PCR and *Neisseria meningitidis* serogroup B-PCR. He complete 7 days of intravenous treatment.

Although rare, this case report highlights the importance of associating the clinical diagnosis to the laboratory findings. This will allow an early empírical treatment and, consequently, better prognosis.

ESPID-1041
SEVERE BACTERIAL AND VIRAL INFECTIONS

TRANSVERSE MYELITIS: AN UNCOMMON CAUSE

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Tranverse myelitis (TM) is a rare neurological syndrome, characterized by motor, sensitive and autonomic dysfunction.

Thirteen-year-old male with no significant past medical history went to the emergency room with acute onset of weakness on the left leg and sensory loss on the right leg up to the abdomen. No other symptoms associated. On physical examination he was afebril, mental status, cranial nerves and upper extremities were normal. The examination besides that was normal. His left leg had a maximum strength of 2/5 and had sensory loss on the right leg and abdomen up to T4. Inicial MRI was related as normal. Methylprednisolone and physiotherapy were initiated with a slow improvement of the symptoms. He had urinary and fecal retention the first four days, with complete recovery after. On the fourth day of disease MRI was repeated, showing a linear hypersignal between D3-4 and D4-5. Brain MRI unaltered. All analytic results were normal, except for a positive PCR for Epstein-Barr virus, although with positive IgG and negative IgM for this virus. Now, at a 2-month follow-up evaluation he remains with a minor difficulty on the dorsiflexion of the left foot and and with a sensory loss below T4, but improving.

TM is a syndrome with various causes, but the parainfectious etiology caused by EBV is a rarely documented situation. So, the etiology of this case remains questioned, since the demyelinating cause, namely a possible multiple sclerosis, will only be excluded by time.

ESPID-1078
SEVERE BACTERIAL AND VIRAL INFECTIONS

Invasive meningococcal disease and complement pathway deficiencies. Is systematic screening warranted?

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Background: Although the relationship between recurrent invasive meningococcal disease (IMD) and complement pathway deficiencies (CPD) is clear, there is scarce data about the complement deficiency prevalence in patients who present his first episode of IMD in our media.

Objectives: The main aim of this study is to analyze the prevalence of CPD in patients with a unique episode of IMD. Furthermore, we want to define demographic, clinical and microbiological features associated with CPD. Patients and methods: Descriptive cross-sectional study including all patients under 18 years of age diagnosed with a single episode of IMD (January 1997-July 2013). IMD was defined as a positive meningococcal culture and/or PCR detection in peripheral blood and/or cerebrospinal fluid. Complement pathway assessment was performed through classical and alternative pathway activity, CH50 and AP50, respectively.

Results: We included a total of 80 children (M/F sex ratio 1.2; mean age: 27 months; caused by serogroup B (64), serogroup C (9), serogroup Y and serogroup E19 (1 each), 5 isolates could not be serogrouped. Only two cases of C5 deficiency were detected in patients with serogroup Y and E19 IMD, respectively. Both were Mahgreb and consanguinity was present in one family. C5 deficiency was also diagnosed in the brother of the first case and parents from both cases were carriers of the mutation.

Conclusion: In our cohort, only uncommon serogroup caused IMD was associated with CDP. Therefore, it seems reasonable to limit this screening in selected cases. However, a national study has started to provide more strong data.

ESPID-1075
SEVERE BACTERIAL AND VIRAL INFECTIONS

ROLE AND IMPORTANCE OF MOLECULAR DIAGNOSIS IN CLOSTRIDIUM DIFFICILE COLITIS IN CHILDREN

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National Institute for Infectious Diseases "Prof. Dr. Matei Bals, Bucharest, Romania

Introduction

Clostridium difficile infection is an increasingly common, both in adults and children. Antibiotics and other drugs have been incriminated as triggers for Clostridium difficile infection. Rapid diagnosis of this form of colitis is extremely important in order to initiate specific therapy.

Material and method

During 2010-2014, we have monitored all children admitted in the Pediatric Department of the National Institute of Infectious Diseases „Prof. Dr. Matei Bals" with suspicion of Clostridium difficile colitis, later diagnosed both through PCR and toxin testing. All cases were severe, thus necessitating rapid initiation of treatment. Cases were separated into two comparative groups in order to assess the efficacy of diagnostic methods.

Results

During December 2010 – October 2014, 15 cases of Clostridium difficile colitis were registred in the Pediatric Department. Most cases were registered in past two years. Two of the children were already at the second relapse of infection, 2 were receiving treatment and 11 were at their first episode. In the first group, diagnosis was established through Clostridium difficile toxin testing and culture, and the second group through both PCR and standard tests. In the second group, treatment was initiated on the first day of hospitalization, with a favourable outcome and no relapses.

Conclusions

Clostridium difficile colitis is becoming an increasingly common condition in Pediatric wards. Antibiotic and proton pump inhibitors abuse has led to a rise in cases. A rapid diagnosis is much more effective in initiating a proper, potentially life-saving treatment.

ESPID-0059
SEVERE BACTERIAL AND VIRAL INFECTIONS

HYDROCEPHALUS AS A RARE COMPLICATION OF CHILDHOOD BACTERIAL MENINGITIS

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Since neurologic complications of childhood bacterial meningitis are encountered frequently, **the aim** of this study was to analyze the risk and outcome of hydrocephalus in children with bacterial meningitis.

Methods: This observational and prospective study included children treated for bacterial meningitis in two study periods. In first study period (1997–2002), 277 children were prospectively enrolled in the study and in the second study period (2009-2010), 77 children were prospectively enrolled in the study.

Results: Of the 277 vs 77 children, 60 (22%) vs 33 (43%) patients developed neurologic complications, while there were 15 (5.4%) vs 2 (2.6%) deaths. Hydrocephalus developed equally in both study periods 7 vs 2 cases (2.5% vs 2.6%). Of the total 9 hydrocephalus cases, 6 developed obstructive and 3 communicating hydrocephalus. The median age of cases with hydrocephalus was 8.6 months. The mean duration of illness prior to admission was 5.7 days and 67% of them have been previously treated with antibiotics. At admission 89% had altered mental state, 67% had seizures, 44% had neurological deficit. The mean time of confirmation of hydrocephalus was 15.8 days (range 2-38 days). The etiology was proven in 7 cases: *H. influenzae* (4 cases), *N.meningitidis* (2 cases) and *S. pyogens* (1 case). Case fatality was 22% among cases with hydrocephalus and 4.3% among other cases.

Conclusions: In two study periods, hydrocephalus developed equally in 2.5% vs 2.6% and was associated with high mortality rate and unfavorable outcome. Late admission was significantly associated with higher incidence of hydrocephalus.

ESPID-0057
SEVERE BACTERIAL AND VIRAL INFECTIONS

NEONATAL MENINGOCOCCAEMIA AND MENINGITIS PRESENTING WITHOUT A FEVER OR A RASH

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Introduction

Neissera Meningitides is an uncommon cause of meningitis in newborns. Fever is often an inconsistent sign of infection in this period. We report a case of a 4 week old with meningococcal sepsis and Meningitis without a fever or a rash.

Case Report

She presented with a day's history of poor feeding, grunting and abnormal skin colour. Past history was significant for IUGR, with birth weight of 1.65kg at 38 weeks, and a duodenoplasty at week 1 for a duodenal web. She was discharged to non-smoking parents at 3 weeks of life.

On re-admission at 4 weeks, she was lethargic with mottled skin, temperature of 37.0^{o}C,heart rate of 180/minute and CRT of 2 to 3 seconds with warm extremities. Anterior fontanelle was level.

She received two, 10ml/kg of normal saline and IV Cefotaxime and Amoxicillin after blood cultute. FBC showed WBC of 1.5, with neutrophils of 0.5 x 10^{9}/L. CRP was 83mg/L. A lumbar puncture showed RBC of 80/micrlitre, and WBC of 65/microlitre, 99% being polymorphs and 1% lymphocytes. CSF glucose was 1.1mmol/L and protein 1.7g/L. Gram stain was negative.

Confirmation of positive blood and CSF culture for N. Meningitides,Type B was reported after 24 hours.

Family received prophylactic Ciprofloxacin. CT scan was normal. She was discharged after 10 days with follow up and audiology assessment.

Conclusion

We cannot tell if this was a nosocomial or community acquired infection, but more important is for physicians to know subtle signs and symptoms that would suggest a seriously ill baby.

ESPID-0418
SEVERE BACTERIAL AND VIRAL INFECTIONS

CURATIVE INTRAVENTRICULAR THERAPY OF PEDIATRIC VENTRICULITIS DUE TO MULTIDRUG-RESISTANT KLEBSIELLA PNEUMONIAE WITH CONCOMITANT USE OF COLISTIN AND AMIKACIN

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Background and aims

Due to poor cerebrospinal fluid (CSF) penetration when administered intravenously, colistin and aminoglycosides are sometimes needed to be instilled directly into ventricles when a difficult-to-eradicate organism is the cause and there is no other remedy. We report an infant with multidrug-resistant *Klebsiella pneumoniae* ventriculitis, who attained microbiological eradication with concomitant use of intraventricular colistin and amikacin.

Methods

A two-month-old male infant with a ventriculoperitoneal shunt was started intraventricular amikacin with intravenous meropenem because of worsening pneumonia and multidrug-resistant *K. pneumoniae* growth in his turbid CSF. This regimen was continued for eight days, during which five *K. pneumoniae* - positive CSF culture results were obtained. Since the characteristics of both the patient's clinical status and CSF persisted, intraventricular and intravenous colistin was substituted for amikacin and meropenem and carried on for 12 days, during which, seven of eight CSF cultures continued to grow *K. pneumoniae*. Intraventricular amikacin was added to the regimen. This dual intraventricular antibiotic regimen (colistin+amikacin) was continued for a microbial growth - free period of 12 days. No organisms were detected in the patient's CSF thenceforwards.

Results

The Infectious Diseases Society of America practice guidelines support the use of intraventricular antimicrobials for the treatment of difficult-to-eradicate CSF infections despite its irritant effects. It is noteworthy that intraventricular monotherapies with either amikacin or colistin was not successful in microbiologic eradication.

Conclusions

This is first reported pediatric case of multidrug-resistant *K. pneumoniae* ventriculitis, microbiologically cured with a combination of intraventricular and systemic therapy.

ESPID-0416
SEVERE BACTERIAL AND VIRAL INFECTIONS

STAPHYLOCOCCAL SCALDED SKIN SYNDROME: A CASE REPORT OF A 3.5 YEAR-OLD MALE TODDLER WITH STAPHYLOCOCCUS CAPITIS INFECTION

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Background and aims: Staphylococcal scalded skin syndrome (SSSS) is an acute epidermolysis usually caused by group II coagulase-positive staphylococci, which elaborate exfoliatin (epidermolysin), a toxin that splits the upper part of the epidermis just beneath the granular cell layer. Infants and children < 6 years are most susceptible as epidemics may occur in nurseries, presumably transmitted by the hands of personnel who are in contact with an infected infant or who are nasal carriers of *Staphylococcus aureus*. The aim of our study is to report a case of a toddler with SSSS and staphylococcus capitis (coagulase-negative species) bacteremia.
Methods-Results: We describe a 3.5 year-old immunocompetent male toddler who presented with low fever and erythematous skin with large, flaccid blisters broken to erosions, mainly on the face and trunk (Figure). Twenty hours before hospital admission he appeared with a scarlet rash on the face and shoulders which was treated with amoxicillin/clavulate per os. During hospitalization he remained in excellent general status. The rash worsened during the first two days (with widespread desquamation, crusting of the lesions, positive Nikolsky sign, penis oedema and anal desquamation), and then gradually improved. Laboratory tests showed mild signs of infection (C-reactive protein 13mg/l), but blood cultures revealed staphylococcus capitis bacteremia. He was treated with intravenous vancomycin for 14 days.

Conclusions: In our knowledge, no case of staphylococcus capitis induced SSSS has been reported recently.

ESPID-0364
SEVERE BACTERIAL AND VIRAL INFECTIONS

IMMATURE GRANULOCYTES AS ADDITIONAL VALUE OF SEPSIS DETECTION IN CHILDREN

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Backgroundand aims: Sepsis is still one of the common causes of children mortality. Early identification and appropriateness of the initial therapy are the key factors influenced the outcome of sepsis. The aim of our study was to evaluate immature granulocyte(IG) percentage in comparison with white blood count (WBC), absolute neutrophil count (ANC) and C-reactive protein (CRP) for early identification of sepsis.

Methods: 75 children with infection admitted to the Children's Clinical University Hospital of Latvia during 2013 were included in the study. Blood samples were collected at the first hours after admission to hospital. The IG and other blood parameters were measured by Sysmex analyzer. Children were categorized into two groups of severity ofinfection: (i) sepsis (n=35), (ii) infection without SIRS (n=40). For sepsis definition International Pediatric Sepsis Consensus Conference classification was used.

Results: Receiver operating characteristics performed in our study showed that IG percentage and CRP were the better predictors of sepsis (AUC values for CRO 0.89 (0.82-0.97) and 0.84 for IG% (0.74-0.94)), lower AUC values were detected for WBC 0.82 (0.71-0.92), ANC 0.81 (0.72-0.94). The IG percentage cutoff value for detecting sepsis patients was 0.45% (71% sensitivity and 93% specificity); CRP cutoff value was 74mg/l (0.68% sensitivity, 100% specificity)**.**

Conclusion: Immature granulocyte percentage is an additional useful marker to predict sepsis in children on routine everyday 24/7 basis. IG percentage adds to WBC and CRP in early identifications of children with sepsis without additional blood sampling and extra costs.

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ESPID-0212
SEVERE BACTERIAL AND VIRAL INFECTIONS

ATAXIA IN CHILDHOOD BACTERIAL MENINGITIS IN LUANDA, ANGOLA

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Background andaims: Childhood bacterial meningitis (BM) and its sequelae are prevalent inlow-vaccine-coverage areas. Ataxia, considered a minor sequela, follows BM in13-18%. We studied ataxia in a large number of BM patients.

Methods: Thisstudy was part of a clinical trial on BM at the Pediatric Hospital of Luanda.Ataxia was defined as truncal (infants) or gait (older children) instability,and its presence, degree, and course were registered. The data were compared withpatient, disease, and outcome variables.

Results: Ataxiawas present in 243/361 (67%) patients on day 7; slight in 21%, moderate in 38%,and severe in 41%. Its course was transient in 41%, prolonged in 24%, and latein 5%, whereas 30% did not present ataxia. Ataxia associated with BM severity, suboptimaloutcome (P<0.0001), and hearing loss (P=0.001). The degree of ataxiacorrelated with the severity of hearing loss (rho, 0.37; P<0.0001).

Variable	**Transient**	**ataxia**		**Prolonged**	**ataxia**	
	OR*	95%CI	P	OR*	95%CI	P
Age <12months	1.29	0.66-2.55	0.46	2.64	1.19-5.83	0.02
Malnutrition	2.73	0.55-13.7	0.22	4.99	0.98-25.3	0.05

S.pneumoniae	2.15	0.98-4.73	0.06	2.20	0.91-5.29	0.08
GCS<12	2.11	0.96-4.61	0.06	4.45	1.89-10.5	0.0006
Malaria-treatment	2.33	1.17-4.64	0.02	1.75	0.80-3.79	0.16
Hearing >40dB at follow-up	1.59	0.27-9.26	0.61	5.81	1.15-29.4	0.03
GCS<15 >5d	9.50	2.12-42.5	0.003	60.8	13.1-283	<0.0001
Glasgow Outcome Score<5 d7	20.3	2.64-156	0.004	149	18.7-1191	<0.0001

***Vs. patients without ataxia.**

Conclusions:Ataxia is more frequent and lasts longer after BM than supposed. The presenceand degree of ataxia associate with hearing loss and its severity.

ESPID-0805
SEVERE BACTERIAL AND VIRAL INFECTIONS

ACUTE CENTRAL NERVOUS SYSTEM INFECTIONS IN CHILDREN– A 2 YEARS RETROSPECTIVE STUDY

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Background and aims:

The aim of our study was to evaluate epidemiology, clinical aspects, aetiology and outcome of acute CNS infections in children hospitalized in our hospital.

Methods:

We conducted a retrospective analysis of patients under 18 years old diagnosed with acute CNS infections between January 2012 and December 2013 in a tertiary facility ('Dr Victor Babes" Clinical Hospital of Infectious and Tropical Diseases, Bucharest).

Results:

184 children were included (105 males). Most cases (64,7% ,119/184) were from urban areas, out of which 75.6% (90/119) came from the capital city, Bucharest. The median age of admitted patients was 7 years. The highest hospitalization rates were recorded in the group age 5-9 years (76 cases; 41.3%) and 10-14 years (43 cases; 23.3%). Neurological features were meningitis - 119 cases, meningo-encephalitis - 32, encephalitis - 28 and others 5. The aetiology was suspected to be viral in 121 cases (varicella zoster virus 6 cases, herpes simplex virus – 3, rubella virus – 2, Epstein-Barr virus in one case) and bacterial in 61 cases (with indentification in cerebrospinal fluid of *Neisseria meningitidis* in 8 cases, *Streptococcus pneumoniae* - 6 , *Mycobacterium tuberculosis* – 4, one case of *Haemophilus influenzae*, *Staphylococcus epidermidis* and *Listeria monocytogenes*). Death occurred in one case.

Conclusions:

The urban area of Bucharest remain the most important reservoir of the cases. Study findings indicate that *Neisseria meningitidis* and *Streptococcus pneumoniae* are the

main bacterial etiologies. Poor viral identification highlights the utility of molecular diagnostics from cerebrospinal fluid .

ESPID-0675
SEVERE BACTERIAL AND VIRAL INFECTIONS

DURATION OF INTRAVENOUS AND ORAL ANTIBIOTIC THERAPY FOR ACUTE OSTEOMYELITIS (OM) AND SEPTIC ARTHRITIS (SA) IN 312 CHILDREN AGED 0-16 YEARS

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AIM: To assess the feasibility of performing a RCT to determine the safety of early oral switch from intravenous therapy, we conducted a UK NIHR HTA-funded

prospective service evaluation to establish the current case load, disease spectrum and clinical practice in the diagnosis and treatment of OM/SA in the UK.

METHODS: 44 centres enrolled all cases of OM/SA over a 6 month period to a secure online database (clinical presentation, laboratory tests, imaging, medical and surgical treatment, complications).

RESULTS: Preliminary statistics show that 15 tertiary centres contributed 220 cases, 29 secondary care centres 142 cases. Of 362 cases enrolled, 213 (58.8%) had simple disease, 99 (27.3%). 50 (13.9%) were incorrectly diagnosed. Of 51 children aged 0-12 months, 26 were simple, 18 complex (7 other diagnosis). Of 179 aged 1-5 years, 114 were simple, 43 complex (22 other). Of 129 aged 6-16 years, 71 were simple, 38 complex (20 other). For simple disease, 195 of 213 (91.5%) received at least one dose of intravenous antibiotic with median duration of IV treatment 8 days, median total (intravenous and oral antibiotic) duration 34 days (n=203). For simple disease, 59 diagnostic surgical procedures were carried out on 58 individuals.

CONCLUSIONS

In this large national cohort, paediatric osteoarticular infection was less common than previous reported during the period of data collection. Early switch from intravenous to oral antibiotics was common for simple disease. There was much variation in antibiotics prescribed and total duration of treatment.

ESPID-0236
SEVERE BACTERIAL AND VIRAL INFECTIONS

NEONATAL VARICELLA: WHEN TO TREAT AND WITH WHAT?

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Introduction:Neonatal varicella is extremely rare and can pose life threatening complications .Prompt diagnosis and treatment are required to lessen those complications.Here reporting a case of 35 weeks neonate with generalized vesicular rash followed by her maternal varicella.

Case:27 days M/preterm 35 wks with generalized vesicular rash, fever and reluctance to feed for one day. Mother acquired eruptions when baby was 10 days old, characteristically of varicella and managed conservatively.Baby was born with weight of 3.0 kilograms and discharged on 2nd day. Examination revealed an active baby .He started on intravenous acyclovir. Next day he became lethargic and had body stiffness.Investigations revealed normal TLC; electrolytes , report was also unremarkable. CSF and blood culture showed no growth. He was monitored and intravenous Acyclovir (2 weeks) continued. He responded to treatment and remained stable. At one month of his follow-up he was normal ,healthy infant.

Discussion: Vesicular rashes in neonates are challenging .It is rare with an incidence of 2–6 per 100, 000 live births/year. Generally the diagnosis of varicella is clinical. According to AAP immunoglobulin is recommended for newborns born from mothers with a varicella infection 5 days before and 2 days after delivery, hence no immunoglobulin was given .Acyclovir is the drug of choice for the herpes infection.It is not recommended for treatment of uncomplicated chickenpox in immunocompetent children.

Conclusion :Postnatal varicella in premature neonates can be complicated therefore strict observation of clinical deterioration followed by prompt treatment is paramount for successful outcome.

ESPID-0678
SEVERE BACTERIAL AND VIRAL INFECTIONS

COGNITIVE SEQUELAE OF PNEUMOCOCCAL MENINGITIS IN CHILDREN

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Objective: To identify the cognitive sequelae as well as predictive factors which can be associated with pneumococcal meningitis in children.
Materials and methods: This descriptive observational study was carried out between May 2013 and March 2014 in Montpellier University Teaching Hospital. The cognitive evaluation was done using Wechsler Intelligence Scale for Children (WISC IV) in children having presented pneumococcal meningitis aged 1 month to 16 years between January 2004 to December 2012. The results were presented in number (percentage), mean (standard deviation) and median; the inter group comparisons were done using Fisher tests, Chi-2 and Mann-Whitney Wilcoxon.
Results: 9 children were included during the study period out of a total of 48 cases. Mean full-squale Intelligence Quotient was 87.67 ± 20.35, the median 94. Perceptive reasoning and speed capacity of work had the lowest score indexes 88.78 ± 19.18 and 89.67 ± 18.92 respectively. The presence of abnormal neuroimaging findings, cerebrospinal fluid leucocytic counts of less than 1000/mm³ and the literacy level of the father were significative factors in leading to low cognitive results.
Conclusion: The reasoning, the speed and the memory of work appear altered in pneumococcal meningitis which can result in low educational performance which underlines the importance of early screening and rapid management of surviving patients.

ESPID-0888
SEVERE BACTERIAL AND VIRAL INFECTIONS

DAPTOMYCIN FOR THE TREATMENT OF PYOGENIC LIVER ABSCESS

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Background and aims
Pyogenic liver abscess (LA) constitute the majority of hepatic abscesses in children. The most common pathogen isolated is S. Aureus. The gold standard of treatment is debatable; we report our experience using Daptomycin.
Methods
We describe the case of a 16 year-old girl affected by pyogenic LA effectively treated with Daptomycin.
Results
A 16 year-old girl with history of recurrent cutaneous abscesses was admitted for fever and asthenia.Physical exam revealed painful right axillary swelling suggestive of abscess and right abdominal pain. Laboratory findings showed normal blood count and elevated inflammatory markers. Ultrasonography of the abdomen revealed a partially liquefied abscess in the VIII and V liver segments (3.5 cm diameter). Immunological evaluation showed no evidence of immunodeficiency. Microbiological work-up on blood resulted negative. Purulent material drained from the axillary abscess was positive for methicillin-resistant Staphylococcus aureus. Antibiotic regimen with Meropenem and Vancomycin showed no improvement; therapy was changed to Linezolid and Tigecycline and a percutaneous drainage was placed in LA. After three weeks of still ineffective therapy, the regimen was changed to Daptomycin (10 mg/kg/day) and Tigecycline. Reduction of fever and inflammatory markers occurred; imaging showed gradual resolution of the liver abscess.
Conclusion
Our experience suggests that Daptomycin can be effective in pyogenic LA caused by S.aureus when no responding to standard care; further studies are needed.

ESPID-0051
SEVERE BACTERIAL AND VIRAL INFECTIONS

THE INFLUENCE OF MEDICAL ERRORS ON THE COURSE OF SEPSIS IN CHILDREN.

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Background and aims: Early recognition, diagnostics, therapy and reduction of sepsis death rate among children, are subjects of multiple studies and recommendations. The aim of our study is the analysis of medical errors, resulting in significant reduction or loss of patients' chances for full recovery.

Methods: 31 medico-legal opinions of sepsis cases in children issued by the Department of Forensic Medicine, Wroclaw, Poland between 2004-2013, were analyzed for medical errors.

Results: Malpractices were found in all cases, 26 children died; in 19 errors were made before hospitalisation, in 22 during hospitalisation. In 30 children doctors were responsible for errors, in 4 - nurses and in 4 - dispatchers. In 26 cases sepsis was incorrectly recognised, in 21 incorrect/insufficient diagnostic procedures were performed. Therapeutic errors concerned 19 victims, organisational errors - 6. The most common first symptoms were fever (24/31), weakness (24/31) and vomiting (18/31), haemorrhagic rash appeared in 12 cases (8 *Neisseria meningitidis*). In 4 patients sepsis was secondary to chickenpox. 9 children died within 24 hours of the onset of symptoms. In 25 cases the authors stated glaring errors, that incur criminal liability. The most common causes of the medical errors were lack of knowledge and ignorance of risk.

Conclusion: The most common medical errors in sepsis in children result from lack of knowledge about symptoms, diagnostics and treatment. Popularisation of standards, regular trainings for health care workers on early identifying and treating sepsis lead to increase of patient safety.

ESPID-0534
SEVERE BACTERIAL AND VIRAL INFECTIONS

IS LUMBAR PUNCTURE NECESSARY IN YOUNG INFANTS WITH URINE INFECTION?

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Background and aims: The necessity of routine lumbar puncture (LP) in infants under 3 months with abnormal urinalysis in ED remains controversial.

Methods: We retrospectively reviewed the records of infants under 3 months with fever without source, UTI suspected, sepsis or meningitis who visited ED from 2008 to 2014. Blood count, urine/blood cultures, CRP, procalcitonin and urine dip-stick were performed. Newborns with suspected UTI or those not well-appearing underwent LP. CSF samples were tested for bacterial, HSV and enterovirus.

Results: During study period 743 infants < 3 months were included, 26 presented bacteremia/sepsis (3.4%), 4 bacterial meningitis (0.6%) and 125 UTI (16.8%). Mean age of infants with UTI was 53.8 days (SD: 41.3) and 26.1% (n=31) were newborns. In infants with UTI LP was performed in 51.2% (n=64) of < 3months old and in 93,6% (n=29) of newborns. 12 cases (19.8%), 7 (27.6%) of them newborns, presented pleocytosis, but only one 12 day-old infant, with CSF fistule, presented a bacterial meningitis and UTI. No enterovirus or HSV infection was identified in children with pleocytosis. UTI was not associated with risk of bacterial meningitis (p=1). Newborns presented higher risk of bacteremia than older infants OR=3.1 (IC95%: 1.42-6.565). Infants with UTI showed higher risk of bateremia OR=2.37 (IC95%: 1.05-5.4).

Conclusions: A cerebrospinal fluid pleocytosis is relatively common in infants younger than 3 months with UTI without bacterial or viral meningitis. Despite bacterial meningitis is uncommon in UTI, newborns presented higher risk of bacteremia; that could justify performing LP in these infants.

ESPID-0819
SEVERE BACTERIAL AND VIRAL INFECTIONS

INFLUENZA A H1N1 ASSOCIATED RHOMBENCEPHALITIS IN CHILDREN – CASE REPORT

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Background and aims: Rhombencephalitis is a rare and severe complication of the infection of the brainstem and is reported to have high mortality and to induce frequent and serious sequelae for survivors. Involvement of the CNS in influenza virus infection is a rare and serious complication, but since the 2009 H1N1 pandemic an increase in the neurologic complications associated with influenza virus infections has been described.

Methods: We report a case of H1N1-associated rombencephalitis in a child.

Results: A 6-year-old girl, with suggestive history, clinical exam, laboratory and IRM studies for acute viral rhombencefalitis was diagnosed with automated multianalyte point-of-care mariPOC test and then confirmed by RT-PCR with Influenza A H1N1 infection. On admission, after 3 days of ambulatory evolution, the patient presented febrile, with an extremely severe general status, SCG 5-6 and despite antibiotic, antiviral and supportive therapies, his respiratory status worsened requiring intubation. After 35 days of intensive care treatment the third IMR study presented an important spread of the initial inflammatory lesions of the white matter, which supported the actual diagnosis of vegetative state and spastic tertaplegia secondary to Influenza A H1N1 rhombencefalitis, subacute-seqular state, in an infant with no previous medical history of chronic disease.

Conclusions: Influenza virus associated rhombencephalitis is a rare and extremely severe disease that highlights the importance on extensive vaccination programs, and must be considered in the differential diagnosis in patients with influenza-like illness and neurological impairment.

ESPID-0479
SEVERE BACTERIAL AND VIRAL INFECTIONS

A CASE OF HEREDITARY SPHEROCYTOSIS ASSOCIATED WITH ACUTE ENCEPHALOPATHY CAUSED BY HUMAN PARVOVIRUS B19

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Human parvovirus B19 (PVB19) links with various clinical symptoms other than erythema infectiosum. Although aplastic crisis is often seen in cases with PVB19 infection in hereditary spherocytosis (HS), there are few reports of central nervous system (CNS) infection by PVB19 with HS.

We present a case of HS associated with acute encephalopathy (AE) caused by PVB19.

A 9-year-old girl with HS was hospitalized for high fever, headache and clouding of consciousness. In laboratory findings, hemoglobin was 9.4 g/dl and cerebrospinal fluid (CSF) examination showed no abnormality. The cranial CT scan showed brain edema and electroencephalography showed generalized high voltage slow waves. PVB19 DNA was detected in plasma and CSF respectively and the patient was diagnosed with AE caused by PVB19 infection. The patient was treated with IV high-dose immunoglobulin and corticosteroid. The patient's consciousness improved gradually and she became completely alert on the second day. As pancytopenia due to aplastic crisis gradually progressed, the patient needed a blood transfusion on the day 7. The patient was discharged from the hospital on the day 12 after she completely improved. On the day 30, red rash appeared on her cheeks. During the clinical period, we examined PVB19 DNA in the plasma and CSF by real-time PCR and those levels were extremely high.

This is the fourth case report of AE caused by PVB19 with HS in our survey. The results suggested an existence of possible relationship between those clinical conditions.

ESPID-0133
SEVERE BACTERIAL AND VIRAL INFECTIONS

SEROTYPES OF FATAL STEPTOCOCCUS PNEUMONIAE INFECTIONS IN CHILDREN :POST-MORTEM DIAGNOSIS

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Herein, we report fatal cases of *Streptococcus pneumoniae* (Sp) infections diagnosed by post-mortem (PM) examinations in children with sudden death. A total of 12 children, aged 3 months to 16 years were invastigated. Of them 10 had a PM diagnosis of pneumonia and 2 had a PM diagnosis of meningitis. SP isolated in 6 patients from lung tissue culture, in 2 patients from CSF, in 3 patients from tracheal samples and 1 patient from blood, CSF and spleen. The serotypes of SP were serotype (st) 6A/B/C in 3 patients, st19F in 3 patients, st16F, st5, st9V/9A, st17F, st23F, and st18A/B/C in one patient, respectively. Among 12 patients CMV was concomitant pathogen in 2 patients, *S. aureus* was in 3 patients, *S. pyogenes* was in one patient and adenovirus was in one patient. Seven, 10 and 13-valent PCV coverage rates were found to be 75%, 83% and 83%, respectively for this patient group.

ESPID-0188
SEVERE BACTERIAL AND VIRAL INFECTIONS

INTRAVENOUS COLISTIN FOR TREATMENT OF MULTIDRUG-RESISTANT GRAM-NEGATIVE INFECTIONS IN CHILDREN

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Introduction: The emergence of infections due to multidrug-resistant Gram-negative bacilli has led to a resurrection of colistin use. In this study, we aimed to evaluate the clinical efficacy and safety of colistin use in critically ill children.

Methods: Sixty-one critically ill children aged 0 months to 18 years old who were treated with intravenous colistin between January 2011 and November 2014 were included in this study.

Results: 29 females and 32 males with a mean (±standard deviation) age of 61.4 (±9.6) months (range 0-216, median 12 months) were enrolled in this study. Bacteremia was the leading diagnosis followed by pneumonia, clinical sepsis, urinary tract infections and wound infections. The isolated microorganisms in decreasing order of frequency were *Acinetobacter baumannii* (n=27, 44.2%), *Pseudomonas aeruginosa* (n=17, 27.8%), *Klebsiella pneumoniae* (n=6, 11.4%), *K. pneumoniae* and *Stenotrophomonas maltophilia* (n=1), *K.pneumoniae* and *A. baumannii* (n=1), *K.oxytoca* (n=1) and *Enterobacter cloacae* (n=1). In seven patients colistin was given empirically since five of these patients were colonized due to carbapenem resistant *K. pneumoniae.* Colistin was administered concomitantly with either carbapenem, ampicillin-sulbactam, aminoglycosides, and quinolons, however carbapenem was the most frequently used. The mean duration of the colistin therapy was 12.8 days (range 3-45). Nephrotoxicity was observed in only 1 patient. We did not observe neurotoxicity in this study. All patients received intravenous colistin in a dosage of 5mg/kg daily in three divided doses.

Conclusion: Colistin was safe and efficacious in children for treating MDR-GNB infections.

ESPID-0189
SEVERE BACTERIAL AND VIRAL INFECTIONS

THE CLINICAL EFFICACY AND SAFETY OF ERTAPENEM FOR THE TREATMENT OF COMPLICATED URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM-BETA-LACTAMASE-PRODUCING BACTERIA IN CHILDREN

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BACKGROUND: Urinary tract infections (UTIs) are a common and important clinical problem in childhood, and extended-spectrum-beta-lactamase (ESBL)-producing organisms are the leading cause of healthcare-related UTIs. In this study, we aimed to evaluate the clinical efficacy and safety of ertapenem in the treatment of complicated UTIs caused by ESBL-producing organisms in children.

METHODS: Seventy-seven children aged three months to 18 years with complicated UTIs caused by ESBL-producing organisms were included in this retrospective study between January 2013 and June 2014.

RESULTS: Sixty-one (79%) females and sixteen (21%) males with a mean (±SD) age of 76 (±52) months (range 3-204, median 72 months) were enrolled in this study, and 51 (66%) had an underlying predisposing factor for UTIs. Ertapenem was initiated after receiving the results of the patients' microbiological cultures. *Escherichia coli* (*E. coli*) (n=67; 87%) was the most common bacterial cause of the UTIs followed by *Klebsiella pneumoniae* (*K. pneumoniae*) (n=9; 11.7%) and *Enterobacter cloacae* (*E. cloacae*) (n=1; 1.3%) which were all ESBL-positive. On the third day of ertapenem therapy, we obtained control urine cultures, and all became sterile. The mean duration of the ertapenem therapy was 8.9 ±1.6 days (range 4-11). No serious drug-related clinical or laboratory adverse effects were observed, and the ertapenem therapy was found to be safe and well tolerated in children in our study with complicated UTIs.

CONCLUSION: Ertapenem is a new carbapenem with the advantage of once-daily dosing and is an effective and safe for treating complicated-UTIs caused by ESBL-producing microorganisms in children

ESPID-0190
SEVERE BACTERIAL AND VIRAL INFECTIONS

BRAIN ABSCESS DUE TO STREPTOCOCCUS INTERMEDIUS SECONDARY TO MASTOIDITIS IN A CHILD: CASE REPORT

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Brain abscess is rare but serious, life-threatening infection in children. It may arise from parameningeal infections such as otitis media, sinusitis and mastoiditis.*Streptococcus intermedius* is usually a commensal microorganism which can cause brain abcess rarely in children.

Herein, we report a child who presented with brain abscess due to *Streptococcus intermedius.*

Case: A ten-year-old boy with glycogen-storage disease and obesity was admitted to the emergency room with complaints of vomiting, decreased level of consciousness, imbalance on walking and also history of ear pain and discharge for the last several days. He had no fever or neck stiffness on physical examination. His cranial magnetic resonance imaging examination showed mastoiditis on the righ side and 39x34 mm abscess formation on the right cerebellar hemisphere. The patient underwent surgery to drain the abcess, and emprical antibiotic treatment with vancomycin and piperacillin-tazobactam were started. Culture of the abscess drainage material yielded *S.intermedius* which was found susceptible to penicilin,ampicillin,ceftriaxone and cefuroxime. On the second week of treatment, the antibiotics were switched to vancomycin and meropenem because of the persistant fever. The therapy was continued for six weeks. His clinical condition improved and he was discharged without any sequele.

Contiguous spread of mastoiditis may result as brain abscess, therefore the clinicans should be aware of children presenting with ear and cranial symptoms concomitantly. Although *Streptococus intermedius* is a commensal microorganism, it can become a pathogen in brain abcess.

ESPID-0192
SEVERE BACTERIAL AND VIRAL INFECTIONS

DEEP NECK INFECTION CAUSED BY EIKENELLA CORRODENS COINFECTION WITH STREPTOCOCCUS MITIS AND ORALIS IN AN INFANT

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Eikenella corrodens is a gram-negative, facultative rod in oral and gastrointestinal flora that can rarely cause infections in children.

Herein we describe a 16 months-old boy who had been admitted to emergency room with symptoms of fever and limited neck mobility for the last five days which was unresponsive to 5 days of intramuscular ampicillin-sulbactam therapy given by another hospital. On admission his physical examination revealed fever, restlesness, exudative tonsillitis and limited neck mobility. His cervical computerized tomography examination showed 10x10 mm abscess formation at the prevertebral space. The patient underwent surgery for drainage of the abscess, and empirical intravenous ampicillin-sulbactam therapy was started. Culture of the abscess drainage material yielded *Eikenella corrodens, S.mitis and S.oralis*. The therapy was changed to vancomycin and cefepime. Antimicrobiological susceptibility tests showed that *E.corrodens* was only susceptible to vancomycin and cefepime while *S.mitis and S.oralis* were only susceptible to vancomycin. Antibiotics were continued for 14 days. He was successfully treated without any sequele.

In conclusion, *Eikenella corrodens* is a critical microorganism which causes infections usually with other organims. Optimal therapy is a combination of surgical intervention and antibiotic therapy in deep neck infections.

ESPID-0194
SEVERE BACTERIAL AND VIRAL INFECTIONS

BACTEREMIA DUE TO ACINETOBACTER URSINGII IN AN INFANT

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Acinetobacter ursingii is an opportunistic microorganism which is rarely isolated among *Acinetobacter* species. There are few reports of infection with *A.ursingii* in the literature. Herein, we describe a 2 month old boy who had been hospitalized in pediatric surgery unit for suspected trachea-esophageal fistula because of recurrent aspiration pneumonia. On the admission he had tachypnea and fever. Twelve hours later, his blood culture yielded growth of gram negative microorganism by the Bact Alert device. Empirical antibiotic treatment with meropenem and amikacin were started. Microorganism was identified as *Acinetobacter ursingii* by Vitek MS with a reliability of %99.9. *Acinetobacter ursingii* was susceptible to ampicilin-sulbactam, gentamicin, ciprofloxacin and imipenem. The antibiotic theraphy was deescalated to ampicillin-sulbactam. On the third day of treatment, control peripheral blood culture was taken and became sterile. He was successfully treated with ampicillin-sulbactam for 14 days. In conclusion although *A. ursingii* has been isolated solely from humans, its natural habitat is not known. It is known as a rare causative agent of invasive infections, but it should be kept in mind as an opportunistic microorganism in children.

ESPID-1051
SEVERE BACTERIAL AND VIRAL INFECTIONS

RETROSPECTIVE CASE REVIEW OF PAEDIATRIC OSTEOMYELITIS, SEPTIC ARTHRITIS, AND DISCITIS, IN A TERTIARY HOSPITAL OVER A 5 YEAR PERIOD

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Background and aims
Bone and joint infections in children present difficult diagnostic and management dilemmas for the emergency, general and specialist paediatrician. There are no evidence based standardised guidelines. We report a series of bone and joint paediatric cases at a major UK paediatric hospital raising awareness of this diagnosis and inconsistencies in diagnostic and treatment guidelines.

Method
A retrospective survey of paediatric patients with bone and joint infections.

Results
88 paediatric patients were identified, 55 with osteomyelitis, 23 with septic arthritis, and 9 with discitis. 55 patients were males, 33 female. Mean age was 4.6 years. Data analysis is underway and results, including detailed results on pathogens, co-morbities, and treatment, will be presented.

Conclusions
Paediatric joint and bone infections present in a variety of ways in the emergency department with frequent delays in diagnosis. Paediatric infectious diseases and orthopaedic referral can be useful in paediatric patients, even in the absence of focal symptoms. Imaging findings can assist in clarifying the diagnosis. A microbiological diagnosis should be attempted in all cases to aid in the choice of antibiotics and duration of therapy. Clinicians should have a low threshold for imaging other potential sites of infection in infants as disseminated osteomyelitis may be missed and results in significant long-term disability. This in turn will also affect management as multifocal involvement might lead to modified drug choice, a longer treatment course and adjunctive therapy. Randomised controlled trials in this patient group will help inform evidence based treatment guidelines.

ESPID-0297
SEVERE BACTERIAL AND VIRAL INFECTIONS

FUSOBACTERIUM NECROPHORUM OTITIS AND MASTOIDITIS IN INFANTS: CASE REPORT AND LITERATURE REVIEW

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Background and aims: *Fusobacterium necrophorum*, an anaerobic Gram-negative bacillus, is a rare cause of otitis and mastoiditis. However, it can cause life-threating infection with intracranial complications as meningitis, abscesses and sinus thrombosis. A paucity of literature exists regarding the management and outcome in infants with fusobacterial infection. We present a case of an infant with biopsy-proven *F. necrophorum* mastoiditis and a review of literature of fusobacterial otic infection in infancy.

Methods: A previously healthy 13-months male infant developed acute purulent otitis and mastoiditis. Otic drainage and surgical debridement were preformed. The culture of mastoid biopsy identified *F. necrophorum* on the 8th day of hospitalization and metronidazole was administered for four weeks. No other bacteria were isolated. Review of the English literature was performed for optimal management.

Results: Following administration of metronidazole and serial drainage procedures, no further complications in the infant developed and a successful treatment was obtained. Among the 8 well described cases of fusobacterial otogenic infections in infancy, complications were common. Sigmoid venous thrombosis, epidural abscess, subperiosteal abscess, Bezold's abscess, and/or osteomyelitis developed in all cases. No pharmacokinetic and pharmacodynamic data of the appropriate antimicrobial therapy exist and optimal duration of treatment is undefined.

Conclusion: *F. necrophorum* otitis and mastoiditis are uncommon but severe infections that are managed by drainage and anti-anaerobic antimicrobial therapy. Complications of epidural abscess, sinus vein thrombosis, and periosteal abscess may ensue with a delay in combination antimicrobial and surgical intervention.

ESPID-0562
SEVERE BACTERIAL AND VIRAL INFECTIONS

CAMPYLOBACTER JEJUNI PANCOLITIS IN A PEDIATRIC PATIENT AND LITERATURE REVIEW

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Background and aims: *Campylobacter jejuni* is a common cause of acute bacterial diarrhea in children. The preponderance of patients with *C. jejuni* diarrhea have some component of segmental colitis, usually of the rectosigmoid or descending colon. *C. jejuni* has been reported as causing colitis mimicking other bacterial infections or ulcerative colitis in adults. Herein, we present a case of *C. jejuni* pancolitis in a pediatric patient.

Methods: A previously healthy 11-year old girl was hospitalized for acute onset of diffuse abdominal pains, fever, and bloody diarrhea for two days. Due to intensity of the abdominal pain, CT with contrast agent was conducted and the inflammatory process was observed in all segments of colon. Fecal culture was positive for *C. jejuni*. No other causes of pancolitis were documented. Review of the English literature was performed with key words including *C. jejuni,* pancolitis and colitis.

Results: Based on the severity of symptoms and the diagnosis of pancolitis, azithromycin 5mg/kg per os was administered for five days. Successful treatment was obtained with resolutions of symptoms by the third day. In the literature, one well-descripted case of pancolitis and another case of segmental colitis starting from the transverse colon were reported in adult patients.

Conclusions: To our knowledge, this is the first reported case of *C. jejuni* pancolitis in a pediatric patient. *C. jejuni* should be included in the differential diagnosis of pancolitis in children. Further clinical studies are needed to assess the approximate frequency of pancolitis caused by *C. jejuni* in children.

ESPID-0368
SEVERE BACTERIAL AND VIRAL INFECTIONS

RISK FACTORS FOR COMPLICATIONS OF PNEUMOCOCCAL BACTEREMIA.

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Background: Pneumococcal bacteremia is sometimes linked to severe infections.

Aim: To investigate risk factors associated with complications in pneumococcal bacteremia.

Methods: Cohort study, from June 2009 to June 2014. We recruited all immunocompetent patients with pneumococcal bacteremia admitted at any of the 11 participating hospitals. Complications were defined as i) complications requiring PICU admission (meningitis, empyema, other) ii) surgical procedure or iii) sequels. We tested patient features, immunization, and laboratory tests.

Results: We recruited 143 patients. Pneumonia represented 50,3%, occult bacteremia 18,2%, sepsis 12%, meningitis 9,8%, and mastoiditis 7,7%. Up to 20% patients had any complication. PCV13 serotypes were associated with meningitis [p=0,09; RR: 4,5 (95%CI: 1.2-15.8)], empyema and surgery [p=0.002; RR 1.2 (95%CI 1-1.3)]. PCV13 (≥2 doses) protected against meningitis [p=0,06; RR: 0.3 (95%CI : 0.1-1.0)] and empyema [p=0.08; RR 0,8 (95%CI 0.7-0.9)]. Immunization with ≥3 doses of PCV13 protected against meningitis [p=0.06; RR 0.19 (95%CI 0.04-0.8)] and surgery [p=0.076; RR 0.2 (95%CI 0.04-0.9)]. PICU associated the following risk factors: male sex [p=0.03 (RR 2.4; 95%CI 1-5.6)], and C-Reactive Protein (CRP) >100 mg/L [p=0.003 (RR: 3.9; 95%CI: 1.4-10.9)]. Risk factors for surgery: CRP >200

mg/L [p=0.001 (RR 8.5; 95%CI: 2-36)]. Sequels were associated with meningitis (RR: 18.9; 95%CI: 1.8-194; p=0.001). After excluding empyema and meningitis, only 6% of patients had any complication.

Conclusions: Severe focal infections and serotypes included in PCV13 are the main determinants for a poor outcome in patients with pneumococcal bacteremia. Immunization against PCV13 (≥2 doses) protect against complications.

ESPID-0072
SEVERE BACTERIAL AND VIRAL INFECTIONS

TRENDS IN FULL BLOOD COUNT INDICES OF CHILDREN WITH DENGUE IN SINGAPORE

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Background and aims

Dengue is a mosquito-borne viral disease endemic in Singapore. The aim of our study was to identify trends of FBC indices in children with Dengue in Singapore.

Methods

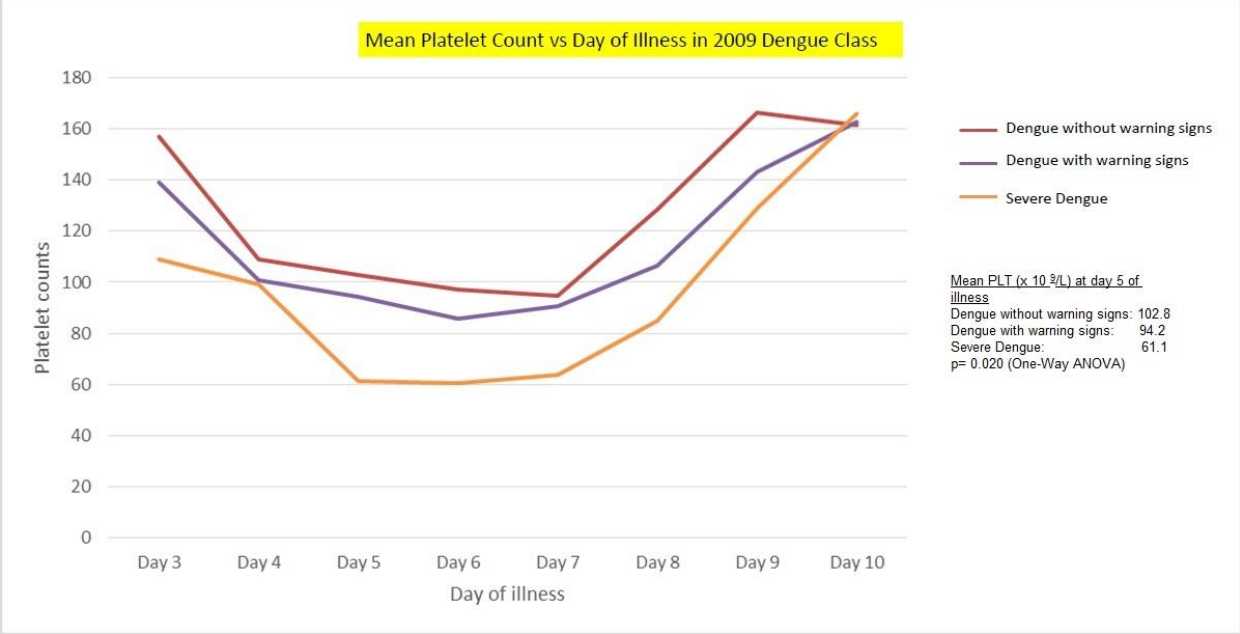
Retrospective study of 290 paediatric Dengue admissions in KK Women's and Children's Hospital (KKH), Singapore, from January 2008 to December 2010. Platelet (PLT) counts and white blood cell (WBC) counts were charted according to day of illness for each patient. The graphs of mean daily values for PLT and WBC were plotted for the various 2009 WHO Dengue classifications.

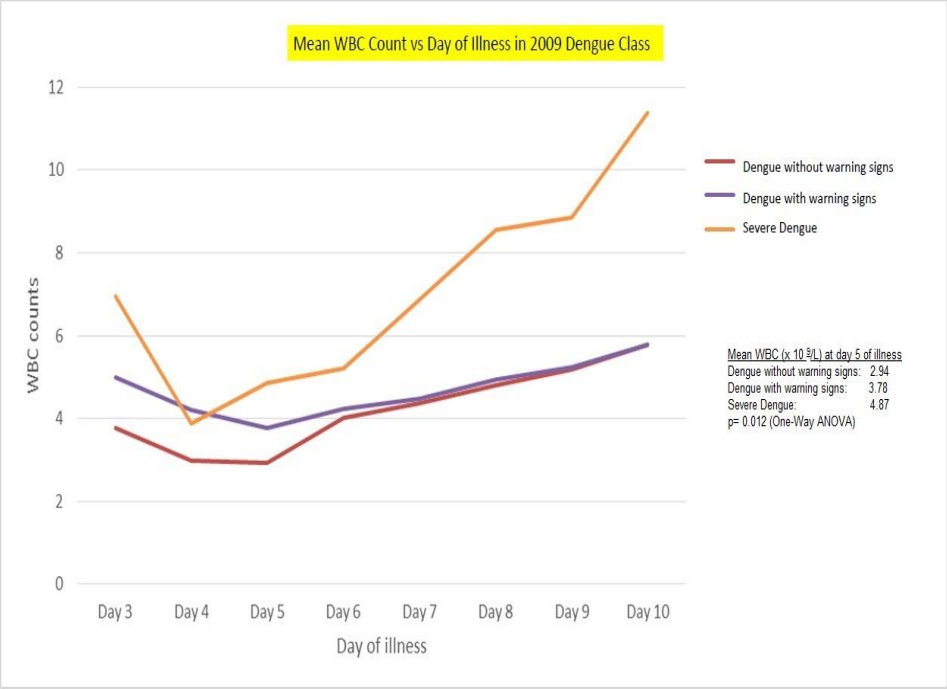
Results

Table 1 shows the demographic and clinical characteristics of the patients.

Table 1:

Male gender, n (%)	174 (60.0%)
Nationality (Singaporean/ foreigner), n (%)	212 (73.1%)/78 (26.9%)
Age, median (IQR years, range years)	12.0 (8.4– 14.0, 0.1-17.0)
Dengue episode (Primary/ Secondary), n (%)	218 (75.2%)/72 (24.8%)
Dengue 1997 classification:	213 (73.4%)/63 (21.7%)/14 (4.8%)
Dengue fever/Dengue haemorrhagic fever/Dengue shock syndrome, n (%)	
Dengue WHO 2009 classification:	97 (33.4%)/168 (57.9%)/25 (8.6%)
Dengue without warning signs/Dengue with warning signs/Severe dengue, n (%)	





There was a trend of lower mean daily PLT counts (Figure 1) and higher mean daily WBC counts with increasing severity of Dengue (Figure 2).

Conclusions

Our findings suggested that lower daily PLT count, and higher WBC count correlated

with increasing severity of Dengue in children. This may aid the paediatrician in predicting and treating the complications of Dengue early in children.

ESPID-0296
SEVERE BACTERIAL AND VIRAL INFECTIONS

HUMAN PARECHOVIRUS (HPEV) ASSOCIATED CENTRAL NERVOUS SYSTEM INFECTIONS IN INFANTS ADMITTED TO A TERTIARY CARE PEDIATRIC HOSPITAL IN VANCOUVER, CANADA.

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Background/aims: Pediatric HPeV CNS infections have been associated with severe outcomes. HPeV prevalence in neonatal CSF samples reportedly ranges from 0 - 17%. HPeV PCR is not routinely performed in all diagnostic laboratories. The true number of HPeV CNS infections may therefore be underestimated. We have examined HPeV CNS infection prevalence in infants seen at BC Children's Hospital, Vancouver, Canada.

Methods: Nucleic acid from CSF samples was extracted using the QIA symphony virus/bacteria kit on an automated DNA extraction platform QIA symphony SP (Qiagen) and tested for the presence of HPeV by a laboratory-developed, validated real-time RT-PCR assay targeting the 5¢-untranslated region of the HPeV genome.

Results: 407 consecutively collected (January 2011- December 2014) CSF specimens from infants < 3 months old were tested for HPeV. 10/407(2%) specimens were HPeV positive. Of those 5/10(50%) were <7 days old; 3/10(30%) were 8-14 days old; 2/10(20%) were <15-35 days old; 6/10(60%) were males. 9/10(90%) infections occurred during summer/fall.

Conclusion: To our knowledge, this is the first prevalence report of pediatric CNS infection with HPeV etiology in Western Canada. Interestingly, in our patient population, 50% of infants who had HPeV positive CSF were less than a week old. Further studies are required to determine the possibility and frequency of perinatal HPeV transmission. Our findings suggest that HPeV should be included in the differential diagnosis of CNS infections in very young infants.

ESPID-0736
SEVERE BACTERIAL AND VIRAL INFECTIONS

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS SECONDARY TO OSTEOMYELITIS

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Hemophagocytic lymphohistiocytosis (HLH) is an aggressive and life-threatening syndrome of excessive immune activation. Systemic infections share many features with HLH, including fever, cytopenias, and hepatic involvement. Here we present a case of secondary HLH occuring after osteomyelitis.

A 9-year old boy complained of fever and foot pain beginning 25 days ago was referred. He received oral antibiotics and ibuprofen but symptoms did not resolve. Bone scintigraphy showed focal uptake in calcaneus revealing osteomyelitis. He was hospitalized and clindamycin plus piperacillin-tazobactam were initiated. During surgical exploration, necrosis and diffuse purulent material were detected. Gram smear of debridement showed Gram positive cocci but no microbial growth. Clindamycin changed to vancomycin. On the 15th day, fever reappeared with rash, and pancytopenia. On admission an irritable child with pain on the right heel, Hb 8.9 mg/dl, platelets 50,000/mm3, leukocytes 1120/mm^3, AST 412 U/L, ALT 76 U/L, C reactive protein 14.1, ferritin 15,000 ng/ml. Bone marrow examination showed no infiltrative cells but hemophagocytosis. Bone culture was repeated but again no growth was detected. Linezolid was initiated and plasma exchange was performed. His fever resolved on the second day, ferritin dropped to 2767 ng/ml. At the end of first week he was discharged by oral linezolid to complete therapy to 6 weeks.

Calcaneus is an uncommon site of osteomyelitis. Slow presentation may lead to a delay in diagnosis. The severe clinical presentation in our patient required evaluation for possibilities including HLH. Directed therapy led to recovery of the patient and resolution of HLH.

ESPID-0782
SEVERE BACTERIAL AND VIRAL INFECTIONS

SCABIES INFECTION IN AN INFANT WITH MENINGITIS

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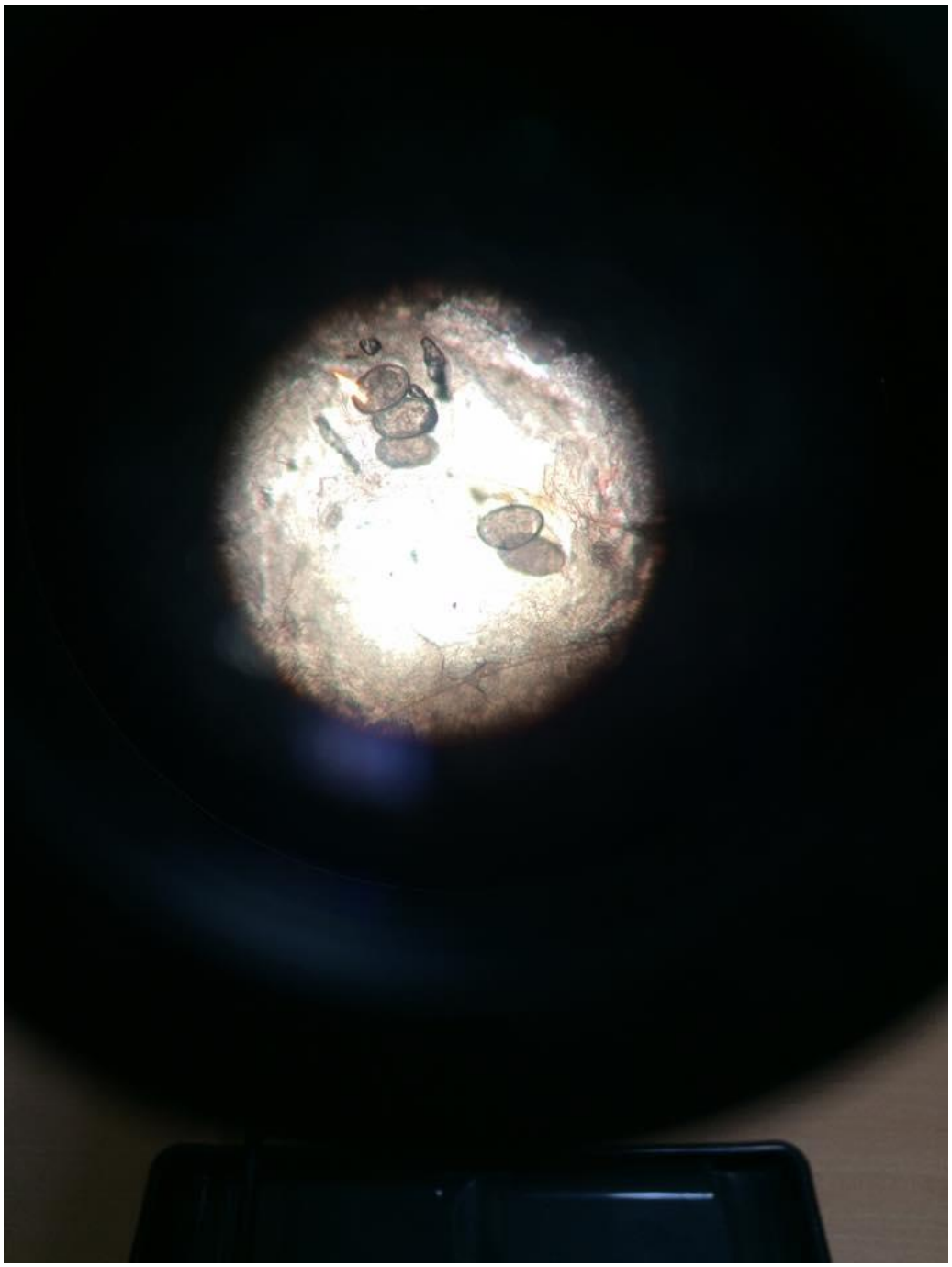
Scabies is a worldwide disease and a major public health problem in many developing countries, related primarily to poverty and overcrowding. A two months old child of a Middle East refugee family presented to emergency clinic with fever and poor feeding. She was born at home and had not received any of the childhood vaccines. On admission she was lethargic, tachypneic and tachycardic. A bulging fontanel and multiple erythematous papules, crusts, xerosis and excoriations involving the back, abdomen, upper and lower extremities were noted. She was transferred to intensive care unit and fluid resuscitation was administered. Blood culture was taken and vancomycin and cefotaxime were initiated. Laboratory examination revealed blood leukocytes 36,000/mm^3, C reactive protein 25.9 mg/dl. Next day lumbar puncture was performed showing a purulent CSF with 15,000 leukocytes/mm^3, glucose 23 mg/dl, protein 230 mg/dl. Focal convulsions were observed. Cranial imaging showed meningeal contast enhancement. Vancomycin was discontinued since blood culture yielded penicillin susceptible *Streptococcus pneumonia* (G+, non vaccine type). Scabies eggs were detected on light microscopic examination of skin scrapings. The patient was treated with permethrin and ketotifen. Other family members had similar eruptions and were also treated with 5% permethrin cream. She was discharged after 14 days of antibiotic treatment.

Scabies in children is often missed until persons in close contact with the child present with similar symptoms. It can occur in both sexes, at all ages, in all ethnic groups, and at all socioeconomic levels. A thorough history and close follow-up are crucial to avoid misdiagnosis.



ESPID-0796
SEVERE BACTERIAL AND VIRAL INFECTIONS

A FAMILY CLUSTER OF MYCOPLASMA PNEUMONIA

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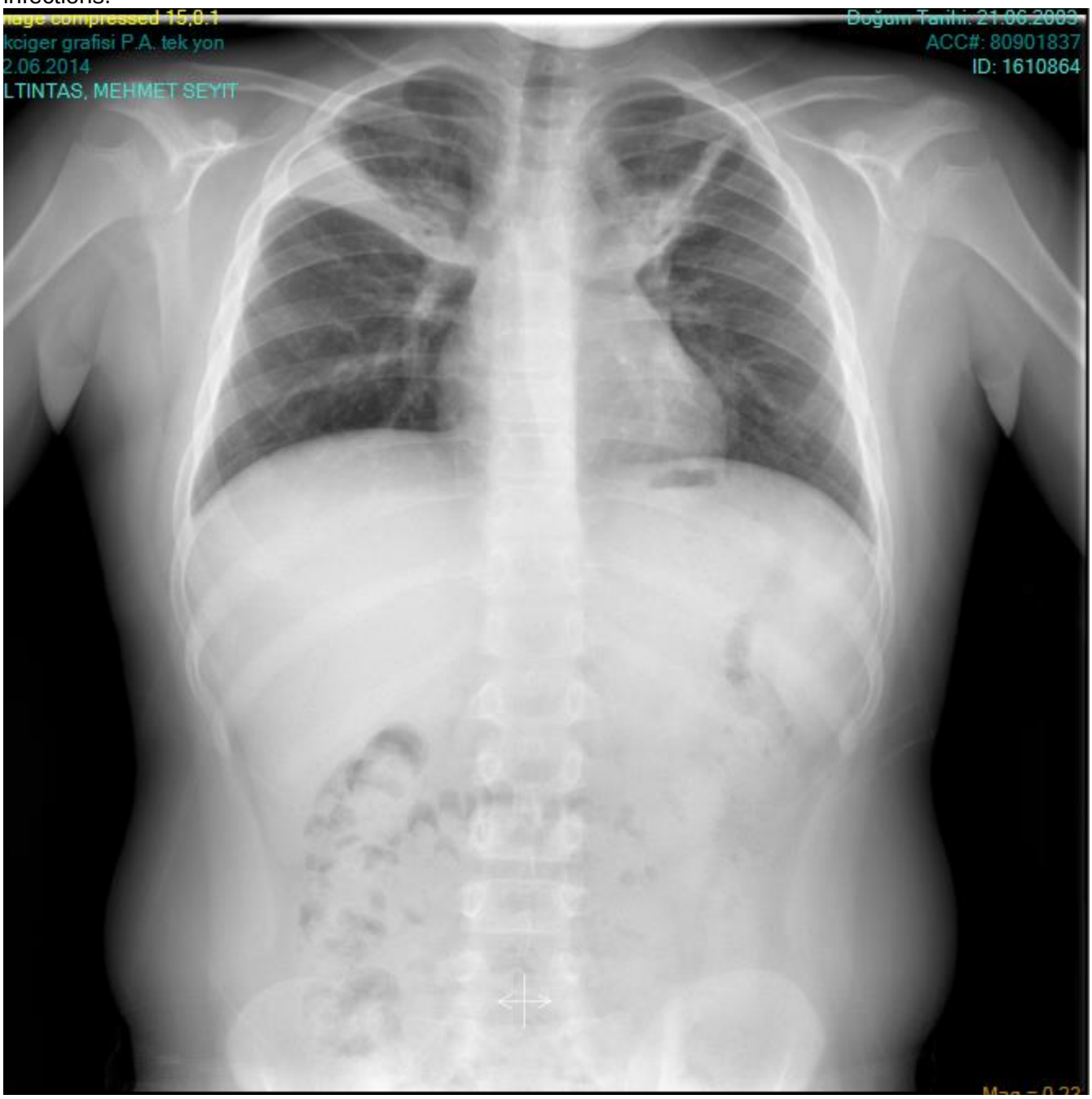
Approximately 40% of community-acquired pneumonia is due to *Mycoplasma pneumoniae* infections, with children and elderly individuals being most susceptible. Outbreaks of *M. pneumoniae* infections tend to occur within groups of people in close and prolonged proximity, including schools, institutions, military bases, and household. In this report, we describe *M. pneumonia* infection among household members of an elderly lady who was suspected to have Middle East respiratory syndrome coronavirus (MERS-CoV) infection since she became ill after visiting Saudi Arabia. Family consisted of grandmother (aged 77 yrs), father (aged 41 yrs), mother (aged 38 yrs), and two sons (aged 6 yrs and 3 months, respectively). Grandmother complained of fever and cough 10 days later from returning from pilgrimage. The mother and father and two sons also complained from cough 10 days after the symptoms of grandmother. The younger brother also had fever. His chest X ray showed bilateral infiltration (Fig 1). Chest X-rays of the mother and father were also abnormal. Two children showed immunoglobulin M (IgM) positivity for *M. pneumonia.* All symptomatic patients were successfully treated with macrolides. Symptoms resolved during follow-up. We want to emphasize the relevance of *M. pneumoniae* in family cluster respiratory

infections.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ESPID-0803
SEVERE BACTERIAL AND VIRAL INFECTIONS

AN INFANT WITH RECURRENT SALMONELLA MENINGITIS

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Patients with inherited deficiency of the interleukin (IL)–12/ IL-23–interferon (IFN)–g axis show increased susceptibility to invasive disease caused by the intramacrophage pathogens salmonellae and mycobacteria. Here we report an infant with recurrent meningitis caused by *Salmonella typhimirium* who was diagnosed to have IL-12 reseptor 1-beta deficiency.

A 2 months old male infant presented with fever and convulsions. On physical examination he was lethargic and Glascow coma scale 13. Cerebrospinal fluid (CSF) examination revealed 22,500 leukocytes/ mm^3, glucose 1 mg/dl, and protein 33.4 mg/dl. Ampicillin and cefotaxime were initiated. CSF culture revealed *S. typhimirium* and meropenem was given according to susceptibility results. He was discharged after 3 weeks with complete clinical recovery. One week later he was readmitted with similar complaints and CSF examination revealed *S*. *typhimirium* again. Recurrent disease suggested inadequate course of treatment and he was treated for 4 weeks following sterile CSF culture. Unfortunately he developed the disease for the third time. Immunity against salmonella.was investigated and IL-12 reseptör 1-beta deficiency was detected. When Interferon Gamma-1b treatment was started we uncovered that his brother had the same defect who was diagnosed as BCG itis at the age of 2 years. During the 6 months follow up no other infection was observed and his neurological devalopment is normal.

Clinicians should consider the possibility of an underlying IL-12/IL-23–IFN-g–axis deficiency in patients with recurrent extraintestinal salmonella disease, as well as in those with disseminated atypical mycobacterial disease.

ESPID-1015
SEVERE BACTERIAL AND VIRAL INFECTIONS

PNEUMOCOCCAL MENINGITIS SECONDARY TO TEMPORAL BONE FRACTURE

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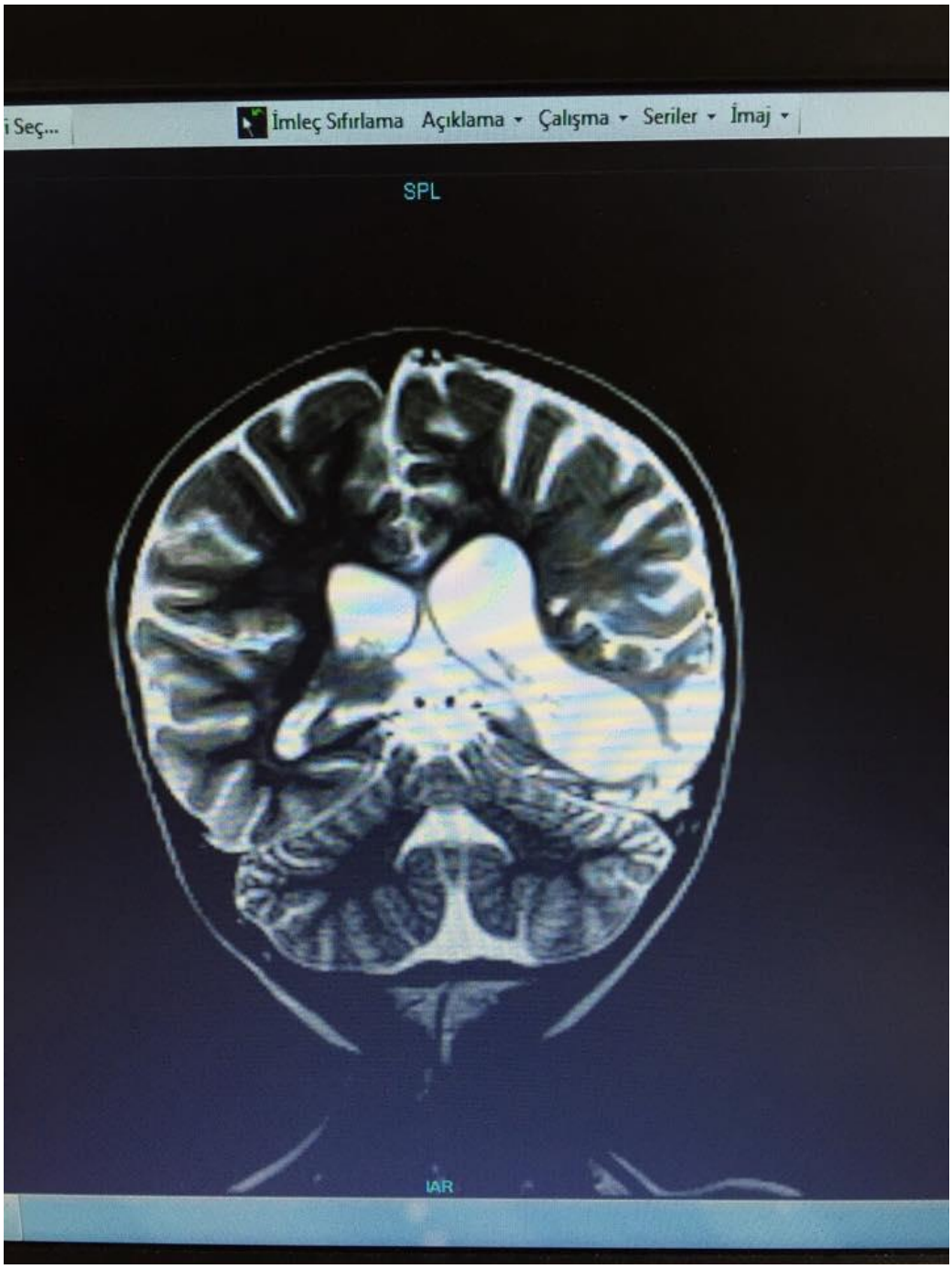
Streptococcus pneumonia infections vary from self-limiting mucosal infections to life-threatening invasive diseases. We present a 2-year-old boy with pneumococcal meningitis secondary to head trauma.

A 4-years old boy is admitted with fever and vomiting. He had received oral antibiotics for respiratory tract infection but had no improvement. Eight months ago he had a head trauma resulting in a fracture involving sphenoidal, parietal and temporal bones and right ftontotemporal hematoma. On initial examination he was lethargic and meningeal signs were positive. Lumbar puncture characteristics were: leucocytes - 1020 mm^3 (80% polymorphonuclear), glucose 0,1 mg/dl, protein 338 mg/dl. Ceftriaxone and vancomycin were initiated pending culture results. At the fifth day, the patient still had meningeal signs and fever. *S. pneumoniae* resistant to and ceftriaxone was isolated from CSF culture. Rifampicin was added to the antibiotic therapy. Two days later his fever resolved and his clinical condition improved. Cerebrospinal fluid (CSF) leak was suspected since he had rhinorrhea. A beta-2 transferrin test of fluid was performed and proved confirmatory. Magnetic resonance cisternography revealed temporal bone fracture, brain herniation to the inferior mastoid segment, and a CSF leak. The patient recovered with 14 days of antibiotic therapy. 13-valent pneumococcal conjugate vaccine (PCV13) was introduced and was referred to neurosurgery for correction of the defect.

Increasing incidence of penicillin resistant pneumococcal serotypes should always be kept in mind especially in children with risk factors for central nervous system infection with pneumococcus, and the therapy should be initiated without delay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ESPID-1039
SEVERE BACTERIAL AND VIRAL INFECTIONS

SEPTIC SHOCK DUE TO LEUCONOSTOC LACTIS IN A 2 MONTH OLD BOY WITH DOWN SYNDROME

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Leuconostoc spp are usually considered as nonpathogenic acid-tolerant organisms that are intrinsically resistant to multiple antibiotics. Identified risk factors for infection include gastrointestinal disease (generally involving bowel resection), prematurity, central venous catheter, recent or ongoing antibiotic therapy (especially with vancomycin). Here we describe an infant with Down syndrome who developed sepsis due to *Leuconostoc lactis* following gastroenteritis.
A 2 month old boy brought to our emergency department with diarrhea and vomiting. He was diagnosed as adenovirus gastroenteritis and received rehydration therapy for 3 days. He had stayed at neonatal intensive care unit NICU) due to sepsis for 19 days previously. He had congenital hypothyroidism and atrial septal defect. The patient was transferred to ICU with a diagnosis of septic shock. On initial examination he had an erythematous rash and skin turgor was decreased. Vital signs included a respiratory rate of 50/min, heart rate of 150/min, blood pressure of 65/34, body temperature 38°C, capillary refill time 4 to 5 seconds. Laboratory tests revealed a white blood cell count of 24,600/mm^3 with 65% neutrophils and C-reactive protein 6.98 mg/dL. Metabolic acidosis was detected. Transthoracic echocardiography was normal. Blood, CSF, and urine cultures were obtained and empiric antibiotic treatment with cefepime was started. Blood culture yielded *Leuconostos lactis* and penicilin G was initiated. Unfortunately the child died on the seventh day of hospital stay due to multiorgan failure.

Even though accepted as nonpathogenic, *Leuconostoc lactis* should be kept in mind as a potential pathogen in patients with risk factors.

ESPID-0764
SEVERE BACTERIAL AND VIRAL INFECTIONS

ECTHYMA GANGRENOSUM (EG) PRODUCED BY GROUP A STREPTOCOCCUS (GAS): AN UNUSUAL PRESENTATION IN A PREVIOUSLY HEALTHY INFANT PRESENTING WITH NEUTROPENIA

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BACKGROUND: EG is an uncommon life-threatening skin lesion that occurs predominantly in children with malignant diseases, immunosuppressive conditions, or transient and chronic neutropenia, and is usually produced by *Pseudomonas aeruginosa*. Although GAS is a leading cause of necrotizing fasciitis (NF), GAS-associated EG is extremely rare, and to our knowledge this is the first report from Latin America.

METHODS: We report a Costa Rican infant who developed GAS EG, necrotizing fasciitis (NF) and septic shock.

RESULTS: A 7-month-old boy was transferred to our institution with a 3-day history of fever and constitutional symptoms. At admission, he was received in septic shock, a small erythematous skin lesion was described on his right knee and leg, and severe leucopenia with neutropenia was documented. Clindamycin and cefotaxime were started, blood cultures showed Gram(+) cocci, and fully susceptible GAS was grown rapidly. He was transferred to the PICU and needed inotropic support and mechanical ventilation. One day later, on infectious and dermatology consultations an extensive violaceous lesion on his right thigh and knee, with hemorrhagic bulla and a black scar consistent with EG was described and later confirmed by biopsy. He underwent surgery where also NF of the thigh and leg were confirmed. He needed further multiple surgical interventions, VAC therapy, skin grafts and 21-day antibiotic treatment prior to discharge. His neutropenia resolved and no immunodeficiency was proven.

CONCLUSIONS: GAS should be included in the list of etiologic agents of pediatric EG. Its prompt recognition is critical for early and aggressive antibiotic and surgical treatment.

ESPID-0971
SEVERE BACTERIAL AND VIRAL INFECTIONS

LISTERIA MENINGITIS COMPLICATED BY SEVERE HYDROCEPHALUS IN AN APPARENTLY IMMUNE-COMPETENT 5-YEAR-OLD CHILD

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Introduction:

Listeria monocytogenes meningitis is very rare in immunocompetent children.

Case report:

A previously healthy 5-year-old-girl was admitted to emergency room with high grade fever for 24 hours, headache, drowsiness and vomiting. On clinical examination, meningeal signs were found.
Blood test revealed a significant inflammatory syndrome. Cerebral spinal fluid showed pleocytosis, hypoglycorrachia and hyperproteinorrachia. The initial culture was sterile. Intravenous (IV) third-generation cephalosporin was started but the child remains febrile after 48 hours of treatment and gradually deteriorated. Lumbar puncture was repeated and IV vancomycin plus aciclovir were added. Second CSF culture grew for *Listeria monocytogenes*. Ampicillin in association with gentamycin was started. Despite antibiotherapy, the child presented a neurological deteriotation and bradycardia. A brain CT revealed hydrocephalus and ventriculitis. An external ventricular drain was placed and systemic corticotherapy was given for 15 days. Finally, a ventriculo-peritoneal drain was put in place after septotomy. The neurological evolution was progressively favorable following antibiotherapy with ampicillin for 21 days.

Conclusion:

Although *Listeria monocytogenes* is a rare cause of meningitis in previously healthy children, it is still a pathogen to consider when treating a child with meningitis, especially when the patient is not responding to empiric antibiotic treatment with IV third-generation cephalosporins. When *Listeria* is isolated from the CSF, treatment should be adjusted to include Ampicillin in combination with Aminoglycoside. Immunodeficiency should be ruled out.

ESPID-0926
SEVERE BACTERIAL AND VIRAL INFECTIONS

UNUSUAL VARIZELLA-ZOSTER VIRUS DISEASE OF THE CNS: REPORT OF TWO CASES

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Central nervous system (CNS) complications of varicella-zoster virus (VZV) are rare. However, they are a leading cause of VZV-associated hospitalization and are associated with significant long-term morbidity and mortality.

Case 1: We report a 21-month-old boy who was not vaccinated with Varivax and who had started suffering from chickenpox 10 days before admission. The parents had discovered him wobbling and observed involuntary movements. Cranial magnet resonance imaging (cMRI) detected evidence for encephalitis. In the cerebrospinal fluid (CSF), cell count was increased but no VZV was detectable. We treated the patient with intravenous aciclovir over 7 days. Three months later he showed complete remission.

Case 2: An 8-year-old girl that was vaccinated with Varivax only once, was admitted to our hospital because of vertigo, vomitus and nystagmus. Her left ear showed almost healed shingles. We detected VZV in the CSF. CMRI showed a local edema from the pons to the left cerebellar peduncle. We treated with prednisone and aciclovir over 21 days. Three months later the patient had still not completely compensated the loss of her left vestibular system.

Discussion: The first case showed a benign neurological complication following chickenpox. Clinically we suspected a cerebellitis. However, cMRI showed mild encephalitis. In the second case, we saw brain stem encephalitis per continuitatem after an untreated zoster oticus. In both cases systemic treatment was indicated..
Conclusion: Sufficient vaccination might have prevented both children from contracting VZV infection. However, there are sparse epidemiologic data on the impact of VZV vaccination on neurologic complications.

ESPID-0157
SEVERE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGICAL SURVEILLANCE FOR INVASIVE MENINGOCOCCAL DISEASE IN ALMATY, KAZAKHSTAN IN 2009-2013.

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The review of invasive meningococcal disease (IMD) data among children under 14 years old in Kazakhstan demonstrated the trend for morbidity decrease from 113 cases in 2009 to 55 cases in 2012. In the same time the level of morbidity stayed rather high in conditions of big city. The aim of our study was to investigate IMD data in children 0-14 years in Almaty, big city of Kazakhstan.

Methods: We retrospectively studied official statistical data on IMD epidemiology surveillance and archived medical records of children 0-14 years old hospitalized in Almaty Children Inflectional Hospital during January 1, 2009 – December 31, 2013 with IMD and bacterial meningitis.

Results: The total number of laboratory confirmed bacterial meningitis cases during 5 years in Almaty was 618. Proportion of meningococcal meningitis was 14, 6% (90 cases), pneumococcal – 3, 8%, staphylococcal –0,3%, meningitis caused by Pseudomonas aeruginosa – 0,1%. Total number of non-typed meningitides was 501 cases (81, 2%).

IMD had the highest prevalence in children less than 3 years old - 44, 6%. Serogroups landscape of Neisseria meningitides isolated from laboratory confirmed cases included A, B and C serougroups with superiority of serogroup B appearance - 66, 7%. The correlation of mortality with any serogroup was not found.

Conclusion: IMD morbidity in Kazakhstan stayed on low level but the number of cases registered from year to year in big cities is constantly high. Vaccination against meningococcal infection could contribute to control of IMD in high risk groups.

ESPID-0268
SEVERE BACTERIAL AND VIRAL INFECTIONS

THE ROLE OF PREMORBID STATUS IN COURSE OF MENINGOCOCCAL MENINGITIS

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Invasive meningococcal disease is dangerous due to potential fatal outcome and the high risk of serious complications. The matters of severe outcomes in childhood are the late appeal to the doctor and burdened premorbid status. The aim of our study was to determine the role of premorbid status in the severity of meningococcal meningitis and length of hospitalization.

Methods: We studied anamnestic and clinical data of 90 children 0-14 years of age hospitalized in Children Inflectional Hospital, Almaty, Kazakhstan with meningococcal meningitis during 2009 – 2013.

Results: 66, 7% of children hospitalized with meningococcal meningitis had burdened premorbid status. Children under 1 year of age presented the major part of these cases. 33, 3% had moderate degree anemia, 11, 7 % had mild degree anemia. In 8,3 % (5 children) – moderate overweight was diagnosed. The protein malnutrition moderate degree was found in 4 cases (6, 7%), the protein malnutrition mild degree was found in 1 case (1, 7%). Meningococcal infection was severe in 95% of the above cases.

The average time of meningococcal meningitis treatment was 12 days. The burdened premorbid conditions extended the course of disease and treatment on 2 days in 45% of patients; on 3 days in 30% of patients; on 4 days in 15% of patients; on 5 days in 10% of cases.

Conclusion: The burdened premorbid status is one of the matters for severe invasive meningococcal infection and extension of hospitalization length.

ESPID-0266
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

A CASE REPORT ON NEONATAL CHIKUNGUNYA: RNA-SEQUENCED VERTICAL TRANSMISSION

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After Discharge

	IgM Elisa	PCR	Dengue PCR	Viral Culture
INDEX PATIENT	NOT TAKEN	POSITIVE	NEGATIVE	POSITIVE
MOTHER	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE

This is a case of a 4 days old male born whose mother had low grade fever, joint pains and petechial rashes 2 days prior delivery. The father had similar symptoms, one week prior to mother's illness. There had been an outbreak of Chikungunya in their community however it was based on clinical diagnosis. Upon consult a day before the mother delivered, her CBC was normal and Dengue NS1 was negative. She was sent home. Impression was Non Specific Viral Illness. Patient was term male whose delivery was unremarkable. He was worked up for presumed sepsis. On the 3rd day of life, his blood culture did not grow any organism. He was sent home. On the night of his discharge, he developed poor suck followed by low grade fever and

generalized petechial rash. He was jaundiced. On the 4th day of life, he was readmitted. Sepsis work up was again done. He was started on empiric antibiotics. His laboratory results were normal.. Chikungunya PCR of the baby was positive for CHIKV EP1 however the mother was negative. Isolation of the Chikungunya Virus in the mother and baby both showed growth. Their Viral RNA was sent for sequencing and the results of the CHIKV NSP1 and CHIKV EP1 were similar for both the mother and child.

ESPID-0185
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

CHARACTERISTICS OF CHILDREN DIAGNOSED OF TUBERCULOSIS AT THE PEDIATRIC CLINIC "LET CHILDREN HAVE HEALTH" IN MEKI, ETHIOPIA. THE CHALLENGE OF DIAGNOSIS WITH LIMITED RESOURCES

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Tuberculosis(TB) is a preventable, curable disease and the first cause of morbi-mortality in Ethiopia. The diagnosis during childhood is a challenge due to the paucibacillary character of the disease. We describe the features of children diagnosed of TB at the Clinic "LET-CHILDREN-HAVE-HEALTH" in Meki(Ethiopia).

Methods:A retrospective-study including children diagnosed of TB from January to December/2013 was performed. Anthropometric, clinical, laboratory and radiological findings were registered. TB was classified as Confirmed, Probable and Possible at the time of diagnosis. A further classification was performed based on Pulmonary, Extrapulmonary (any type of extrathoracic manifestations, including Miliary-form) or Mixed-TB.

Results:38children were diagnosed of TB: 35Probable, 3Possible(mycobacterium culture was not available). The median age was 8years. 50% of them had PulmonaryTB, 37%Mixed, 13%Extra-pulmonary(1Miliary-form). At the time of diagnosis 32(84%)reported cough, 31(81%)fever, 15(39,5%)lymphadenitis. 39.5% had a family history of TB and none of them had received chemoprophylaxis. Malnutrition(MUAC<12cm or weight/height<70%) was detected in 13children(34%). Four-children had a positive-smear(all older than 7years). In one-child diagnosis was confirmed by lymph-node byospie. Another one required surgery due to intestinal-obstruction and smear-positive was detected in surgical specimens. Mantoux was performed in 13children, remaining 9positive. Rapid HIV-Test were done to 22children, all of them were negative. The evolution of all children was favorable.

Conclusions: TB diagnosis remains a challenge, as most of the children are detected late. Identification of exposed-children and an active searching using specific programs such as local program-malnutrition, should be promoted. Extrapulmonary presentation seems to be very prevalent in this area, so TB should always be considered.

ESPID-0666
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

VP-SHUNT DYSFUNCTION CAUSED BY MALARIA CNS INFECTION

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Background: Shunt dysfunction caused by bacterial infections is a common problem.
Case report: We present a case of a 2-year old boy from Saudi-Arabia with shuntdependent occlusive hydrocephalus, who underwent shunt revision and developed intermittent fever and progressive dysfunction of the vp-shunt three weeks postoperatively. CSF cultures were negative for bacteria.
Nevertheless elevated CSF protein content, CSF pleiocytosis and IL-6 concentrations prompted removal of the shunt system and temporary external ventriculostomy. Recurrent fever of 40°C and origin of the patient were suspicious for an infection beyond the spectrum of bacteria usually found in Europe. With positive antigen and smear examination, Plasmodium falciparum was identified in a blood specimen. Under treatment with atovaquone and proguanil, the patient recoverd quickly and CSF composition normalized. After 30 days of external drainage, VP-Shunt re-implantation was performed without any further difficulties.
Conclusion: Patients' origin of tropical countries should direct differential diagnosis to unusual specimen of European countries such as malaria.

ESPID-0688
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

FOCAL MYOSITIS CAUSED BY FILARIOSIS (LOALOA)

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Background: Filariosis is a common tropical disease transmitted by mosquitos. Up to 200 million patients are affected. The clinical picture includes elephantiasis and onchocercosis. The subtype loaloa is found mainly in central and West Africa.
Case report: A 14-years-old female patient who used to live in Cameroon until three years before reported of recurrent self-limiting swelling of the hands, the arms and the face during the last four years. Two days before admission the girl developed a marked swelling of the upper arms with inhibition of extension. No fever was observed. Creatinkinase was increased to 204 µkat/l [< 2.9 µkat/l]. Ultrasound scan and whole body magnetic resonance imaging showed an isolated myositis of both Mm. brachialis, Mm. biceps and the right M. extensor carpi radialis longus. Serology was positive for IgG4 antibodies against Diofilaria immitis suggesting a productive infection. Filarias could not be microscopically observed in the blood smear. While treating the patient with stromectol symptoms ceased within days. There was no relapse since that time.
Conclusion: Tropical diseases might present with atypical symptoms. Especially previous stays in tropical areas, affections of the soft tissues should direct to differential diagnosis of filariosis. Remarkably in our case, the isolated myositis with focal distribution pattern was the only clinical sign.

ESPID-0147
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

TYPHOID FEVER IN PUNJABI CHILDREN:CLINICAL FEATURES AND DIAGNOSTIC CHALLENGES

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Backgound & Aims:Typhoid fever is endemic in Northern India including the state of Punjab.It is often overdiagnosed and unnecessary antibiotics continued for long. This study was done in children ,diagnosed as typhoid/paratyphoid fever based on blood culture positivity.In these children detailed clinical features and laboratory tests were performed and results thus obtained were statistically analysed to check the reliability of diagnosing typhoid fever in children.

Methods:This was a prospective study conducted over from July 2012-June 2014.In this study all the consecutive children admitted to the pediatrics department ,Dayanand medical college and hospital,Ludhiana,Punjab and diagnosed as cases of Typhoid/Paratyphoid fever on blood culture test,were included.A detailed history,clinical examination and relevant investigations were done in all tghese cases.Results thus obtained were statistically analysed.

Results:A total of 101 cases with blood culture positive for Typhoid/Paratyphoid fever were admitted during this time period.Fever was seen in all the 101 cases(100 %),followed by vomiting in 38 (37.6 %),pain abdomen in 31(30.6 %) cases.Hepatomegaly was present in 68 patients (67.3 %%),splenomegaly in 65 patients(64.3 %).Serum LDH was raised in 100 patients((98 %).Wida test was done in 87 patients out of which it was positive in 44 (65.5%).Typhoid vaccination was already done in 20 patients(19.8%).Out of 101 cases ,Salmonella strain grown was resistant to nalidixic acid and aminoglycosides in all the cases.

Conclusions:Typhoid fever is endemic in children of Punjab.Besides blood culture positivity,raised serum LDH,Positive Widal test and soft splenomegaly clinch the diagnosis in most of the patients

ESPID-0493
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

KEEP CHILDREN OUT OF REACH OF MACAQUE MONKEYS!

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Background and aims – Severe human infectious diseases can be transmitted by monkeys. Monkey's bite can be a health hazard with short-term and long-term morbidities. We alert about the risk of simian Herpes (B-virus) infection.

Methods – We report 2 pediatric cases of macaque's bite. Both children were admitted at a French Pediatric Emergency Department.

Results – Case 1: A 4 year-old child was bitten on the hand by a macaque monkey of a Tunisian zoo. Back in France two days later, he was admitted for a dermohypodermitis located on the hand due to methicillin-sensitive *Staphylococcus aureus*. He recovered entirely after intravenous amoxicillin-clavulanic acid therapy, antiviral prophylaxis (acyclovir) for 14 days and rabies vaccination. Herpes serology using ELISA technique was positive, specific simian Herpes PCR was negative but Herpes simplex virus type 1 PCR was positive in blood samples.

Case 2: A 10 year-old girl was deeply bitten on the thigh by a free-ranging macaque in Bali. Local treatment permitted favorable evolution. Back to France 14 days later, she received rabies vaccination and antiviral prophylaxis (valaciclovir) for 14 days. Herpes serology using ELISA technique was positive, specific simian Herpes PCR was negative but Herpes simplex virus type 1 PCR was positive in blood samples.

Conclusion – Due to the attractiveness of Indonesian destination and illegal pet monkey's importation, cases of monkey's bites increase. Such bites can cause serious wounds and expose to simian Herpes infection burdened with high mortality if

symptomatic.

ESPID-0103
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

VISCERAL LEISHMANIASIS WITH SECONDARY HEMOPHAGOCYTOSIS IN SICKLE CELL ANEMIA

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Visceral leishmania (VL) is a parasitic infection which is transmitted by sandflies & cause many morbidities & mortalities in different areas of the world. Sickle cell anemia (SCA) is a common hemoglobinopathy which is inherited in autosomal recessive pattern. Affected patients may suffer from number of crisis & they are prone for infection as well.

A 2-year-old boy who is a known patient of SCA presented to a hospital with two weeks history of fever, hepatosplenomegally & anemia. Because of no focus of infection or any other causes had been detected to explain the persistent fever, patient then referred to our hospital for further evaluation. In our hospital , patient started to develop pancytopenia. Many investigations involving bone marrow aspiration had been done & revealed visceral leishmaniaiasis with secondary hemophagocytosis. Patient responded to treatment with liposomal amphotericin B. Fever subsided, pancytopenia corrected & hemophagocytosis improved.

To our knowledge, this is the first reported case of VL infection in patient with SCA. Secondary hemophagocytosis to VL infection had been discovered in this patient as well . Administration of liposomal amphotericin B was enough to clear the infection & subsequently the secondary hemophagocytosis.

Patients with SCA despite of being potentially resistant to some parasitic infection like malaria, however, they still prone for other parasitic infection like VL. Liposomal amphotericin B is effective for the treatment .

ESPID-0466
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

CONSULTATION OF PAEDIATRIC TROPICAL DISEASES AND INTERNATIONAL ADOPTED CHILDREN AND DIAGNOSIS OF EOSINOPHILIA.

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Background and aims: Eosinophilia is defined as an increase of absolute number of eosinophils in peripheral blood exceeding 500/mm3. Aims: To expose the characteristics, diagnosis and treatment of children with eosinophilia that have been analyzed in our Consultation.
Methods: A descriptive retrospective study during one year period 2013-2014.
Results: 19 children of 212 (8,9%) had eosinophilia (68,4%males); average age: 9,8 years old; 10 children (52,6%) International Adopted-children; 4(22,2%) from Institucional Homes and 5 referred by their paediatrician. All of them came from Tropical Areas: Africa (8), Asia (6) and South America (2). Three of them were spanish but had visited a Tropical Country. Related symptoms were: itching (16,6%), diarrhoea (16,6%), abdominal pain (16,6%), and 68,4% without symptoms. The most common diagnosis was: 7 (38,8%) schistosomiasis, 3 strongyloidiasis, toxocariasis and ascaridiasis (16,6%); 3 of them remain without diagnosis. The average absolute number of eosinophils was 3.764/mm3 (19,65). The treatment consisted of: Praziquantel *(Schistosoma)*, Albendazole *(Toxocara)*, Mebendazole *(Ascaris)* and Ivermectin *(Strongyloides).*
Comments: Eosinophilia is frequently found in International-Adopted children and travellers to tropical countries. Parasites are the main cause of eosinophilia in this group. As a result of severe eosinophilia we can mainly diagnose Strongyloidiasis, toxocariasis and acute schistosomiasis; all of them tissular helminthiasis pontentially serious. Real diagnosis and specific drugs are needed, usually foreign drugs in our country; trying to avoid empiric treatments with antiparasitic drugs.

ESPID-0779
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

STAFF PREPAREDNESS FOR EBOLA VIRUS DISEASE IN A WESTERN EUROPEAN TERTIARY PEDIATRIC HOSPITAL.

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Background and Aims: Ebola virus disease (EVD), its rapid spread, high mortality, and heath care worker (HCW) impact, provoked concern that staff might disengage and refuse care to suspect patients. To inform staff education and training, we sought to determine staff EVD knowledge level in a European tertiary pediatric hospital and to characterise perceptions and fears that might impede care provision.

Methods: In October 2014, prior to specific training, an anonymous online survey was circulated to all medical and nursing staff. Objective questions had yes/no answers. For others, the five point Leikart scale was used. An open comment box was included.

Results: 100% response from 106 surveyed staff (52% nursing) was obtained. 94 - 100% correctly identified it as a virus and its transmission mode. 60% anticipated an overall survival of 10 – 40%, 15% predicted a poorer outcome. 49% felt informed but most reported reliance on non-medical media outlets for information. 73% worried about an EVD case presenting, with only 26% confident in infection control procedures. 92% considered themselves personally at risk if caring for an EVD case and 73% concerned for transmission to their families. 72% expressed willingness to care for an EVD patient but 79% felt colleagues might refuse.

Conclusion: In October 2014 hospital staff were concerned that they were not adequately prepared to care for a suspect EVD case. Despite the negative impact of EVD on HCWs, a large majority expressed willingness to engage. A clear need for EVD specific training and information updates was identified.

ESPID-0861
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

STRONGYLOIDES STERCOLARIS, 47 CASES IN PAEDIATRIC PATIENTS

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Background and aims:

Strongyloides stercolaris is a nematode with a worldwide distribution. It usually causes infection in humans who live in tropical areas, but, international adoption, travellers around the world and migration… have increased the risk of infection in other areas. The aim of this report is to describe epidemiological items of paediatric cases in a Paediatric Tropical Unit.

Methods:

We describe the patients with diagnosis of infection *S. stercolaris* in our Paediatric Unit of Tropical Infectious diseases along the last 3 years.

Results:

Forty seven cases (4.9%) out of 959 patients attended during 3 years in this specific practice, presented a positive serology to *S. stercolaris*: 51% boys, (5 months to 22 years old; average 6.5 years, median 4.8 years).

Most of these patients came from international adoption (75% - 35 cases), and 21% were travellers or immigrants. The distribution according to the origin countries: Ethiopia 32%, India 15%, China 10.6%, and 14 other countries. Forty children were diagnosis of strongyloidiasis as a primary infection, and 7 patients were re-infections. Co-infections were found in 40% of patients.

Conclusions:

Travels, immigration and international adoption let common tropical infections appear in no tropical areas. Thus, if a patient comes from an endemic area and has been risk of exposure to *S. stercolaris*, it should be carefully checked, even more if suggestive symptoms or eosinophilia are detected.

ESPID-0589
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

ADOPTION OF VIETNAMESE CHILDREN WITH SPECIAL NEEDS: IS THE INITIAL DIAGNOSIS CONFIRMED?

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Background and aims.

Vietnam has reformed its adoption system since January 2011. According to this, old adoption applications are not accepted, except for children with special needs in list II.
'Special needs" (SN) refers to children with chronic diseases or development disabilities that will need medical or surgical treatment. Consequently, prioritizing the adoption of these children would allow to provide them early therapy.
Our main objective is to describe the initial diagnoses of adopted children according to SN list, and corroborate subsequent confirmation. The secondary goals are to expose other additional diagnoses and know the status of vaccine immunization.

Methods.

Medical charts of Vietnamese adopted children in a Spanish cohort of international adoption during 2014 were reviewed.

Results.

There were identified fourteen children adopted from Vietnam, median age of 27.7 months, 72% female. 78% were identified as SN. The diagnoses that included in the SN were: six HBV infection, four malnutrition, one inguinal hernia, and one patent ductus arteriosus. The 29% of the initial diagnoses were confirmed. Other additional diagnoses were: iron deficiency, strongyloidiasis, schistosomiasis, scabies and toxocariasis. Four cases (28%) had adequately signed and stamped vaccine primer. Only 21% were protected against HBV and 28% against measles.

Comments.

Most of the children adopted from Vietnam were included in SN and we only could confirm the diagnoses in a small percentage of cases. We focus in the high incidence of HBV infection, being the most frequently origin of the SN for adoption.

ESPID-0289
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

UNUSUAL PRESENTATION OF PLASMODIUM VIVAX MALARIA WITH ANEMIA, THROMBOCYTOPENIA AND CEREBRAL MALARIA

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"Malignant tertian" and "benign tertian" are terms that have long been used for two of the major diseases we
recognize as malaria. The former is generally considered to be synonymous with *Plasmodium falciparum* and the latter with *P. vivax* infection. As the terms "malignant" and "benign" suggest, the current dogma is that *P. falciparum* can be severe and life-threatening while *P. vivax* tends to be mild. However, recent studies have concluded that P.vivax can cause both sequestration-related and non-sequestration related complications of severe malaria, including cerebral malaria, renal failure, circulatory collapse and severe anemia.
This is a report of two children, one of whom presented with cerebral malaria and other one with severe malaria. The presence of P.vivax only was demonstrated in their peripheral blood smear. Both responded well to antimalarial drugs.

Conclusion:
Definition and classification of severe and cerebral malaria need to be revised to include plasmodium vivax
as a possible causative parasite.

ESPID-0400
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

OPHTHALMOLOGICAL FEATURES OF VISCERAL LEISHMANIASIS

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Visceral leishmaniasis (VL) is a systemic disease that affects all the body organs including the nervous system. Ophthalmological effects of VL carry a considerable morbidity that may eventually end in blindness. It is therefore becoming a pressing need to determine the burden of ophthalmological effects as early as possible to prevent blindness in the first place and to reduce long term morbidity. As far as we are aware this was the first study to look at the ophthalmological effects in children due to VL.

Methodology:

This study was a cross-sectional, prospective observational study. It was conducted during the period from 1st of October 2012 to 30th of March 2013 at AL Gadarif Teaching Hospital which is located in the heart of the endemic area in Gadarif state, the main endemic area for VL in Sudan. Data were collected through a questionnaire which included demograhic data and eye symptoms. Standard ophthalmological examination was conducted by consultant ophthalmologist.

Results:

Opththalmological assessment of 64 patients revealed that 93.8% (60/64) of them with hypermetropia. One patient was found to have uveitis 1/64(1.6%), chorioretinal degeneration was found in another patient 1/64(1.6%). Retinal hemorrhages was confirmed in two patients2/64(3.2%) with bleeding in upper temporal arcade.

Conclusions:

There is no distinctive characteristic sign of VL in the eye. However, the significant percentage of patients of VL with refraction error- hypermetropia- definitely need further clarification in future studies. Larger sample sized studies are needed to characterize the possible relationship between VL and upper temporal arcade hemorrahge reported in this study.

ESPID-0847
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

AUDIT OF CLINICAL MANAGEMENT OF DENGUE HEMORRHAGIC FEVER GRADE III IN EMERGENCY ROOM DR. SOETOMO HOSPITAL

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Background : Dengue hemorrhagic fever (DHF) contributes high morbidity and mortality in children. WHO had established guidelines to manage DHF properly. It is needed a clinical audit to evaluate clinical management based on WHO guidelines.

Objective : To audit clinical practice on DHF grade III management to improve the quality of patient care.

Methods : A cross-sectional study was performed, reviewing DHF grade III medical records diagnosed at the pediatric emergency room Dr. Soetomo Hospital between 2012 to 2013. It investigated the completenes of history taking, physical examination, rumple leed, laboratory examination and treatment data. The data were analysis using EpiData 2.1 and STATA 7.0

Results : We reviewed 93 medical records and mostly between 1 to 5 years old (98%). Male:female ratio was 50 : 43. All patient had onset of fever, but cold clammy extremities and less urine production were recorded 68% and 38% respectively. Vital signs and capillary refill time were recorded above 95% and 94%, but only 41 % patients underwent rumple leed test. Complete blood count was presented in all cases and 90% chest radiography were done. Ig M and Ig G anti dengue serologic were performed in 23% patients. The crystalloid or colloid fluid resuscitation were received by 78% patients, with 52 (71%) had sufficient amount of fluid resuscitation. Ninety five percent received crystalloid-dextrose fluid administration after stable condition achieved.

Conclusion : This clinical audit resulted many important data are missing. Improvement efforts in making complete records are needed to promote good clinical practice and DHF grade III patient's care.

ESPID-0807
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

TWO CASES OF GLANDULAR TULAREMIA PRESENTING WITH SERVICAL LYMPHADENOPATHY

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Background and aims: Tularemia is a zoonotic infectious disease that is caused by *Francisella Tularensis*, especially seen in North hemisphere. Depending to inoculation dose, virulancy, host immune response and where the bacteria inoculated into the host, tularemia has several clinical manifestations. Tularemia has six different clinical forms, depending on the route of transmission. In Turkey, the most common type is the oropharyngeal form. **Cases:**We present two cases of glandular tularemia with cervical lymphadenopathy (LAP) which was not respond to betalactams. Excisional LAP biopsies was compatible with chronic infection and granulomatous inflammation. Although hunting or hunted animal meat consumption was not found, tularemia serology was sent due to consumption of source water in patients' hometown. The tularemia microagglutination tests; 1/160 positive was detected. Gentamycin treatment was given to case 1 for 10 days and combination therapy with doxycycline and streptomycine was given to case 2 for 21 days. After the treatment given, lymphadenopathy sizes got smaller and two patients discharged from the hospital. **Conclusions:** Tularemia; in relation to consumption of contaminated water began to appear with increasing frequency in different regions of our country in recent years. As a result; tularemia should be thought in differantial diagnosis in patients with lymphadenopathy which is not response to betalactams.

ESPID-0979
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

MEDICAL TREATMENT AND SURGICAL APPROACH FOR A CONDUIT INFECTION CASE SECONDARY TO CHRONIC Q FEVER

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Background and aims: Q fever is a worldwide zoonosis caused by an obligate intracellular bacterium, *Coxiella burnetii* (1). Q fever endocarditis is associated with surgery for 15%-73% of patients and can induce a large number of relapses(1). We aimed to present a case of pulmonary atresia-ventricular septal defect with a conduit placed between the ventricle and pulmonary artery that developed conduit infection secondary to Q fever.

Case: The 8-year-old female case from North Africa had a Rastelli operation at the age of 4 with the diagnosis of ventricular septal defect and pulmonary atresia. It was learned that the case was administered on doxycycline and hydroxychloroquine for 18 months according to infective endocarditis secondary to Q fever. The case was referred to our clinic due to constricted conduit. We identified calcification and constriction in the conduit and a mobile, hyperechoic lesion sized at 6x10 mm in the proximal part of the conduit. Since the history of the case included Q fever, it was initially thought that it could be conduit infection. Coxiella Burnetti IgM was negative, phase 1 and phase 2 IgG≥1/1024 was positive; therefore, it was concluded that she had conduit infection secondary to relapsing Q fever. Eventually, the decision was taken to replace the conduit. It was planned that treatment with doxycycline and hydroxychloroquine be administered for another 18 months and she was discharged.

Conclusions: The conduit infection should be kept in mind in patients undergone surgery with Q fever and the conduit should be surgically replaced.

ESPID-0213
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

FASCIOLOSIS IN MEXICAN PEDIATRIC PATIENTS

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Fasciolosis is an infection caused by *Fasciola hepatica*, geographical distribution of human fasciolosis is found in all countries. Fasciolosis is presented in Mexico importantly in bovines;

In Mexico the first human case was reported in 1936 in an 11 year-old boy, since then many cases have been reported: two in 1942, ten in 1992, one in 1999, four in 2000, one complicated case in 2002 and 5 in 2006. The diagnostic of this 24 cases were made by isolation of the parasite in 14 and by immunologic test in 10.

The parasitologic isolation were made by coproparasitologic test in 13 patients, in the 2002 case, the isolation was made by identification of the parasite directly from the gallbladder tissue, obtained by quirurgic procedure.

Last 3 years we diagnosed 3 pediatric patients by coproparasitologic studies where we observed *Fasciola hepatica* eggs.

In clinical evaluation two of this patients presented inespecific symptoms, only one presented symptoms as weight loss, hepatomegaly, hepatic pain, intermitent jaundice in last 10 months.

We consider the human fasciolos is more frequent than reported in literature, but etiologic diagnosis is not made in every case, it is important that physicians suspect this disease, and include a concentration coproparasitoscopic test as a routine test in geographic zones where the fasciolosis is an endemic disease in bovines and ovines.

ESPID-0571
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

GRANULOMATOUS AMEBIC ENCEPHALITIS CAUSED BY ACANTHAMOEBA IN AN IMMUNOCOMPETENT BOY: A RARE CASE

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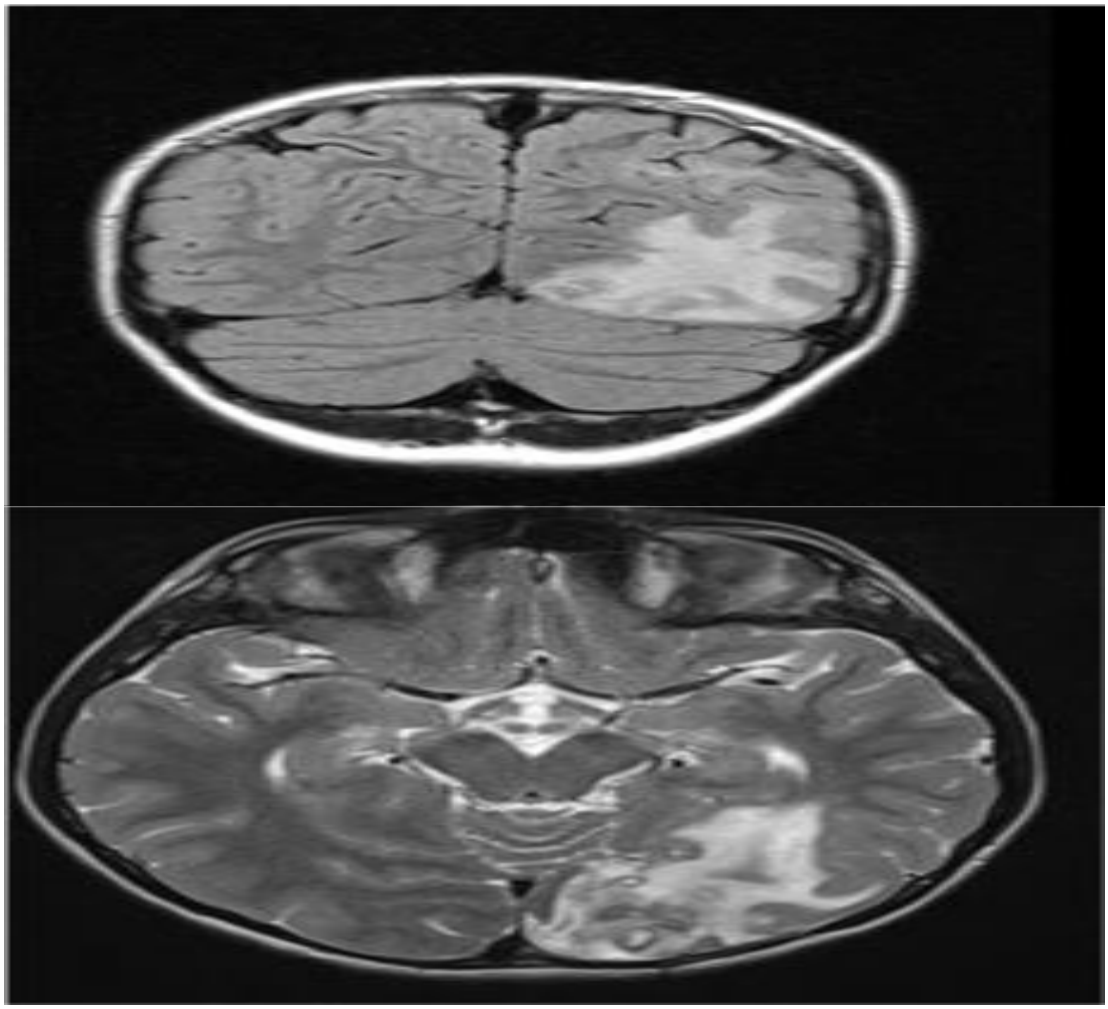
Introduction: Acanthamoeba, a rare cause of encephalitis, is associated with high mortality, Granulomatous amebic encephalitis(GAE) has been described rarely in the immunocompetent host. This case report presents a previously healthy, immunocompetent 9-year-old male patient who diagnosed to GAE, with the intention of raising awareness of this rare infection.

Case: This 9-year-old Georgian male patient was originally brought to a local community hospital by her parents after he presented generalized tonic-clonic seizures. His full blood count, urea, glucose and electrolytes were all unremarkable. Noncontrast computed tomography (CT) demonstrated multiple hypodense cerebral lesions on right parietal lobe. Brain biopsy was performed on the lesion. Histopathologic examination revealed necrotizing encephalitis, amebic trophozoites, and cysts in brain parenchyma. His immunoglobulins, yeast and HIV 1 and 2 serology, nitroblue tetrazolium(NBT) mycobacterial and fungal culture, chest radiograph and abdominal ultrasound were all unremarkable. His CD4 count was 1150 (range: 775–1385) with a normal CD8 count. The patient had head trauma one year ago and he often swam in the river. After receiving the diagnosis GAE, immunocompetent child received fluconazole, rifampin and trimethoprim-sulfamethoxazole at usual doses. He has been taking antimicrobial therapy for two months and the general condition of the patient is good.

Conclusion: Although GAE is encountered rarely, it should be considered as a diagnosis for any patient with meningoencephalitis without evidence of bacteria by staining, antigen detection tests, or culture. Biopsy is critical to establish the etiology so that appropriate combination therapy can be developed.



ESPID-0827
TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

MANAGEMENT OF A 16 YEAR OLD PATIENT WITH CARDIAC AND PULMONARY CYSTIC ECHINOCOCCOSIS WITH MASSIVE OBSTRUCTION OF THE PULMONARY VESSEL SYSTEM

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History:

A 16 year old girl was admitted to our hospital with mild cough, mild dyspnoea, weight loss and the diagnosis of a cardiac cyst. She originated from Romania, had moved to Austria 2 years ago, and had had close contact to dogs in Romania.

Diagnostic investigations:

Diagnostic imaging confirmed a cardiac cyst in the apex of the right ventricle close to the pericardia of 3,3 x 3,4 cm in diameter, surrounded by several daughter cysts, up to 1 cm in diameter. In addition, multiple cystic lesions up to 4 cm in diameter in lung-tissue, a complete obstruction of the right pulmonary arterial system, and a 2/3 occlusion of the left pulmonary arterial system were detected. She had a highly increased pulmonary arterial pressure of 68/33/47 (systolic/diastolic/mean). Serological and parasitologic investigations revealed infection with echinococcus granulosus.

Treatment:

The advanced stage of the disease required several interdisciplinary councils, including contacting specialists from Spain, Turkey and Germany. She first underwent cardiac cystectomy and treatment with albendazole. In a second stage pulmonary thrombendarteriectomy was performed eliminating numerous echinococcal cysts from the pulmonary vasculature. After the operation, lung perfusion improved only partly, but pulmonary arterial pressure was markedly reduced to 45/18/29; s/d/m.

Outcome:

In a follow up investigation after 6 months her clinical status had markedly improved. She shows complete disappearance of her excertional dyspnoea and a weight gain of

10 kg.

ESPID-0895
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

ABDOMINAL TUBERCULOSIS IN AN 8 YEAR-OLD GIRL

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AIM : Extrapulmonary tuberculosis is rare, especially in young immunocompetent children. We describe the case of an 8 year-old child with abdominal lymph nodes tuberculosis.

METHOD : An 8 year - old girl was admitted to the hospital because of acute abdominal pain and vomiting. The x-ray and the ultrasound of the abdomen revealed a mass in the lesser pelvis. An exploratory laparotomy revealed a mass consisting of necrotic tissues and calcifications. Because of the macroscopic characteristics of the mass the most likely diagnosis was tuberculosis.

RESULTS : The tuberculin test was strongly positive (30mm induration) and the Quantiferon test was also positive. The mother had a positive tuberculin test (22mm induration), while the girl's uncle was a drug user and had been hospitalized for pulmonary tuberculosis a year ago. The girl had also a history of positive tuberculin test (20mm induration) a year ago but no further examination or medication was administered. Post surgery abdominal and chest CT scan excluded other organ involvement . The histological report concluded that the findings are compatible with a *Mycobacterium tuberculosis* infection in a necrotic stage. The patient began a 3-drug treatment, isoniazid and rifampicin for 6 months combined with pyrazinamide for the first 2 months of treatment.

CONCLUSION : Abdominal tuberculosis is unusual in children. In order to reach a diagnosis invasive procedures are required**.** Nevertheless, when there are infectious patients with tuberculosis in the child's environment, even if the symptoms are non specific, extrapulmonary tuberculosis must be included in the differential diagnosis.

ESPID-1071
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

Immunodiagnosis of tuberculosis infection in children under the age of five - which testing is feasible?

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Immunodiagnosis of tuberculosis infection (TB) in children under the age of five is challenging. Current German guidelines recommend tuberculin skin testing (TST), but not interferon gamma release assays (IGRAs) as first line diagnosis. In 71 TB exposed, non BCG vaccinated and asymptomatic children under the age of five TST (cut off < 5mm) and IGRA (QuantiFERON TB Gold in tube) were performed simultanously. In four children (6%) the IGRA was inconclusive. In seven (10%) of the remaining 67 children both TST and IGRA were positive. One of those children had pulmonary TB. In one child only the TST and in five children (7%) only the IGRA was positive. One of these children developed active TB during the follow up. Conflicting results were detected in six children (9%) in total. All children with negative tests were treated with isoniazide (INH) for three months, all children with at least one positive test result were treated with INH/rifampicine for three months. This study shows that there is a number of inconclusive IGRAs in children under the age of five. Therefore, IGRAs should not replace the TST in TB diagnosis in this age group. Nevertheless, they could add sensitivity to the results of the TST testing.

ESPID-0749
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

ONE CASE OF PEDIATRIC PULMONARY MDR-TUBERCULOSIS SUCCESSFULLY TREATED WITH HIGHER-DOSE-ISONIAZID AND QUINOLONES.

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Background

MDR-tuberculosis in children represents a challenge because of poor availability of palatable and fully orally administrable drugs.

Case report

A 4-years italian girl was referred to our department for a history of intermittent fever in the last two months and recent erythema nodosum. The child was in very good clinical condition without any cough.
We made the diagnosis of pulmonary tuberculosis (intrathoracic lymph node and parenchyma) without cavities. The culture of gastric lavage isolated Mycobacterium tuberculosis resistant to etambutol (ETB) and to isoniazid (INH) at 0.1 mcg/ml, so that the first-line therapy (INH, rifampicin RMP, pyrazinamide PZA) had to be changed. Streptomycin has high toxicity and needs daily intramuscular injections. Quinolones had not been tested and are not recommended in children. Additional laboratory investigation allowed us to define an INH sensibility at >0.4mcg/ml, no INH-A mutation and quinolones effectiveness. On the basis of these results, we doubled the INH dose (20 mg/kg/die), added levofloxacin and extended the treatment to 9 months. The therapy was well tolerated and, because of the full oral regimen, compliance was good. One year after diagnosis the child is well with complete regression of the pulmonary lesion.All the family members resulted negative to the Mantoux-test as well as all the teachers children attending her kindergarden.

Conclusions

In case of pediatric MDR-TB, it is advisable to force the local laboratory to try not only standard MIC before ruling out a drug potentially effective at higher doses. Quinolones represent a safe and effective alternative to streptomycin.

ESPID-0294
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

UNSUSPECTED CONGENITAL TUBERCULOSIS

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BACKGROUND AND AIMS: Congenital tuberculosis is a rare disease, fatal when untreated and with non-specific symptoms.

METHODS: We reviewed confirmed congenital tuberculosis cases (according to Cantwell criteria) diagnosed at Hospital La Paz (Madrid, Spain) in the period 1978-2014.

RESULTS: 555 cases of pediatric tuberculosis were diagnosed, 3 (0.5%) of which fulfilled Cantwell criteria. Clinical symptoms had started between 8 and 36 days after birth, and consisted in pertussoid cough (1 patient) and fever and respiratory distress (2). There was no maternal history of tuberculosis, so initial diagnoses were pertussis (1) and sepsis (2). All infants had abnormal chest X-ray (one hilar adenopathy, two miliary pattern). One patient died within 24 hours of hospital admission, and diagnosis was confirmed at necropsy. His mother developed miliary disease with meningitis shortly afterwards. The other two cases had positive gastric aspirate acid-fast smears and cultures and were successfully treated with antitubercular drugs and corticosteroids. Both mothers were immigrants from high tuberculosis-burden countries and had normal chest radiograph and negative sputum acid-fast smears and cultures. Endometrial biopsies demonstrated tubercular granulomas and *M. tuberculosis* was identified by PCR. One of the mothers had been diagnosed with primary sterility due to tubal obstruction and pregnancy had been achieved by in vitro fertilization.

CONCLUSIONS: Congenital tuberculosis is a severe disease that can mimic other perinatal infections and occur in the absence of maternal symptoms. In these cases, endometrial biopsy should be considered, particularly in immigrants from tuberculosis-endemic countries or in women with previous history of tubal infertility.

ESPID-0689
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

DIAGNOSTIC POTENTIAL OF A WHOLE BLOOD LYMPHOCYTE PROLIFERATION ASSAY FOR DETECTING TUBERCULOSIS IN INFANTS AND CHILDREN

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Background: Diagnosis of tuberculosis (TB) remains problematic in children, especially in the youngest age group, as clinical presentation can be non-specific and existing immunodiagnostic tests tend to be falsely negative in the youngest children. Therefore, better diagnostic tests are needed to fill in the void.

Methods/results: An earlier study on pediatric flow cytometric data (PBMC) taught us that the frequency of CD4+lymphoblasts, used as a readout for antigen-specific proliferation, offers an excellent discrimination between infected and non-infected children. Although the identification of lymphoblasts is based on easily measurable and interpretable markers, i.e. cell size and granularity, the isolation of PBMC is time-consuming and requires relatively large blood volumes. Therefore we have adapted a "Flow cytometric Assay of Specific Cell-mediated Immune response in Activated whole blood" (FASCIA) and are currently investigating its diagnostic value in the context of TB diagnosis in children. FASCIA is a heparinized whole blood assay that is relatively simple to perform and necessitates small blood volumes. Cells are stimulated 7 days with mycobacterial antigens (PPD, ESAT-6 and HBHA), stained for surface markers CD3,CD4 and CD8, followed by lysis of red blood cells and flow cytometry analysis for the detection of lymphoblasts.

Conclusions: FASCIA is a whole blood proliferation assay that holds promise for the diagnosis of TB, especially in infants, as high sensitivity for detecting infection is crucial in this age group. In contrast to IGRA, that tends to provide false negative results in the youngest, FASCIA is not based on IFNγ secretion.

ESPID-1040
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PERINATAL TUBERCULOSIS: DIAGNOSIS CHALLENGE FOR AN OLD CONDITION

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Background and aims: Perinatal tuberculosis (PT) is an uncommon but agressive condition with a high mortality risk. Diagnosis is frequently a real challenge. Four PT cases are described.

Methods: Description of cases of PT assisted between 1991-2014 in a Tertiary Paedatric Hospital where children from Moroccan Hospitals are frecquently transferred.

Results: Four patients were included. Epidemiological, clinical, and diagnostic data of the cases are shown in the table 1. All patients presented good evolution after starting tuberculosis treatment. All their mothers showed positive TST and radiological findings compatible with tuberculosis.

Conclusion: PT should be suspected in neonates/infants with suggestive epidemiological history and a respiratory infection which do not improved after broad-spectrum antibiotic therapy. Bronchoscopy is a very useful diagnostic tool due to the high prevalence of intrinsic or extrinsic bronchial obstructions.

Table 1.				
Cases (year of diagnosis)	Case 1 (2013)	Case 2 (2005)	Case 3 (1999)	Case 4 (1991)
Age at diagnosis (days)	45	170	90	55
Original country	Morocco			
Family history	Prematurity	-	Prematurity	-
Clinical features	Progressive respiratory failure	Persistent cough Intermitent fever Failure to thrive	Progressive respiratory failure Intermitent fever	Tachypnea
Age of onset (days)	30	75	7	5
Tuberculin skin test (TST)	Negative	Negative	Negative	-
IGRA test	Positive	-	-	-
Chest x-ray	Several consolidations	Atelectasis	Atelectasis	Lung collapse
Chest CT	Cavitary infiltrates	Paravertebral adenopathies	Mediastineal adenopathies	Subcarinal adenopathies
Bronchoscopy	Extrinsic bronchial obstructions	Endobronchial granuloma	Granulation tissue	Extrinsic bronchial obstructions
Mycobacterium tuberculosis cultures (Gastric aspirates/ bronchoalveolar lavage)	Positive	Positive	Positive	Positive

ESPID-0914
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

EXTRAPULMONARY AND COMPLICATED FORMS OF PULMONARY TUBERCULOSIS

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BACKGROUNDS AND AIMS

There is an increased number of extrapulmonary (EPT)and complicated forms of pulmonary tuberculosis (CFPT) worldwide.

The aim of this study is to describe epidemiological,diagnostic and therapeutic characteristics of EPT and CFPT.

METHODS

Descriptive retrospective study of EPT and CFPT cases diagnosedin patients <14-year-old during 2008-2014.

RESULTS

Over this period, 14 children were diagnosed as havingEPT and 8 as CFPT.

EPT group included: 4 lymphadenopathy (L), 3meningitis (M), 2 abdominal disease (AD) and 5 disseminated disease (DD) andCFPT: 6 endobronchial disease (ED) and 2 pneumonia with pleural effusion (PE). Meanage was 4.8 year-old (0.16-13.16).

Mycobacteriumtuberculosis was isolated in 15cases (68.2%), 3 of whom were *Mycobacteriumbovis (*1 L and 2 AD). MDR was observed inone L and isoniazid resistance in one PE.

Second line drugs were used in 4: the MDR case, one AD who developed a Dresssyndrome caused by rifampicin, and 2 patients with DD due to hepatotoxicity.Steroids were used in all ED and M cases. Treatment duration was 6 months inCFPT and 2 L; 9 to 14 months in 2 AD and DD; 12 months in one M; 18 in MDR.Three cases are currently under treatment and one was lost to follow up. ThreeL required removal and 3 M cases CSF shunts. There were no deaths and 2 M developed neurological sequelae.

CONCLUSIONS

- EP and CFPT management used to becomplicated.

- A high *Mycobacterium* isolation index wasobserved.

ESPID-0886
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PERITONEAL TUBERCULOSIS PRESENTING AS SALPINGITIS: A CASE REPORT

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Background and aims: Extra-pulmonary manifestations of tuberculosis (TB) in children and adolescents occur in about 25% of cases. Peritoneal and genital TB are uncommon, especially in children without any comorbidity. Due to the non-specific nature of the clinical findings, diagnosis is often delayed or mistaken for pelvic inflammatory disease (PID).

Case report: A previously healthy 14-year-old girl, was admitted to the emergency department with a four weeks complaint of unintentional weight loss and anorexia and one-week of abdominal pain and fever. She had been living in Angola until the last 6 months and her mother had a past history of TB. On examination, she was febrile, with pale mucous membranes, and a moderate distension and tenderness in the lower abdomen associated with peritoneal reaction. Laboratory tests revealed microcytic hypochromic anemia, elevated C-reactive protein and lactate dehydrogenase (LDH). Mantoux test was positive (23mm x 20mm). Chest and abdomen radiography were normal. Abdominal ultrasound showed intra-abdominal fluid and complex cystic lesions in the adnexal region. Laparotomy evidenced multiple peritoneal cysts, purulent exudate and frozen pelvis with pyosalpinx. Histology showed granulomatous inflammation with giant multinucleated cells with central necrosis. Ziehl-Neelsen stain was negative. *Micobacteria tuberculosis complex* was isolated in culture. Anti-tuberculosis quadruple therapy and corticosteroids were started, with good clinical response.

Conclusions: Peritoneal and genital TB are uncommon in childhood but, when occurring, they have a high fatality and infertility rate. This case stresses, therefore, that clinicians should be aware of the disease for accurate differential diagnosis, in particular with PID.

ESPID-0460
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

STUDY OF EFFECTIVE TESTS FOR DIAGNOSIS OF MYCOBACTERIUM TUBERCULOSIS INFECTION. - WHAT IS THE BEST DIAGNOSTIC TOOL FOR MYCOBACTERIUM TUBERCULOSIS INFECTION? -

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Background and aim
Many people still suffer from Mycobacterium tuberculosis (TB) infection all over the world. One of the reasons that TB can't be eliminated is difficulty of diagnosis. At the same time TB infection drastically become severe systemic infection for children especially infants. In adult, some studies suggested that Interferon-Gamma Release Assays (IGRA) is regarded as reliable test for TB diagnosis. On the other hand, in children some studies suggested that IGRA treated as controvercial test. The aim of this study is to reveal the most effective method for early and conclusive detection of TB infection in children.
Method
From April 1st 2009 to March 31 2014, 116 children were referred to Kurume university hospital due to contact with TB excretion patients. Twelve children were diagnosed as TB infection. In these cases, we retrospectively investigated the diagnostic plan for TB infection.

Result
Age ranges 6 months to 14 years. Breakdown of definite diagnosis are 8 cases of latent TB infection, 2 cases of TB lymphadenitis and 2 cases of lung TB. Tuberculin skin tests (TST) were tested in 8 cases. And all of those cases were judged as positive. IGRA was tested in all cases. Only 7 cases were detected as positive. In TST positive cases, IGRA positive were only 50%. All lung TB cases were judged as negative by IGRA but detected abnormality by chest CT.

Conclusion
In children definite diagnosis of TB should be judged by multiple test such as chest CT, tuberculin skin test and IGRA.

ESPID-1061
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PERITONEAL TUBERCULOSIS: A DIAGNOSTIC CHALLENGE

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Introduction: We present two cases of Peritoneal Tuberculosis (PTB), a rare manifestation of extra-pulmonary tuberculosis that often presents as a diagnostic challenge.

Case Report: An 11 years-old male and 12 years-old female, previously healthy adolescents, both with an epidemiological background of tuberculosis, presented with asthenia and abdominal distension for more than 4 months. The girl mentioned weight loss and night sweats and the boy vespertine fever.

Both had anemia without leukocytosis and slightly elevated inflammatory markers. Serum protein levels, renal and hepatic function were normal. HIV serology was negative. The ascitic fluid showed elevated leukocytes (predominance of lymphocytes on the boy and polymorphonuclear leucocytes on the girl), reduced glucose, high protein and LDH levels. Girl´s ADA was 251. None had neoplastic cells. Chest and abdominal CT showed “pure ascites without ileitis” and the girl had “hilar enlarged lymph nodes and a pulmonary condensation in the superior left lobe”.

Mycobacterium Tuberculosis was isolated on the boy’s ascitic fluid, sensitive to all first line anti-tuberculous therapy; A presumptive diagnosis of TBP was made on the girl based on epidemiology, clinical findings and elevated ADA levels. Both patients were successfully treated with standard anti-tuberculous therapy. On long term, both are asymptomatic.

Conclusion: PTB is a difficult diagnostic due to non-specific clinical manifestations and the low cultures yield. We intend to alert for the necessity of high level of suspicion and importance of indirect findings (especially ADA levels) for diagnosis.

ESPID-0152
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CHILDHOOD TUBERCULOSIS IN A TERTIARY HEALTH FACILITY IN NORTH EAST NIGERIA 2002 -2012.

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BACKGROUND AND AIMS

TB incidence rate in Nigeria is 388/100,000; with childhood TB emerging a significant contributor. thisdescribes the pattern of childhood tuberculosis from 2002 – 2012.

Method

Review of 2002- 2012 registers from central DOTS unit

Results

55% (117) males and45% (95) females. 32 %(69/213) were 11-15years, 29 %(61/213) were <5years,23 %(50/213)16 – 18 years and 15 %(32/213) were 6-11years. 63 %(134/213)had PTB; 37 %(78/213) had EPTB. Of those with Pulmonary TB, 17 %(24/134) testedpositive for AFB ZN. 81% (110/134) were diagnosed clinically using TB score.AFB was positive in 10 %(2/24) of early morning gastric washings of infantsless than 6 years.

Lymph node TB constituted 57 %(45/78) of EPTB: 84 %(38/45)cervical disease; 16 %(4/45) axillary. Other EPTB were CNSTB 22 %(17/78) withTB meningitis 6/17(35%); Potts disease 4 %(3/78); Abdominal TB 18 %(14/78); Tbulcer of thigh 2/78(4%); 1(2%) case of aural Tb. 62 %(48/78) of EPTB were 9 to 18 years. 45cases of Lymph node Tb showed 100% concordance between Fine Needle Aspiration Cytologyand histology reports.

20 %(44/213) were HIV positive; 70% (31/44) of PTB and 29%(13/44) of EPTB were HIV positive. HIV/TB co- infection was highest in <5year olds, 15% (9/61); lowest in 16 -18years 6% (3/50).

70 %(149/213)completed treatment; 13 %(27/213) died. 74 %(20/27) of the dead hadHIV/TB co-infection.

ESPID-0153
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TUBERCULOSIS BURDEN, TREATMENT OUTCOMES IN CHILDREN AND ADULTS IN A TEACHING HOSPITAL, IN THE POOREST REGION OF NIGERIA; 2002 – 2012.

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BACKGROUND AND AIMS

Nigeria ranks 3rd, amongst countrieswith the highest tuberculosis burden globally. This is to describe the spectrumof the disease.

Method

Review of registers in DOTS centre.

Results

Of 2745 tb patients; 93 %(2554) were new; 213(8%)were 0-18years, 19-55 years 80 %(2130); >55years 17%. 81 %(2029) of adults;63 %(134/213) of children had PTB. 19 %(480/2532) and 37% (78) of adults andchildren had EPTB respectively. Leading EPTB was Tb spine 61 %(288/480) inadults, adenitis 57 %(45/78) in children. Both PTB, 58 %(8/134) and EPTB, 32%(44/134) in children were highest in 10-18years. 24% of adults (560/2310); 17% of children(24/134) were sputum AFB+ by ZN.

81%(2032/2517) of adults tested for HIV; all children 100% (213) tested for HIV.64 %(1296/2032) of adults; 20 %(44/213) of children were HIV +. 88 %(1142/1296)of adult TB-HIV co-infection occurred in 30-39 years; in children was highestin <5 year olds 15 %(9/61). 56 %(1142/2029) of PTB and 30 %(142/480) of EPTB in adultswere HIV+. 70 %(31/44) of PTB; 29% (13/44) of EPTB cases were HIV + amongst children. 2months after treatment,83 %(464/560) of adults were AFB negative.

42 %(1152/2532) of adults; 12% of childhoodcases were transferred out. 13% each of adults (322/2532) and children (27/213)died. 65 %(210/322) of adults; 75 %(20/27) of children with HIV died.

Conclusion

TB/HIV co-infection has high mortality.

ESPID-0553
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

NONTUBERCULOUS MYCOBACTERIAL LYMPHADENITIS IN CHILDREN

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Background and aims: Cervical lymphadenitis is the most common manifestation of Nontuberculous mycobacterial (NTM) disease in children. While the incidence of this infection appears to be increasing the optimal therapy is still controversial. The epidemiology, diagnosis and treatment of a series of children with this condition in Cyprus are described.

Method: 19 children with cervical lymphadenitis by NTM were admitted to our hospital from 2006 to 2014. In all cases a Mycobacterium species was isolated by culture. The patients were followed-up for up to 2 years.

Results: The patients' age ranged from 16 to 55 months.The median time between onset of symptoms and diagnosis was 5 weeks. The tuberculin skin test revealed some induration in 72.2% of cases (4-17mm). Median ESR on diagnosis was 10mm. All patients underwent surgical excision of infected lymph nodes. In 9 patients total removal was not achieved and additional antimycobacterial treatment was given with a clarithromycin including regimen for 3 to 12 months. No complications occurred after surgery. Recurrence occurred in 3 patients, 2 of which had not received postoperative antimycobacterial treatment. All biopsies detected granulomatous lymphadenitis with or without Langhans cells and caseous necrosis. *M.avium* was isolated in fifteen cases, *M.intracellulare* in two, *M.paraffinicum* in one and *M.Kasansii* in one case.

Conclusions: Despite being a rare disease, NTM infections pose a significant morbidity with prolonged treatment regimens, recurrences and family disturbance when present. Surgical excision with or without clarithromycin including regimen was proved to be a safe and effective treatment.

ESPID-0752
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

HOW CAN WE DIAGNOSE TUBERCULOSIS IN CHRONIC PATIENTS?

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Tuberculosis (TB) is still one of the most important three infectious diseases that cause morbidity and mortality in the world. It is aimed to revise the diagnose TB methods in chronic patients and investigate whether the diagnostic criteria can be classified.This prospective study analyzes 726 pediatric patients with chronic diseases (chronic kidney disease, rheumatologic diseases, asthma, diabetes, inflammatory bowel disease). From all patients the PPD and lung film are requested and clinical or laboratorial suspicious cases Quantiferon and lungs tomography were asked. ARB, culture and PCR are considered to diagnose from sputum or fasting gastric juice or any other material. TB is identified in 90 cases out of 171 cases with chronic illnesses (81 control group). In this study we aimed to search whether we can evaluate the criteria that are used for the TB diagnosis for children with chronic disease as major and minor. According to the results we cannot have such a definite classification. Nevertheless, contact with TB (82.7% specificity and sensitivity to 43%), more than 10 mm PPD level (84% specificity and 80% sensitivity), Quantiferon positivity (57.7% specificity and sensitivity 88,6%), systemic use of steroid and the presence of lymph node that is bigger than 10 mm on CT can be considered as strong evidence for TB diagnosis in patients with chronic disease. On the other hand, inhaled corticosteroid use, the presence of pathological findings on chest radiograph (79% specificity and 77.7% sensitivity) and clinical findings (fever, weight loss, cough, sweating) can be regarded as auxiliary evidence.

ESPID-0082
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MULTIFOCAL TUBERCULOSIS INCLUDING MYOCARDITIS IN AN ADOLESCENT

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Background:

Multifocal Tuberculosis is a rare disease in Central Europe but has to be taken in account in migrants with suspicious symptoms.

Multifocal manifestation has been recently described as typical in adolescents of the migrant community in Canada[1,2] and France[3], where pulmonary, peritoneal, pleural, lymphnode, meningeal and splenic involvement could be found.

Our case presented with an additional tuberculous myocarditis in the histologically rarest manifestation – the diffuse infiltrative form.[4,5]

Case presentation:

We describe the clinical course, diagnostic work up and therapy of this patient.

Conclusion:

A high index of suspicion and a thorough diagnostic work up has to be applied in adolescent patients with migratory background and symptoms indicating tuberculosis.

Involvement of the myocardium by TB is rare, but nowadays better diagnostic opportunities in the form of MRI and endomyocardial biopsy can render it into a "curable" form of cardiomyopathy.

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ESPID-0253
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TUBERCULOSIS IN CHILDREN WITH SICKLE CELL DISEASE: DIAGNOSIS AND EVOLUTION IN A FRENCH RETROSPECTIVE STUDY

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Tuberculosis (TB) and sickle cell anemia (SCA) may affect the same population of patients particularly in sub-saharian Africa but also in tuberculosis high incidence urban area in northern countries. However very few data are available in children with SCA developing TB.

The aim of this study was to assess the incidence, the diagnosis features and the evolution of TB in children with SCA. We conducted a monocentric and retrospective descriptive study in the pediatric Hospital Robert Debré, Paris, France.

Among the 264 children evaluated in our institution for TB between 20/03/2000 and 01/06/2013, 9 had SCA (5 males, 4 females). They all had a past history of severe infection. The mean age at TB diagnosis was 11 years old [6-16.5]. Three patients were asymptomatic, six were symptomatic. One child had pulmonary TB, four had an extra pulmonary tuberculosis (osteoarticular lesion, (n=1), or mediastinal lymph nodes, (n=3)). The last four children had both pulmonary and extra pulmonary involvement. Mycobacterium tuberculosis was isolated in 5 out of 9 cases. For 5 patients, therapeutic drug monitoring was performed and allowed a dose adaptation for 2 patients. All the patients recovered after a median 7,77 months duration of anti-TB treatment [6-14] and a median follow up of 31.1 month [6-149] .

Despite the low number of patients, our study highlights that tuberculosis seems to be rather extra-pulmonary and/or disseminated in children with SCA. Risk of tuberculosis should be closely evaluated in the follow up of children with SCA.

ESPID-0917
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PAEDIATRIC CASE SERIES: OCULAR TUBERCULOSIS – A CLUE TO CENTRAL NERVOUS SYSTEM DISEASE

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Background and aims

Ocular TB is a rare presentation of paediatric TB and may be an indicator of disseminated infection including unrecognised CNS disease. We report a series of ocular TB cases at a major UK paediatric hospital raising awareness of this diagnosis and inconsistencies in diagnostic/treatment guidelines.

Method

A retrospective survey of patients with TB with ocular involvement.

Results

Six paediatric patients were identified with ocular TB. One case had lateral rectus palsy. Opthalmological examination identified 3 patients that would not have been otherwise recognised as having CNS TB disease. Diagnostic yield was increased by using combined TST (tuberculin skin test) plus TB-IGRA (TB-interferon gamma release assay), microbiology and brain imaging. All cases were HIV negative. All cases received 12 months TB therapy and 3 cases received topical eye therapy. One case had residual reduced visual acuity. All cases required adjunctive steroid therapy due to significant CNS disease.

Conclusions

TB eye disease in children is rarely recognised and presents in a variety of ways, often with little or no systemic symptoms. Ophthalmology referral can be useful in paediatric patients for whom TB is a differential, even in the absence of visual symptoms. Ophthalmic findings can assist in clarifying the systemic diagnosis. A diagnosis of ocular TB can suggest more widespread disease and alert the clinician to CNS involvement. This in turn will affect management as CNS involvement might entail modified drug choice, a longer treatment course and adjunctive therapy. In addition, the eye lesions themselves may require ophthalmic follow-up.

ESPID-0167
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

INVESTIGATION INTO AN INCREASE IN PAEDIATRIC TUBERCULOSIS INCIDENCE IN GREATER MANCHESTER

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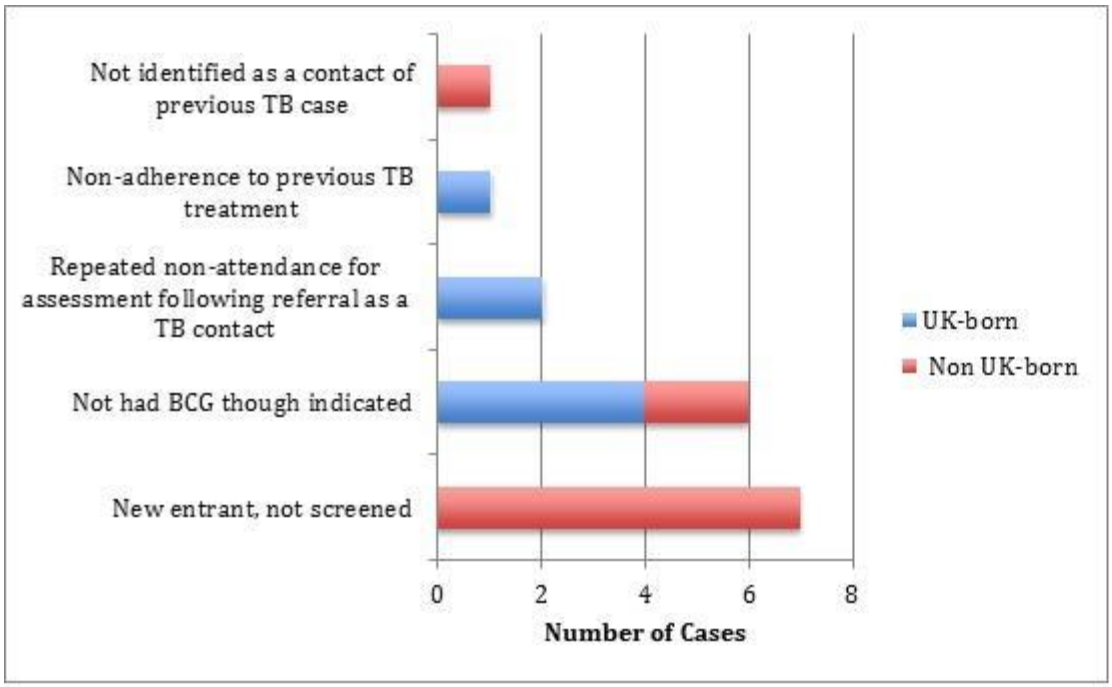
AIMS: From 2003 to 2009 there was an almost 3-fold increasein the incidence of tuberculosis (TB) in children in Greater Manchester (GM).The aim of this investigation was to understand the factors driving thisincrease, with a view to improving prevention and reversing the increasingtrend.

METHODS: Data were prospectively collected from paediatric TBcases diagnosed within GM between 1 January 2012 and 31 December 2013. Informationwas collected from the parents/guardians of each case using a standardised proforma.At the end of the investigation period, teleconferences were held with eachclinical service to assess the potential preventability of reported cases.

RESULTS: 60 TB cases were ascertained during the study period.Proforma were completed for 56/60. 31/56 (55%) were UK-born, 9/56 (16%) were born in Pakistan and countryof birth for the remainder was distributed across 11 different countries. A total of 17 cases (30%) were judged to have been potentiallypreventable. 7/17 of the potentially preventable cases were UK-born.

CONCLUSION:A third of cases were judged to be potentially preventable. The two main themesthat emerged were failure of the new entrant screening process and failure tobe vaccinated with BCG vaccine despite being eligible. It is important toensure effective mechanisms are in place to maximise ascertainment of eligiblenew entrants to the UK. With regards to BCG vaccination, a review ofarrangements across GM is currently underway.

Figure: Factors contributing to preventability of TBinfection by number of cases and country of birth (UK/Non UK-born)


Not identified as a contact of previous TB case
Non-adherence to previous TB treatment
Repeated non-attendance for assessment following referral as a TB contact
Not had BCG though indicated
New entrant, not screened
0
2
4
6
8
Number of Cases
UK-born
Non UK-born

ESPID-0646
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

OUTCOME OF TUBERCULOUS MENINGITIS IN CHILDREN: THE FIRST COMPREHENSIVE RETROSPECTIVE COHORT STUDY IN INDONESIA

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Background. Tuberculous meningitis (TBM) is the most severe extrapulmonary complication of tuberculosis with high mortality and sequelae. The objective of this study was to assess hearing, visual, motor function, neurological and mental development outcomes.

Methods. A cohort retrospective study of 129 TBM children post-hospitalization were followed based on documented TBM registry from January 2007 to December 2010 at Department of Child Health, Dr. Hasan Sadikin Hospital, Bandung. We did home visit and if they could not be found. Hearing function was examined using Brainstem Auditory Evoked Response (BEAR) method, visual acuity using Snellen chart or cardiff, optic disc appearance using indirect ophthalmoscope, motor function using Growth Motor Functional Measurement (GMFM), neurological and mental development using The Griffiths General Developmental Quotient/The Wechsler Intelligence Scale for Children-Third Edition (WISC-III).

Results. Thirty-four (26.5%) of 128 patients were identified death after hospital discharge, 58 patients's address could not be found and 7 parents refused to participate. Of the 29 patients included, 16 male and 13 female has mean age of 44 months old. Almost all patients presented in stage II or III TBM. Hearing loss and low vision/blindness were identified in 11/28 and 10/25 patients, respectively. More than half patients identified had motoric disorder. Neurologic and mental developmental delay was found in nearly three quarter which 11 patients had normal or borderline IQ.

Conclusions. TBM is still high with high mortality and sequelae involving hearing, visual impairment, neurological and mental development. Several survivor could attend regular school.

ESPID-1009
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

ELBOW TUBERCULOSIS DUE TO SUBOPTIMAL TREATMENT: THE IMPORTANCE OF GETTING THE BASICS RIGHT

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Skeletal tuberculosis (TB) represents 1%-3% of TB cases and the elbow joint is not commonly involved. We report a case of an 11-year-old Bangladeshi girl referred to our unit with acute swelling of her left elbow. She had a history of non-resistant pulmonary TB 18 months before, treated with isoniazid, rifampicin and pyrazinamide for 10 months. Six months after completing treatment she was diagnosed with TB lymphadenitis and treatment was restarted. Despite good compliance to treatment she developed a new lymphadenopathy a month later. On physical examination she was afebrile, her left elbow was hot and painful with functional impairment. Laboratory findings were normal except for CRP 4 mg/dl and ESR 98 mm/h. MRI revealed humeral and soft tissue abscesses with anterior cortical rupture (figure) and arthritis. Pus drained from the elbow resulted positive by real time PCR for *Mycobacterium tuberculosis* although cultures were negative. During her admission immunodeficiency was ruled out, including T-cell defect, CGD and IFNg-IL12 axis defects. Reassessing adherence, she confirmed taking her medication but confessed frequent vomiting shortly after intake. Furthermore, the hospital-made pyrazinamide syrup was found to be a heterogeneous solution. Before discharge, medical compliance was assured and medication was given as fixed dose combination pills. Clinical outcome has been favourable during follow-up.
Careful medical history taking and guided questions are key when treatment failure is suspected. Adherence should be addressed in every clinical visit as suboptimal treatment may lead to disseminated TB disease.

T1 weighted sagittal MRI with fat suppression and intravenous gadolinium.

A metaphyseal humeral abscess is depicted (black thick arrow) with anterior cortical rupture (thin white arrow), anterior soft tissue abscess and posterior recess synovial enhancement indicating septic arthritis (white thick arrow).

ESPID-1037
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MYCOBACTERIUM BOVIS ABSCESSES AT AN UNUSUAL SITE: THREE CASE REPORTS

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Introduction: Bacillus Calmette-Guérin (BCG) vaccine contains a live attenuated strain of Mycobacterium bovis. Localized abscess in the site of inoculation is a known complication, however in another location is rare.
Case reports: We describe 3 cases, a 22 months child and two infants with 6 and 7 months, that came to the Emergency Room presenting a swelling in the right thigh, with scarce local inflammatory signs and no significant changes in the overall state. At ultrasound, the swelling was interpreted as possible sarcoma, abscess and hemangioma, respectively. However, the MRI was suggestive of pyomyositis in the first case and abscess in the last. All 3 patients underwent needle aspiration, with subsequent surgical drainage. The polymerase chain reaction for Mycobacterium Tuberculosis (MT) Complex was positive in purulent content. They had a BCG scar on the left arm and didn´t share the place of birth or the primary healthcare center. Quantiferon and MT research were negative. In the first case the mycobacterial direct examination and culture were negative, but acid-fast resistant bacilli and BCG strain were isolated on the other two. All patients started treatment with antituberculosis drugs, with favorable outcome.
Conclusions: Mycobacterium should be considered in the presence of abscess of unknown etiology, particularly in areas where tuberculosis is endemic and BCG vaccine is universally administered. In these cases, authors pose as hypothesis BCG administration intramuscularly in the thigh, probably due to exchange vaccines. The authors wish to draw attention to this issue and reflect the need to adopt preventive measures.

ESPID-0238
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

VISUAL IMPAIRMENT IN TUBERCULOSIS MENINGITIS

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Introduction:
Visual impairment is one of the feared complications of Tuberculous Meningitis (TBM). The pathogenesis is diverse and may involve many factors including raised intra-cranial pressure, compression of optic chiasm and direct involvement of the optic nerve and may lead to blindness which is mostly irreversible. Here, we report three such cases with dimished vision of varying extent and history of fever;
Cases: A 3 ½ year old boy with non-reactive, mid-dilated pupils, bilateral abducent nerve palsy and optic pathway dysfunction; a 15 year old girl with optic neuritis, diminished direct and consensual light reflexes, fixed, dilated pupils, and weak ocular movements and a 14 years old boy with anisocoria, right occulomotor and left abducent nerve palsies, pale optic disc with visual acuity of 20/150 bilaterally.The patients responded well to ATT and supplemental steroids.
Conclusion:Since TB is treatable and to a great extent preventable, it deserves international priority to increase the awareness about its possible complications and the need to manage these patients before any of the complications set in. The patients responded well to Anti TB treatment. Therefore it is necessary to identify vision impairment early in TBM and initiate treatment promptly especially in our country which ranks fifth on the list of countries with a high burden of TB worldwide, according to the worldHealth Organization (WHO) estimates.

Table 1: Comparison of CSF Analysis of study patients

CSF Analysis	Case 1	Case 2	Case 3
Glucose	72	22	62
Protein	44	103	42
TLC	10	95	15
N/L	30/70	10/90	10/95
RBC	4	30	25
AFB Culture	negative	negative	negative
AFBPCR	negative	negative	negative

Table 2: Clinical and Radiological Features of patients before and after treatment with antituberculous therapy and steroids.

	Case 1	Case 2	Case 3
Age (years)	3.5 years	14 years	15 years
Gender	Male	Female	Male
Diagnosis of TBM	TBM with visual impairment	TBM with optic neuropathy and caudate lobe infarct	Complicated TBM with communicating hydrocephalus +cranial nerve palsies
Ophthalmological findings before treatment	Suggestive of optic neuritis VEP: bilateral optic pathway dysfunction	Suggestive of optic neuritis VEP: Normal	Suggestive of optic neuritis VEP : relative integrity of optic Visual field: Right: 79% Left : 95%
Ophthalmological findings after treatment	Lost to follow up	Lost to follow up	Lost to follow up
MRI findings before treatment	Moderate ventricular dilation of all ventricles suggestive of communicating hydrocephalus, slight meningeal enhancement of the cortical sulcus and basal cisterns:	Multifocal acute infarctions with multiple small tuberculomas within the brain parenchyma involving both supra and infratentorial compartments .These are associated with diffuse nodular enlargement more marked in basal region	Not done
CT findings before treatment	Showed evidence of hydrocephalus involving all the ventricles and diffuse cerebral edema in the left cerebral hemisphere close to the vertex with effacement of cortical sulci and gyri. The possibility of impending ischemia in left cerebral hemisphere cannot be entirely excluded	Redemonstration of multifocal established infarcts, mild hydrocephalus, infratentorialtuberculomas and diffuse, nodular leptomeningeal enhancement. No new abnormality identified.	Ventricular dilatation and cerebral edema. Multiple hypo attenuating partly defined rounded area in basal ganglia and thalamus bilaterally

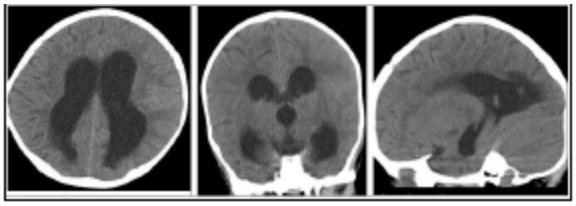

Fig 1: CT head showing evidence of hydrocephalus involving all the ventricles and diffuse cerebral edema in the left cerebral hemisphere close to the vertex with effacement of cortical sulci and gyri. The possibility of impending ischaemia in left cerebral hemisphere cannot be entirely excluded.

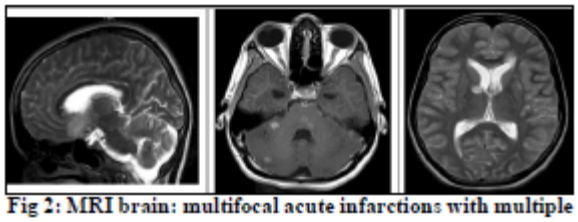

Fig 2: MRI brain: multifocal acute infarctions with multiple small tuberculomas within the brain parenchyma involving both supra and infratentorial compartments. These are associated with diffuse nodular enlargement more marked in basal region.

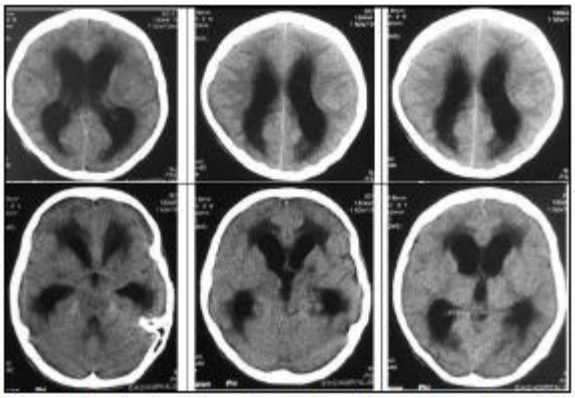

Fig 3: Ventricular dilatation and cerebral edema. Multiple hypo attenuating partly defined rounded area in basal ganglia and thalamus bilaterally.

ESPID-0227
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TUBERCULOSIS IN INFANTS

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Background and aim: Children younger than 12 months of age have up to 50% risk to develop tuberculosis (TB) disease following infection. They also have an increased risk of severe forms of the disease. Here we evaluated the clinical picture of TB in infants.

Methods: The medical records of 11 children younger than 12 months of age followed at our department with a diagnosis of TB between November 2007-October 2014 were reviewed.

Results: Median age of the children was 5 months (min:2 months, max:10 months). The most common symptoms were cough (72.7%), wheezing (63.6%), and fever (45.4%). Source cases in the families were identified in 10 (90.9%) of the cases. All infants had pulmonary TB. Extra pulmonary TB accompanied in 3 (27.2%) cases. One had central nervous system (CNS) TB and two had disseminated TB. One of the cases with disseminated TB had pulmonary, CNS, and hepatosplenic involvement, and the other one had pulmonary, lymph node, bone, cutaneous and CNS TB. Mycobacterium tuberculosis was isolated in the early morning gastric aspirate samples of 6 (50%) cases. Two infants diagnosed within the last 2 years had multidrug resistant (MDR)-TB. Ten cases recovered completely with antituberculous treatment. The last case is still on therapy.

Conclusion: Infants are the most risky population for TB and severe forms of disease after exposure/infection. They should be followed up closely after exposure. Besides, MDR-TB should be kept in mind for young children, too.

ESPID-0243
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MULTIDRUG-RESISTANT DISSEMINATED TUBERCULOSIS IN A NINE-MONTH-OLD INFANT

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Background and aim: Confirmed multidrug resistant-tuberculosis (MDR-TB) in children is usually undetected, and little is known about the clinical profile, treatment, and prognosis of MDR-TB in children. Here, we report an infant with disseminated MDR-TB.

Case report: A nine-month old girl was admitted to our department with a two-month history of swelling on her neck and a draining lesion on her right forearm. Her uncle had been diagnosed with MDR-TB five months ago. Physical examination revealed multiple lymph adenopathies in the right cervical region and a fluctuated, hyperemic lymph node in the left cervical region. A draining lesion on her left forearm was also observed. Direct microscopy of the lymph node exudate showed acid-fast bacilli. X-ray assay of the right extremity showed osteolytic lesion in the distal end of the right ulna, with soft tissue heterogeneity extending to the skin surrounding the bone. Cranial magnetic resonance imaging assay revealed multiple ring-enhancing lesions in the cerebral and cerebellar hemispheres. Mycobacterium tuberculosis was isolated from the gastric aspirate sample and lymph node exudate, and it was resistant to isoniazid, rifampin, ethambutol, and streptomycin. High dose of isoniazid (18 months), pyrazinamid (9 months), amikacin (4 months), levofloxacin (18 months), linezolid (3 months), cycloserine (18 months), and clofazimine (18 months) were given to the patient. She recovered completely.

Conclusion: Child contacts of infectious MDR-TB source cases should be closely followed up for a minimum of two years. Appropriate treatment should be given as soon as TB is diagnosed.

ESPID-0118
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

A CASE REPORT OF MYCOBACTERIUM INTRACELLULARE INFECTION PRESENTED WITH MASSIVE INTRAABDOMINAL LYMPHADENOPATHY

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The most common forms of Nontuberculous mycobacteria (NTM) in children are cervical lymphadenopathy, skin and soft tissue infections, and disseminated disease in immunocompromised patients.

Here in we present a case with massive intraabdominal lypmhadenopathy due to *Mycobacterium intracellulare*.

Case: He was a 3 years-old-boy of consanguineous Azerbaijan parents who was transferred to our hospital from Iran. In Iran, he had chemotherapy with the diagnosis of Histiocytosis X. He transferred to Turkey because of lack of response to therapy at the end of 2 months. He had massive (biggest one is 4x5 cm in diameter) and multipl intraabdominal lymphadenopathy. To strenghten the diagnosis, biopsys was repeated from mesenteric lymph nodes and the new biopsy showed multiple irregular histiocytes which were full with acid-fast bacilles. Izoniasid, rifampicin, ethambutol, pyrazinamid and chlarythromycin therapy was given for two months. Lymph node PCR was performed for mycobacterial strains and it was 100% consistent with *M. intracellulare.* Then the therapy changed to linezolid, levofloxacin, azithromycin, rifabutin and amikacin combination. His lymphocyte subset analysis, immunoglubuline levels and di-hidro-rhodamin tests were normal and HIV serology was negative. Interferon-gamma therapy was started with presumed diagnosis of Mendelian Susceptibility to Mycobacterial Diseases. The genetic analysis of possible mutations was not resulted yet. The diameter of abdominal lymph nodes decreased after 3 months with antimicrobial therapy. His clinical condition improved and he gained weight.

Atypical mycobacterial infections in children are an important clue for rare primary immundeficiency syndromes especially if there is a consanguineous marriage history.

ESPID-0197
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CUTANEOUS TUBERCULOSIS IN A CHILD WITH ANIMAL CONTACT

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Tuberculosis is still common in Turkey. Cutaneous tuberculosis is a rare form of extrapulmonary tuberculosis. We describe a case with cutaneous tuberculosis (lupus vulgaris) after contact with a sheep. **Case:** A 15- years-old boy admitted to our hospital with prolonged wound on left index finger and left axillar lymphadenopathy. In history, he cut his finger when he was slaughtering a sheep three months ago. One month after his injury, his left axillar lymph node enlarged at the same side with his wound and the wound became dark-black. The skin and lymph node biopsies were showed granulomatous reaction but acid fast bacilli (AFB) could not be shown with Ehrlich-Ziehl Neelsen (EZN) stain. Interferon-gamma releasing assay test was positive. His thorax computerized tomography was normal and sputum/gastric lavage were negative for AFB . His wound and axillary lymphadenopathy were disappeared after anti-tuberculosis therapy for 6 months. **Conclusion:** Chronic skin lesions with granulomatous reaction should be considered for tuberculosis in countries with high tuberculosis prevalence.

ESPID-0507
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

A 15 YEAR OLD GIRL PRESENTING WITH AN UNUSUAL NECK MASS

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Aim

To present a case of tuberculosis presenting with an unusual thyroid mass and review related literature.

Methods

We present the patient's history, examination, results and management.

Results

A 15 year old girl presented with 1-week history of lethargy, pallor, dysphagia and midline anterior neck swelling. Past medical history revealed successful treatment of miliary tuberculosis 2 years earlier, On examination she had a large solid midline neck swelling, 5cm width, Fig 1. Ultrasound revealed a cystic cavity filled with necrotic tissue pushing into the thyroid gland. MRI showed a large mass extending from midline infrahyoid neck into the mediastinum, Fig 2. Fine-needle aspiration cytology showed abundant necrotic debris, with interspersed degenerate neutrophils and macrophages. Auramine stain showed small numbers of acid fast bacilli. GeneXpert was positive for Rifampicin sensitive *Mycobacterium tuberculosis* confirmed to be fully sensitive on culture. She was diagnosed with extra-pulmonary thyroid tuberculosis and anti-tuberculosis treatment was commenced with worsening of symptoms. She subsequently required multiple aspirations to avoid upper airway obstruction and spontaneous rupture/fistula formation. She required high dose steroids over several weeks.

Conclusions

Thyroid tuberculosis is a rare condition even in endemic areas. As far as we know this is the first paediatric case of thyroid tuberculosis reported in the UK. This case reflects an unusual diagnosis of paediatric thyroid tuberculosis and treatment complications. Paediatricians should have a low threshold for tuberculosis in the differential of any unexplained mass.
Figure 1: Neck mass at presentation

Figure 2: MRI neck

(F)

ESPID-0763
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MANAGEMENT AND OUTCOME OF PAEDIATRIC LATENT TUBERCULOSIS INFECTION IN A LOW BURDEN COUNTRY – A SINGLE CENTRE RETROSPECTIVE ANALYSIS

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Introduction:

There is a paucity of data on the management and outcome of children with latent tuberculosis infection (LTBI) in low burden countries.

Methods:

Retrospective descriptive case series of children diagnosed with LTBI between 01/2009-02/2014 at Charité Universitätsmedizin, Berlin. Diagnosis of LTBI was based on tuberculin skin test (TST) and/or interferon- γ-test (Quantiferon®) without radiologic (chest-x-ray) or clinical signs of TB disease. Children were followed for 2 years after chemopreventive therapy including clinical evaluations and chest-x-ray. During chemopreventive therapy patients were evaluated at least twice for side effects and adherence.

Results:

Seventy-eight children were included, 33 male (42.3%), median age 9.7 years, 26 (33.3%) were BCG vaccinated; no child was HIV-infected. Index case was known in 56 (71.8%) children, of those 7 (12.3%) were exposed to drug-resistant TB. Initial TST was available in 69/78 (88%) children [positive 63/69 (91.3%), negative in 6/69 (8.7%)], initial Quantiferon® in 52/78 (66.7%) children [positive 44/52 (84.6%), negative 8/52 (15.4%)]. Except for one child all children received chemopreventive therapy: 6-9isoniazid (INH) in 13/78 (16.7%) children, 3INH/rifampicin (RMP) in 56/78 (71.8%), 4RMP (index case with INH resistance) in 5/78 (6.4%), 3 children received individualised regimens (index cases with multi drug resistant TB).

Adverse events with discontinuation of treatment were recorded in 2/78 (2.5%) children. No child showed elevated liver enzymes or clinical signs of hepatotoxicity. None of the children developed TB disease.

Conclusion:

Chemopreventive therapy for LTBI in children consisting of either INH and/or RMP is safe and may efficiently prevent progression to TB disease.

ESPID-0506
TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

ATYPICAL MYCOBACTERIA IN PAEDIATRIC CYSTIC FIBROSIS PATIENTS: EXAMINING CHANGES IN COLONIZATION RATES AND STRAIN DISTRIBUTION.

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Background and Aims

Cystic Fibrosis (CF) patients can be colonized or infected with atypical mycobacteria (ATB) amongst which, *M.abscessus* is considered most pathogenic. An apparent increase in *M.abscessus* detection in paediatric CF patients attending our centre, from 2011, necessitated examination of local colonization rates and risk factors. Genetic relatedness of strains was compared and Infection Control Specialists examined the potential for cross infection events.

Methods

- The Scottish Mycobacteria Reference Laboratory provided data on all Glasgow respiratory ATB isolates. Patient CHI numbers were cross matched with the registry of adult CF patients.

- Retrospective data on paediatric ATB isolates were retrieved from the Microbiology computer system and historical CF databases.

- Isolates of *M.abscessus* were sent to PHE, Colindale, for genetic analysis.

Results

A genuine increase in ATB colonization amongst our paediatric CF population was confirmed. Sampling patterns varied over time but isolation rates were independent of numbers of sputum samples and patients tested.

When all ATB strains isolated from respiratory medicine patients were compared *M.abscessus* had a clear predilection for CF patients across the age groups.

Five of 14 paediatric patients colonized with *M.abscessus* harboured strains belonging to clonal lineage ST26. Of the 5, none had any direct contact or epidemiological evidence of cross infection. Remaining patient isolates were distinct.

Conclusions

Since diverse ST26 strains have been reported in the context of CF, further genetic analysis including whole genome sequencing may be required to determine any relatedness between isolates and assess the impact of specific strains.

ESPID-0112
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

VIRAL ETIOLOGY OF RESPIRATORY INFECTIONS IN CHILDREN IN SOUTHWESTERN SAUDI ARABIA USING MULTIPLEX REVERSE-TRANSCRIPTASE POLYMERASE CHAIN REACTION

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Objectives: To investigate 15 respiratory viruses in children with acute respiratory tract infections (ARTIs) using multiplex reverse-transcriptase polymerase chain reaction (RT-PCR), and to analyze the clinical andepidemiological features of these viruses. Methods: In a cross-sectional study, 135 children, ≤5 yearsof age who presented with ARTIs in Najran Maternity and Children Hospital, Najran, Saudi Arabia between October 2012 and July 2013 were included. The clinical and sociodemographic data, and the laboratory results were recorded using a standardized questionnaire. Two nasopharyngeal swabs were collected from each child: one for bacteriological examination, and the second for viral detection using multiplex RT-PCR. Results: A single viral pathogen was detected in 76 patients, viral coinfections in 9, and mixed viral and bacterial pathogens in 15. Respiratory syncytial virus was isolated in 33 patients, human rhinovirus (hRV) in 22, adenovirus (AdV) in 19, human metapneumovirus in 13, influenza virus in 10, parainfluenza virus in 7, human corona virus (hCoV) in 4, and human bocavirus in one. Conclusion: Respiratory syncytial virus, hRV, and AdV were the most frequent viruses, accounting for more than two-thirds of the cases. Other viruses, such as MPV, hCoV NL63, and hCoV OC43, may play a role in pediatric ARTIs. Of significance is the potential use of multiplex RT-PCR to provide epidemiological and virological data for early detection of the emergence of novel respiratory viruses in the era of the Middle East respiratory syndrome coronavirus.

ESPID-0850
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PULMONARY INFECTION WITH S.AUREUS IN PATIENTS WITH CYSTIC FIBROSIS

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Aim. Evolutionary research of *S.aureus* pulmonary infection frequency in children with cystic fibrosis (CF) in the Republic of Moldova.

Methods. The study presents an analysis of pulmonary infection with *S. aureus* in children with CF carried out for 5 years (2010 – 49 patients, 2011 – 55 patients, 2012 – 58 patients, 2013 – 62 patients, 2014 – 61 patients). To identify the etiology of pulmonary infection was performed seeding sputum, bronchial and pharyngeal secretion with diagnostic titer determination. The diagnosis of CF was confirmed in all children with sweat test (>60 mmol/l) and/or diagnosis of CFTR mutations.

Results. Colonization of the respiratory system with *S.aureus* in infant child with CF, in this period, is increasing from 50% (2010) to 75% (2014). In children with CF from 1 to 7 years this infection persists in 52-64%. In children between 7-18 years *S.aureus* pulmonary infections is increasing from 37,5% (2010) to 64% (2014). Pulmonary infections with *S.aureus* in patients >18 years with CF is diagnosed in 30-50% cases. Generally the frequency of *S. aureus* lung infection in patients with CF in Moldova in the period 2010-2014 varies from 50% to 57%.

Conclusions. *S.aureus* pulmonary infection in patients with CF is installed in the infant age and persists with an insignificant reduction in this period of children and adults with CF.

ESPID-0423
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

Unusual presentation of mycoplasma pneumoniae infection with fever without focus: report of 3 cases

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Mycoplasma infections are common *and* cause a wide variety of clinical manifestations in children. Herein we present an unusual manifestation of mycoplasma infection presented with fever without focus initially.

CASE 1.

A 3 year-old-girl complaining about fever for 12 days despite of a prolonged beta-lactam therapy. She had no other complaints. Physical examination revealed no localizing signs. She was hospitalized and on the second day rales occured at middle zone of the right lung and chest X ray is shown in figure 1.

Figure 1.

CASE 2.

A 10 year-old-girl was consulted with fever accompanied by mild headache for the last 2 days. Her physical examination was normal initially. During follow up dyspnea and rash occured (figure 2-3).

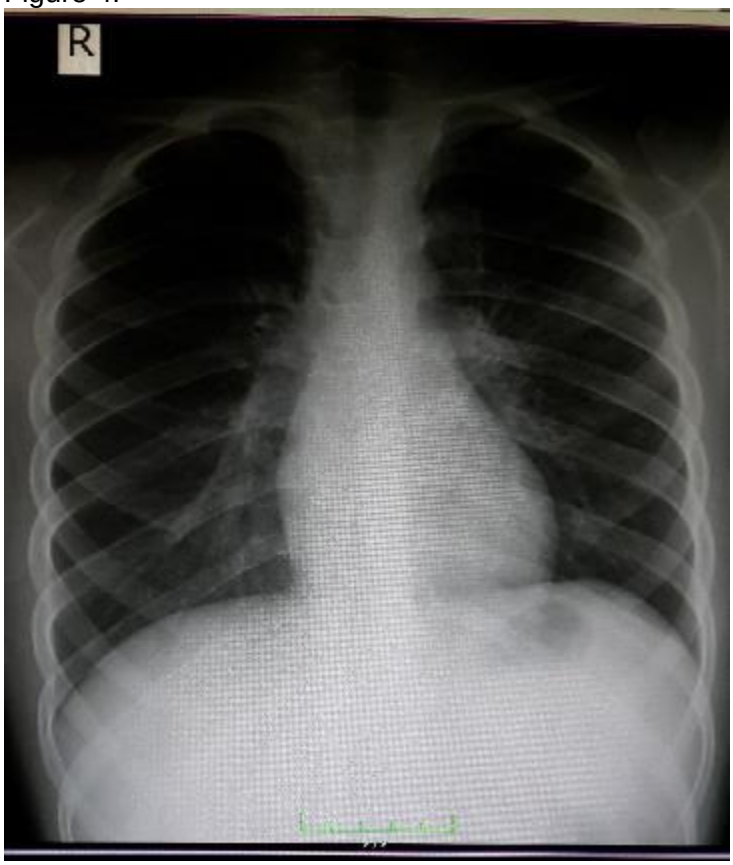
Figure 2.

Figure 3.

CASE 3.

A 9 year-old-boy was complaining about fever for a month. Cough, joint pain and malaise accompanied for the last 2 weeks unresponsive to beta lactam therapy. Initial physical examination was normal. After a few days of hospitalization rales were determined on the left lung. There were bilateral infiltration on the chest X-ray (figure 4).

Figure 4.



Nasopharyngeal viral multiplex PCR was negative but mycoplasma PCR was positive for all three cases. All patients responded well to macrolid therapy.

CONCLUSION: Symptoms and signs of *M. pneumoniae* infection are not unique and abnormalities on physical examination can be minimal initially. Pulmonary symptoms may start to occur later on the course of the disease.

ESPID-0712
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

AMINOPENICILLIN PREFERENCE FOR CHILDHOOD COMMUNITY-ACQUIRED PNEUMONIA IN EUROPE VARIES BY PRACTITIONER TYPE AND REGION

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Background/aims: International guidelines recommend aminopenicillins as first line therapy for mild-moderate suspected community-acquired pneumonia (CAP) in childhood. We compared the regional preferred first-line antibiotic choices of European primary care paediatricians (PPs) and general/family practitioners (GPs) for this indication.

Methods: A targeted cross-sectional online survey was conducted in 2014 amongst 1574 members of the European Academy of Paediatrics Research in Ambulatory Settings network (EAPRASnet). The survey was also distributed to approximately 100 GPs through PREPARE (Platform for European Preparedness Against (Re-emerging) Epidemics). Differences in proportion of PPs and GPs expressing aminopenicillin preference for younger and older children were evaluated using $\chi 2$ or Fisher's exact test.

Results: The EAPRASnet response rate was 46.4% (n= 730, 528 PPs, 54 GPs, 148 other) with 78 additional responses obtained through PREPARE (74 GPs, 3 PPs, 1 other). The results for comparisons of PPs and GPs by European region are shown in Tables 1 and 2.

≤5 year-olds		North Europe		East Europe		South Europe		West Europe	
		n	% (95%CI)	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Type of physician	PP	9	77.8 (48.0-97.2)	85	27.1 (18.0-37.8)	323	66.9 (61.4-72.0)	114	49.1 (39.6-58.7)
	GP	49	91.8 (80.4-97.7)	34	44.1 (27.2-62.1)	28	71.4 (51.3-86.8)	17	88.2 (63.6-98.5)
p-value		0.231		0.071		0.622		0.002	

Table 1: % GPs and PPs preferring aminopenicillin for treatment of CAP in children ≤5 years of age by European region

>5 year-olds		North Europe		East Europe		South Europe		West Europe	
		n	% (95%CI)	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Type of physician	PP	9	55.6 (21.2-86.3)	85	14.1 (7.5-23.4)	323	30.0 (25.1-35.4)	114	27.2 (19.3-36.3)
	GP	48	85.4 (72.2-93.9)	33	27.3 (13.3-45.5)	28	39.3 (21.5-59.4)	17	76.5 (50.1-93.2)
p-value		0.059		0.094		0.309		<0.001	

Table 2: % GPs and PPs preferring aminopenicillin for treatment of CAP in children >5 years of age by European region

Overall, PPs showed slightly lower aminopenicillin preference than GPs for both ≤5 and >5 year-olds and across all regions. However, this difference was statistically significant only for respondents from Western Europe. Except for Northern Europe and Western European GPs, both GPs and PPs reported lower aminopenicillin preference for older children.

Conclusions: Aminopenicillin preference for treatment in Europe varies by region and practitioner type. The reasons for this and implications for community antibiotic stewardship need to be explored further.

ESPID-0754
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DETECTION OF MYCOPLASMA HOMINIS, UREAPLASMA PARVUM AND UREAPLASMA UREALYTICUM IN SEQUENTIAL, NEONATE CLINICAL SAMPLES USING A NOVEL MULTIPLEX ASSAY.

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Background and aims

Mycoplasma hominis and *Ureaplasma* species are associated with infections in neonates (pneumonia, bacteremia, meningitis, abscesses and chronic lung disease). This study established a quantitative real-time PCR to simultaneously detect *M. hominis*, *U. urealyticum* and *U. parvum* in neonate clinical specimens to improve current clinical diagnostic services.

Methods

The multiplex assay developed included two gene targets; *yidC* gene of *M. hominis, ureaseB* gene of *Ureaplasma* species with species-specific probes and control. Specificity and sensitivity were determined. Endo-tracheal secretions were tested from 53 intubated, preterm neonates (anonymised; Plymouth) and 6 intubated, preterm neonates treated with clarithromycin (clinical diagnosis samples; Cardiff).

Results

The assay was 100% specific and had positive predictive values of 81.82% and 82.86% and negative predictive values of 98.11% and 92% for *U. urealyticum* and *U. parvum*, respectively, when compared to culture. A total of 238 clinical samples were tested of which 6 were positive for *M. hominis*, 23 were positive for *U. urealyticum* and 52 were positive for *U. parvum*. Four mixed infections were identified. Treatment with clarithromycin cleared *U. parvum* infection by 48 hours post-treatment in 4 out of the 6 neonates however 2 neonates tested PCR positive for *U. parvum* at 48 hours and 72 hours post-treatment, respectively.

Conclusions

In conclusion, we developed a specific, sensitive and reproducible real-time PCR to detect *M. hominis*, *U. ureaplasma* and *U. parvum* in oral clinical samples. This PCR assay was used to successfully diagnose infections in neonatal samples and monitor infection levels over the period of intubation.

ESPID-0527
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PREVALENCE OF DIFFERENT RHINOVIRUS SPECIES IN HOSPITALIZED AND NON-HOSPITALIZED CHILDREN IN THE NETHERLANDS

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Background and aims: Rhinovirus(RV) infections are frequently occurring respiratory infections in young children. Epidemiology and clinical significance of RV types (A,B or C) are far from clear. Some studies suggest RV-C might cause more severe disease than other RV-species. Our aim is to compare the prevalence of RV-species and association with clinical symptoms in RV-infected non-hospitalized and hospitalized children.

Methods: Non-hospitalized children were selected from an unselected birth cohort in the Netherlands (EUROPA-study, focusing on prediction of early signs of asthma). Hospitalized children were identified from RV-positive nasopharyngeal samples (NPS). All RV-positive-NPS, detected using qPCR and collected from November 2009 till December 2012, were typed and analyzed.

Results:121 RV-positive NPS from 114 children (49 hospitalized,65 non-hospitalized) were analyzed. The most prevalent RV-species in both groups was RV-A (n=67) with a prevalence of 48.1% in hospitalized and 60.9% in non-hospitalized children. RV infected hospitalized children were younger than non-hospitalized children (p=0.014). An RV-B-infection was the least identified (9.9%). The prevalence of RV-C in hospitalized children did not significantly differ from the prevalence in non-hospitalized children (40.4% versus 30.4%).Subgroup analysis of children admitted to the ICU revealed that 53.8% of RV-infected children were infected with RV-A and 34.6% with RV-C.

Conclusions:RV-A is the most dominant species in both studygroups. The distribution of RV-species in hospitalized and non-hospitalized children did not significantly differ. In children admitted to the ICU the prevalence of RV-A and RV-C was comparable, suggesting that RV-A and RV-C are equally capable of inducing severe disease in young hospitalized children.

ESPID-0670
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ANTIBODY RESPONSES TO STREPTOCOCCUS PNEUMONIAE, HAEMOPHILUS INFLUENZAE AND MORAXELLA CATARRHALIS IN CHILDREN WITH OR WITHOUT RADIOLOGICALLY CONFIRMED PNEUMONIA

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Background and aims: Acute lower respiratory tract disease (ARLI) is an important cause of child morbidity, particularly community-acquired pneumonia (CAP). The role of chest radiograph to distinguish probable aetiological agents of ALRI is still to be defined. We aimed to evaluate the predictive role of a radiological diagnosis of pneumonia for the detection of antibody responses against typical bacterial agents of CAP.

Methods: We compared the frequency of antibody responses and the level of antibodies at admission against *Streptococcus pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis* inchildren with ARLI aged 2-59 months with or without radiologically confirmed pneumonia (n=249 and 366, respectively). Antibody responses were studied as a ≥1.5-, 2-, and 4-fold increase in the antibody levels.

Findings: Radiological pneumonia was independently associated with detection of antibody responses against the studied bacteria increasing the odds from 1.764 to 3.451 times depending on the threshold-fold increase applied. The negative predictive value of the normal chest radiograph for the detection of antibody responses against typical bacterial agents of CAP varied from 68.58 to 96.45%.

Conclusion: Children with ARLI and radiological pneumonia present a higher rate of antibody responses against bacterial agents of CAP than those with a normal chest radiograph.

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ESPID-1028
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

BACTEREMIA IN HOSPITALIZED CHILDREN WITH RESPIRATORY SYNCYTIAL VIRUS INFECTION

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Introduction: Bacteremia risk is considered low in children with acute bronchiolitis and fever. However the concrete rate of occult bacteremia in infants with RSV infection is not well established. Objective: Determine the actual rate and predictive factors of bacteremia assessed by both conventional culture and molecular techniques in children admitted to hospital due to confirmed RSV acute respiratory illness. Methods: A prospective multicenter study (GENDRES-network) was conducted between 2011-2013 in children under the age of 2 admitted to hospital because of an acute respiratory infection. Among those RSV positive, bacterial presence in blood was assessed using PCR for Meningococcus, Streptococcus pneumoniae, Haemophilus influenzae, Streptococcus pyogenes, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus in addition to conventional cultures. Results: 66 children with a positive RSV respiratory illness were included. In 10.6% patients bacterial presence was detected in the blood, predominantly H.influenzae (n=4); S.pneumoniae (n=2). In those patients with bacteremia there was a previous suspicion of bacterial superinfection in 5 of 7 patients (71.4%) and 6 of 7 (85.7%) had received empirical antibiotic therapy. There were significant differences in terms of severity between children with positive or negative bacterial PCR: PICU admission (100% vs. 50%, P-value=0.015); respiratory support necessity (100% vs. 18.6%, P-value

ESPID-0605
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

IDENTIFYING RHINOVIRUS THROUGH RT-PCR USING NASOPHARYNGEAL ASPIRATE OR NASOPHARYNGEAL SWAB IN CHILDREN IN MIDWEST BRAZIL

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Background and aims: Viral respiratory tract infections in children are responsible for the majority of medical visits and hospitalizations worldwide. However, identifying respiratory pathogens in children requires choosing the best sampling method. The objective of this study is to compare positivity rates of rhinovirus through RT-PCR between nasopharyngeal aspirate (NPA) and nasopharyngeal swab (NPS).

Methods: In this cross-sectional study, 72 children (ages 4 to 14) with acute respiratory infection (ARI) were selected between August-2012 and August-2013 in Goiania, Brazil. Respiratory secretions were collected through NPA or NPS and tested for rhinovirus through a RT-PCR kit. The study was approved by the ethics committee of the Federal University of Goias. Statistical analysis were performed using SPSS v.20 software (SPSS Inc., Chicago, IL). The Exact Fisher test compared variables between sampling methods; p-value <0.05 was considered significant.

Results: Samples of respiratory secretions were obtained from 72 children with ARI. In 59 (81.9%) of them, samples were collected through NPA while in 13 (18.1%) of them through NPS. The positivity for rhinovirus were respectively 91.5% (54/59) and 76.9% (10/13) (p=0.151).

Conclusions: The results of nasopharyngeal swab were similar to nasopharyngeal aspirate for rhinovirus detection using RT-PCR, allowing both to be useful for surveillance for rhinovirus in children.

ESPID-0869
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DETECTION OF MYCOPLASMA PNEUMONIA IN CHILDREN WITH RESPIRATORY INFECTIONS: A SINGLE CENTRE RETROSPECTIVE ANALYSIS

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Introduction

M. pneumonia (MP) infection can be diagnosed by detection of MP-DNA from nasopharyngeal swabs (NPS). A recent study suggests detection of MP-DNA is common in symptomatic and asymptomatic children. The aim of this study was to investigate the frequency of MP-DNA in NPS from children with respiratory tract infections (RTI) and to describe clinical characteristics and management.

Methods

NPS were routinely taken from children with clinically severe RTI presenting to the emergency department and analysed using Respifinder (Pathofinder, Maastricht, Netherlands). Results from June 2010 to December 2014 were analysed and clinical data were extracted from hospital records for MP-positive patients.

Results

In 4499 samples analysed over 4.5 years, 70 (2%) were positive for MP-DNA. Complete medical records were available in 64 patients. Median age was 6.5 (IQR 2.8–9.8) years, 60% were male and 66% presented during autumn/winter. 66% were admitted and 27% required oxygen. Co-infection with other organisms detected by Respifinder was found in 19%, with rhinovirus most frequently detected. 88% were treated with a macrolide: 5 before presentation, 25 at presentation and 27 patients after detection of MP-DNA. Children with treatment at presentation compared to after detection of MP-DNA were statistically not different for age, oxygen requirement or duration of hospitalisation.

Conclusions

Detection of MP-DNA in children with RTI is rare in our setting. This is in contrast to other studies that detected MP-DNA in up to 16% of cases. Detection of MP-DNA influenced antibiotic treatment. Factors influencing detection rates of MP-DNA need to be further determined.

ESPID-0601
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

BIOMARKERS AND CLINICAL OUTCOMES IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA

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Background: Host biomarkers reflect the host's response to infection. We aimed to determine the association of host biomarkers and disposition outcomes in children with community-acquired pneumonia (CAP).

Methods: This is a prospective cohort study of pediatric CAP severity at a single, urban, academic emergency department (ED) in the US. Eligible patients are ages 3 months to 18 years with a lower respiratory tract infection and a focal opacity on chest radiograph. Patients with recent hospitalization or chronic medical conditions were excluded. White blood cell (WBC) count, C-reactive protein (CRP) and procalcitonin were obtained at ED visit. Proadrenomedullin was performed retrospectively. The primary outcomes were patient disposition and ICU admission. We compared median values using the Mann-Whitney test.

Results: The mean age of the 51 included patients was 5.3 years (SD, 4.4) and 61% were female. Mean duration of illness was 5.4 days (SD, 4.5). Differences in the 4 biomarkers between admitted (n=40) and discharged (n=11) patients are shown in Figure 1 and between those who required intensive care (n=4) and those who did not (n=47) are shown in Figure 2.

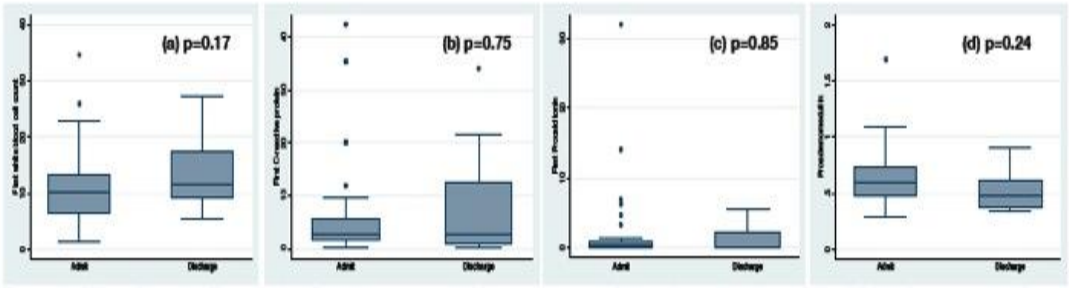

Figure 1. White blood cell count (a), C-reactive protein (b), procalcitonin (c), and proadrenomedullin (d) levels of patients by disposition (admitted to hospital vs. discharged home)

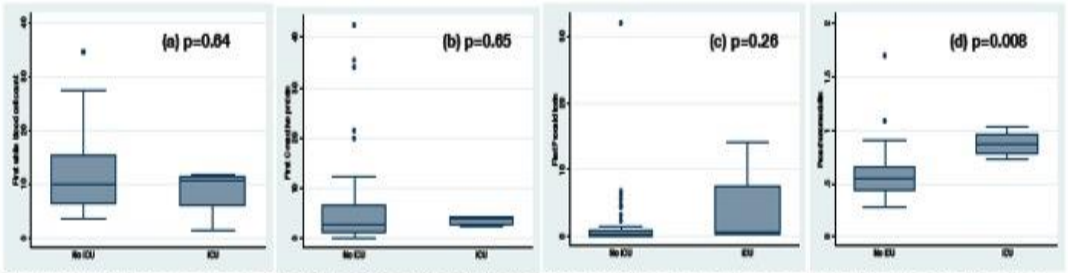

Figure 2. White blood cell count (a), C-reactive protein (b), procalcitonin (c), and proadrenomedullin (d) levels of patients by need for intensive care (no ICU vs. ICU)

Conclusions: WBC count and CRP do not significantly differentiate patients who require hospitalization or intensive care. Proadrenomedullin levels were significantly elevated in patients who required intensive care compared with those who did not. This preliminary data suggests that proadrenomedullin may provide the strongest discrimination of disease severity in children with CAP.

ESPID-0499
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

FREQUENCY, SEASONALITY AND ANTIBIOTIC RESISTANCE IN STREPTOCOCCUS PYOGENES PHARYNGITIS AT A PRIVATE HOSPITAL IN BUENOS AIRES, ARGENTINA

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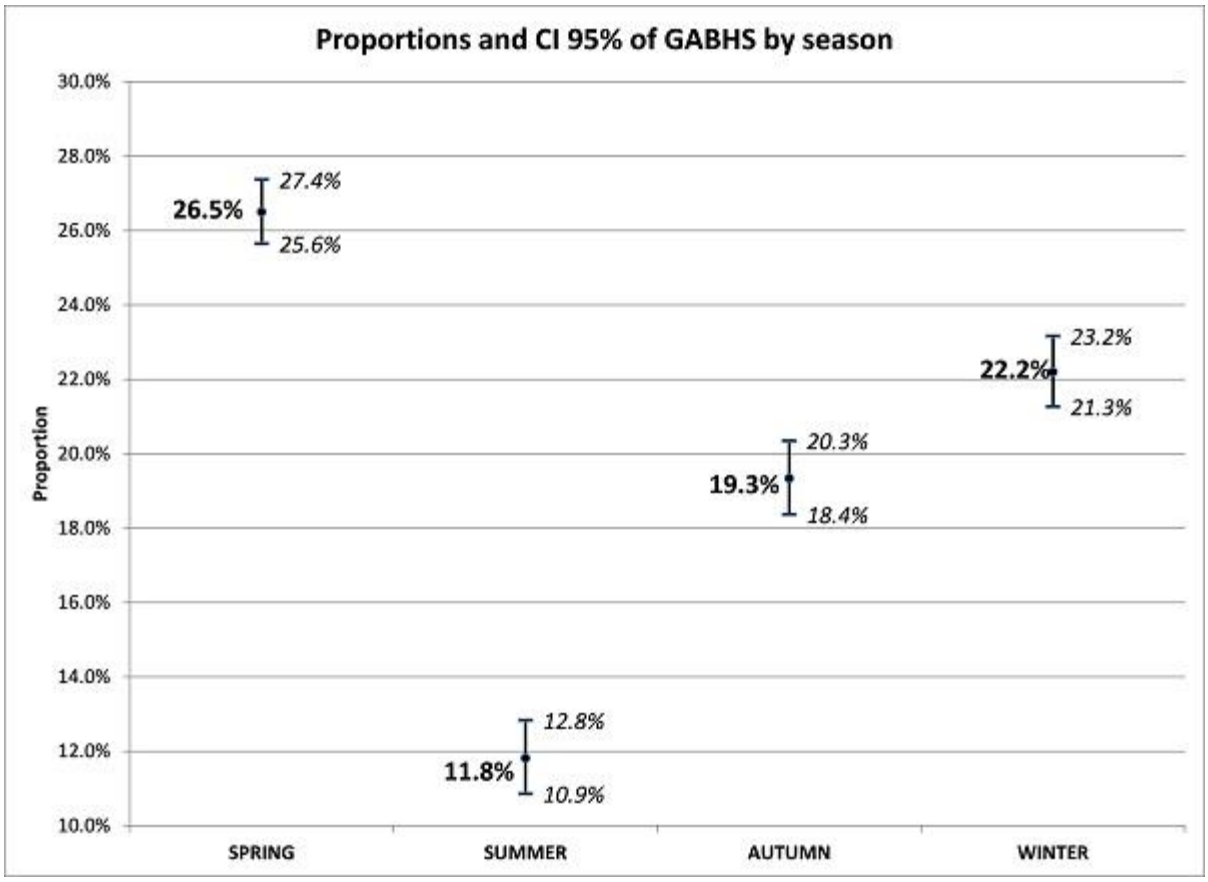
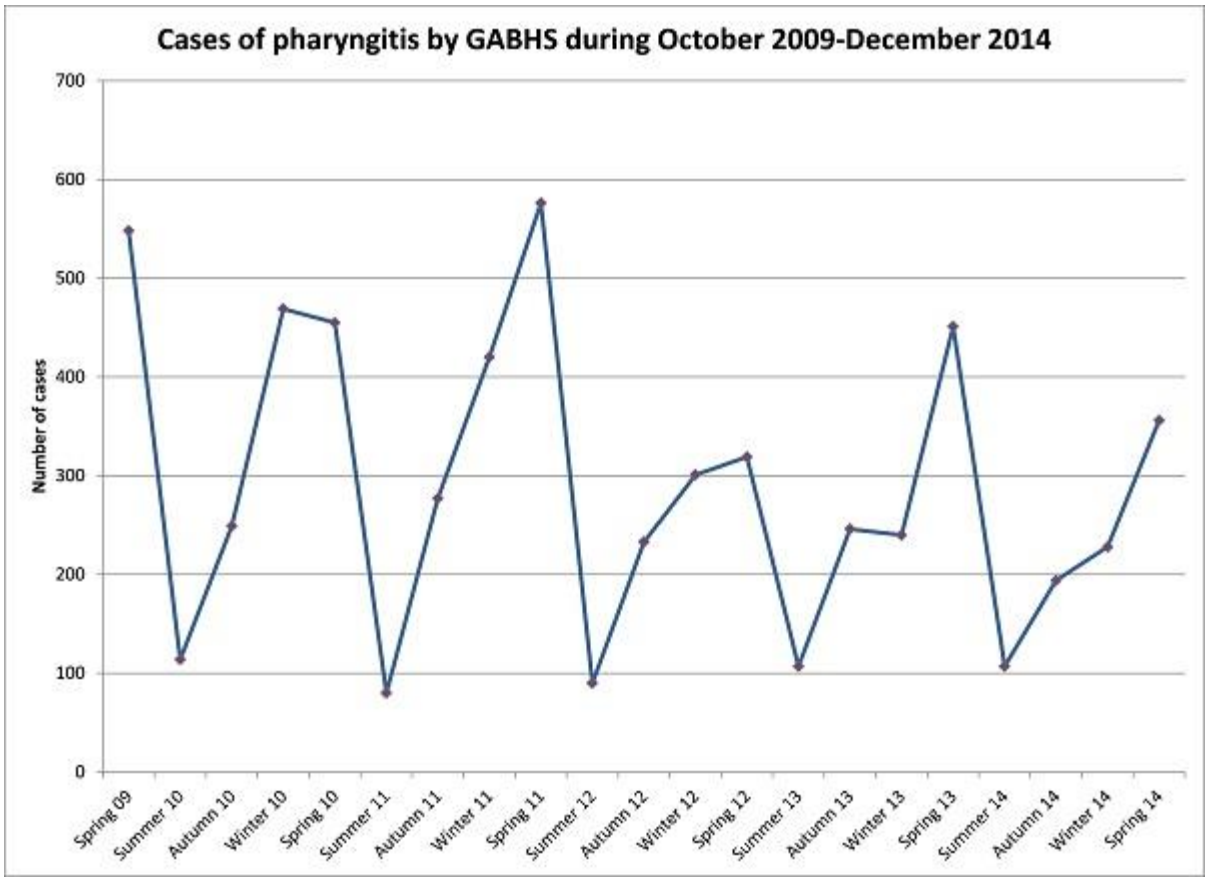
BACKGROUND AND AIMS: Streptococcus pyogenes (GABHS) is the pathogen more often isolated from throat cultures of patients up to 18 years of age. Its frequency, seasonality and antibiotic resistance has been changing along last decades.
METHODS: We performed a retrospective analysis of throat cultures of 28092 patients under 18 years with acute pharyngitis and fever between October 2009 and December 2014. Samples were inoculated on Columbia agar base plates containing 5% sheep blood, and incubated for 48 hours in ambient atmosphere. Beta haemolytic colonies were identified according to guidelines of the Manual of Clinical Microbiology (ASM, 9th and 10th edition). Susceptibility to penicillin, erythromycin, and clindamycin was determined according to CLSI standards.
RESULTS: GABHS was present in 21.6% of samples.Spring was the season with the highest incidence of GABHS (Figure 1). Each year showed an increase from autumn to spring and an evident decrease in summer (Figure 2). It was observed a decreasing incidence along time.
A small proportion (0.9%) of positive samples showed antibiotic resistance: 0.2% to erythromycin, 0.1% to clindamycin and 0.6% to both. Resistance showed a decreasing trend.
CONCLUSIONS: GABHS was present in 21.6% of patients.
Cultures GABHS positive occurred more often in spring.
Antibiotic resistance was low.
Figure 1


Proportions and CI 95% of GABHS by season
30.0%
28.0%
26.0%
24.0%
22.0%
20.0%
18.0%
16.0%
14.0%
12.0%
10.0%
Proportion
27.4%
26.5%
25.6%
12.8%
11.8%
10.9%
20.3%
19.3%
18.4%
23.2%
22.2%
21.3%
SPRING
SUMMER
AUTUMN
WINTER
Figure 2


Cases of pharyngitis by GABHS during October 2009-December 2014
Number of cases
700
600
500
400
300
200
100
0
Spring 09
Summer 10
Autumn 10
Winter 10
Spring 10
Summer 11
Autumn 11
Winter 11
Spring 11
Summer 12
Autumn 12
Winter 12
Spring 12
Summer 13
Autumn 13
Winter 13
Spring 13
Summer 14
Autumn 14
Winter 14
Spring 14

ESPID-1060
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

KAWASAKI DISEASE MIMICKING RETROPHARYNGEAL ABSCESS: ONE DISEASE?

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Background: Kawasaki disease (KD) is an acute, systemic, self-limited vasculitis. The diagnosis is clinic and not always straightforward. Rarely, retropharyngeal phlegmon has been described as first manifestation of Kawasaki disease, which makes the differential diagnosis more difficult.

Case reports: We report two children, a four-year-old girl and six-year-old boy, who presented with fever and cervical pain. Neck swelling, torticollis, neck stiffness and trismus were observed. Retropharyngeal cellulitis (low density without rim enhancement) was diagnosed on CT and penicillin plus clindamycin were started. No pus was obtained on drainage and cultures were negative. By the seventh illness day fever persisted and a skin rash, conjunctival injection, mucositis and edema of the hands dorsum and feet developed. Both patients desquamated and one had arthralgia. Analyses revealed leukocytosis, left-shift in white blood cell count, elevation of acute phase reactants, anemia and elevation of transaminases. No cardiac involvement was noted. One patient received high-dose intravenous immunoglobulin therapy plus aspirin with defervescence in twenty-four hours. The other patient remained feverish till the tenth day of disease without specific treatment. At two months follow-up, there was no cardiac involvement in both cases.

Conclusion: These cases highlight KD atypical presentations.
Although no cardiac involvement was noted, the negative cultures and lack of clinical response to antibiotics suggested KD. Furthermore, the typical KD clinical features and the flu edema on imagiology supported the diagnosis.

ESPID-0146
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICAL AND LABORATORY CHARACTERISTICS OF COMMUNITY-ACQUIRED ALVEOLAR PNEUMONIA (CAAP) ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN CHILDREN

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Background and aims: Respiratory viruses (RV), mainly RSV, are commonly found in children with CAAP, often considered a bacterial infection. The aims of the study were to compare the clinical and laboratory characteristics of children with CAAP, in whom RSV was also detected (RSV-CAAP) to those in children with other RV (ORV-CAAP) or with no RV (Non-RV-CAAP).

Methods: Clinical, laboratory data and nasopharyngeal washes for viruses were prospectively obtained from hospitalized children <5yrs with CAAP in winter (November-March**)** during 2001-2011. RV were detected by antigens or by PCR. P-values were adjusted for age and ethnicity**.**

Results: 1,264 patients were enrolled: RSV-CAAP- 860, ORV-CAAP- 240 and Non-RV-CAAP- 164. RSV-CAAP patients were younger, with higher prematurity rate, but less co-morbidity compared with ORV-CAAP and Non-RV-CAAP patients (TABLE). O_2 saturation was lower and common cold was more prevalent in RSV-CAAP. In the RSV-CAAP group, mean CRP, WBC and ANC values were lower than in ORV-CAAP and Non-RV-CAAP patients. No differences in ethnicity, number of siblings, exposure to smoking, breast-feeding duration, hospitalization duration and death were observed between the groups.

Conclusions: Children with RSV-associated CAAP have less frequently underlying diseases, less marked inflammatory responses and have more often symptoms usually attributable to viral infection compared with children with CAAP in whom other viruses or no viruses were detected.

Table: Comparison of demographic clinical and laboratory characteristics: RSV-CAAP *vs.* ORV-CAAP and *vs.* Non-RV-CAAP children <5 years old.

	RSV-CAAP N=860	ORV-CAAP N=240	P* vs RSV-CAAP	Non-RV-CAAP N=164	P* vs RSV-CAAP
Age (months±SD)	10.1±10.3	15.6±12.6	**<0.001**	16.3±13.5	**<0.001**
Ethnicity - Bedouin n (%)	599 (69.9)	162 (67.5)	**0.840**	306 (53.6)	**0.455**
Prematurity (%)	20.4%	11.9%	**0.004**	17.2%	0.272
Co-morbidity (%)	27.7%	44.6%	**0.011**	41.7%	**0.018**
Mean O_2 saturation (±SD)	90.5±5.7	91.5±4.6	**0.033**	91.9±4.6	**<0.001**
Common cold (%)	81.5%	73.5%	**0.013**	73.5%	**0.002**
CRP (mg/L±SD)	6.0±7.4	7.8±11.3	0.319	9.2±9.8	0.094
Mean WBC (cells x 1000/µL±SD)	13.4±5.6	14.0±7.0	0.060	17.1±8.5	**<0.001**
Mean ANC (cells x 1000/µL±SD)	712±431.3	833.6±533.8	**0.008**	1105.3±778.4	**<0.001**
Mean Hb (gr/dL±SD)	11.1±1.5	10.8±1.3	**0.007**	10.8±1.5	**<0.001**

*P - adjusted for age and ethnicity

SD - Standard deviation; CRP – C-reactive protein ; WBC - White blood cell; ANC - Absolute neutrophils count; Hb - Hemoglobin

ESPID-0513
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MICROBIOLOGY ASSOCIATED WITH ACUTE PHARYNGITIS

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Background and aims

Acute pharyngitis accounts for a substantial portion of visits to pediatricians, but there have been only few comprehensive studies on the microbiological etiology, besides group A streptococcus (GAS). The aim of this study was to determine the viruses and the bacteria that are associated with acute pharyngitis in an outpatient setting.

Methods

In this 14 months prospective study oropharyngeal swab samples and acute serum samples were collected from children 1-16 years of age presenting to the emergency department with an acute pharyngitis (fever > 38°C and exudations or intense redness in the oropharynx). Throat culture, serology, antigen detection and polymerase chain reaction were used to investigate the microbiological etiology.

Results

A potential causative agent was detected in 69 of the 80 patients (86%; mean age 7.5 years). Sixty-four percent of the patients had evidence of viral infection, 23% had GAS infection and 11% had evidence of concomitant GAS-viral infection. Enteroviruses (24%), rhinovirus (18%), adenovirus (14%) and Epstein-Barr virus (11%) were the most common viral agents associated with acute pharyngitis. Multiple viruses were detected in 15 patients. Haemophilus influenzae (HI), group C streptococcus, group G streptococcus, streptococcus pneumoniae and moraxella catarrhalis were detected in the oropharynx of 9, 3, 2, 1 and 1 patients, respectively.

Conclusions

Viral infection is the most common cause of pharyngitis in children and adolescents. These data fortify the current practice to withhold antibiotic treatment in non-GAS illness. Role of HI as a possible pharyngitis pathogen needs further investigations.

ESPID-1014
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

IN DEPTH CHARACTERIZATION OF MATERNAL ANTIBODIES IN INFANTS WITH RSV INFECTION

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Background: Respiratory syncytial virus (RSV) infections are a major burden and disease severity upon RSV infection ranges from mild respiratory symptoms to mechanical ventilation. Severe RSV infections affect infants below 6 months, a period in which RSV-specific maternal antibodies are present but apparently not fully protect. Therefore, the properties of maternal antibodies required for protection are still unknown. We investigated multiple antibody properties to correlate with disease severity in RSV infection which might lead to effective immunization strategies.

Methods: Children below 3 months of age with PCR confirmed RSV infections were prospectively included. Patients were classified into three severity groups; mild infections without oxygen support, moderate infections with supplemental oxygen and severe infections required mechanical ventilation. Blood samples was collected and plasma was stored. Neutralizing effect was determined by plaque reduction titers against recombinant RSV-X and its derivative lacking the G-protein. RSV-specific IgG antibodies and avidity were determined by ELISA.

Results: Antibody titers, antibody avidity and neutralizing effect of plasma did not correlate with disease severity. RSV containing G-protein was more efficiently neutralized compared to its derivative lacking the G-protein. Anti-G antibodies did not correlate with disease severity. Pre-fusion antibodies were comparable between severity groups, whereas post-fusion antibodies were lower in moderate and severe infections compared to mild infections.

Conclusion: In depth characterization of maternal antibodies in RSV-infected infants did not show correlations with regard to titer, avidity and neutralizing effect of antibodies between the different severity groups. Low titers of post-fusion antibodies might play a role in disease severity.

ESPID-1074
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DEVELOPMENT AND VALIDATION OF A NEW CLINICAL SCALE FOR INFANTS SUFFERING FROM ACUTE RESPIRATORY INFECTION.

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[1]Translational Pediatrics and Infectious Diseases Section Pediatrics Department, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, Spain
[2]Genetics Vaccines Infections and Pediatrics Research Group (GENVIP), Healthcare Research Institute of Santiago de Compostela, Santiago de Compostela, Spain

BACKGROUND AND AIMS Respiratory infections in infants (especially bronchiolitis) remain as one of the main concerns in pediatric infectology. We lack a validated scoring system that categorizes patients objectively and that could also be used by non-health professionals. We aimed to create and validate a new clinical assessment scale which could be replicated by parents and people with no special healthcare training.

METHODS We devised a new clinical scale (GENVIP scale) based on seven different items and assigned them different values (Table 1), making for a total of 20 points. The clinical status of 187 children was assessed by three independent pediatricians using this scale. Parents also evaluated their offspring with an adapted version of the scale in a subset of cases. The scale was tested for internal consistency, Pearson correlation coefficient for the items of the score, interobserver agreement and correlation between observers (for independent investigators alone, for parents alone and for parents and independent investigators altogether) using R Software.

RESULTS For the total score the Cronbach's reliability alpha was 0.94. The lowest Kappa agreement index for the mean score for each compared pair of investigators was 0.74. When comparing the results of the score obtained by parents and by pediatricians a strong correlation was found (Table 2).

CONCLUSIONS GENVIP scale may be useful and reliable in the evaluation of infants with respiratory infections for clinical and research purposes.

		0 points	1 points	2 points	3 points	TOTAL POINTS
1	Feeding intolerance	No	Mild .	Partial	Total	
2	Medical intervention	No	Basic	Intermediate	High	
3	Respiratory difficulty	No	Mild	Moderate	Severe	
4	Respiratory frequency	Normal	Mild or occasional tachypnea	Prolongued or recurrent tachypnea	Severe alteration	
5	Apnea	No			Yes	
6	General Condition	Normal	Mild	Moderate	Severe	
7	Fever	No	Yes, mild Central Tª <38,5ºC	Yes Central Tª >38,5ºC		
					TOTAL SCORE	

	Correlation
Investigator 1 vs Investigator 2	0.82 (<0.001)
Investigator 1 vs Investigator 3	0.78 (<0.001)
Investigator 2 vs Iinvestigator 3	0.76 (<0.001)
Parents vs Mean investigator's Score	0.73 (<0.001)
Parents vs I1	0.72 (<0.001)
Parents vs I2	0.56 (0.002)
Parents vs I3	0.75 (<0.001)

ESPID-0637
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

UPPER RESPIRATORY TRACT INFECTION IN CHILDREN WITH DEVELOPMENTAL DISABILITIES AND IRON SUPPLEMENTATION

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Background: Iron deficiency anemia and recurrent infections of upper airways are common among children in early ages.

Aim: The objective was to evaluate the effects of iron supplementation on iron status and morbidity with recurrent respiratory infections in children with DD .

Methods: Children aged 3-5 year with DD were recruited for study in the Children's Hospital, Tbilisi, Georgia. Clinical and iron statuses were stated at beginning and after the intervention. Children with a history of RURT infections and with laboratory and clinical evidence of a current URTI establish the studygroup (26) and children without infection - the control group (29). Patients in both groups were supplemented with ferrousfumarate(50 mg Fe) or placebo once daily for 3 month (12 weeks). Morbidity was recorded every 4 week.

Results: The overall prevalence of anemia in study group of children with DD was 47,5 %. Iron supplementation significantly improved iron status by increasing serum ferritin ($P < 0.001$) concentrations from start point values in the children with or without infection. There was no significant improvement in iron status in the children who received placebo. In both the infection group and the control group, the number of URTI episodes and the total number of sick days with an URTI during the period of intervention were significantly lower ($P < 0.005$ and $P < 0.001$) in the children who received iron supplements than in those who received placebo.

Conclusion: Iron supplementation significantly improves iron status and reduces morbidity from URTIs in children with developmental disabilities

ESPID-0729
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

VIRAL ETIOLOGY OF ACUTE RESPIRATORY TRACT INFECTION IN HOSPITALIZED CHILDREN OF A TERTIARY REFERRAL HOSPITAL IN AN-YANG, KOREA : IN TWO SEASONS (2012-2013)

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[2]Pediatrics, The National Medical Center, Seoul, Korea

Background : Our aim was to analyze the most frequent viruses in children of under 5 years of age.

Methods : We used mass Tag PCR, a multiplex assay plateform, to test for the presence of 12 viral respiratory agents. Patients were identified through a review of all ARTI patients discharged with a diagnosis of respiratory virus confirmed.

Results : We analyzed 1,782 viruses in children under 12 years old from Jan 2012 through Dec 2013. The 802 virus-positive patients were evaluated in 2012 and the 980 virus-positive patients were evaluated in 2013. Children aged under 5 years were 771 patients (96%) out of 802 in 2012 and 932 patients (95%) out of 980 in 2013.

In 2012, we detected adenovirus 73(9.1%), metapneumonovirus 47(5.9%), coronavirus 20(2.5%), parainfluenza1 33(4.1%), parainfluenza2 1(0.1%) parainfluenza3 54(6.7%), influenza A 24(3.0%), influenza B 20(2.5%), rhinovirus 181(22.6), RSV A 326(40.5%), RSV B 23(2.8%), bocavirus 0(0%). And in 2013, we also detected adenovirus 168(17.1%), metapneumonovirus 57(5.8%), coronavirus 25(2.6%), parainfluenza1 23(2.4%), parainfluenza2 24(2.5%) parainfluenza3 76(7.8%), influenza A 31(3.2%), influenza B 0(0%), rhinovirus 190(19.4%), RSV A 76(7.6%), RSV B 231(23.6%), bocavirus 79(8.1%).

The viruses most frequently detected in children were RSV. The next viruses were rhinovirus and adenovirus.

Conclusions : The RSV peak epidemiology was Nov in 2012 and Oct in 2013. The peak incidence of rhinoviruses were May and Oct in 2012 and May and Sept in 2013. The adenoviruses were spread during the June in 2012 and Nov in 2013. The bocavirus takes place in An-Yang, Korea from 2013.

ESPID-0647
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICAL PRESENTATIONS OF HUMAN CORONAVIRUS INFECTION AT 2014 WINTER SEASON IN A SINGLE CENTER

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Background:The Human Coronaviruses (HCoVs) group has thought to be one of the importantpathogen causing common cold. Interestingly in 2014 in Korea, HCoV infection causednot only upper respiratory infection but also lower respiratory infection moreseverely than any other years. We sought to determine the epidemiology,clinical characteristics, outcomes and severity of illness associated with HCoVinfections in a single center.

Methods:We retrospectively identified patients with positive HCoV respiratory specimensbetween October 2013 and December 2014 in a Severance Children's HospitalYonsei University Medical Center. Clinical characteristics, underlying conditions,outcomes and disease severity were reviewed.

Results:During the study period, HCoV was the 3rd (13.7%) most commonrespiratory virus. Coinfection was detected in 43.8% of children with HCoV.Interestingly, one patient had both HCoV-OC43 and HCoV-NL63. Mild pneumonia wasmost common (60.4%) with HCoV and when combined with RSV, bronchiolitisoccurred. Two patients had ICU care. But compared with RSV infection, diseasecourse was short.

Conclusions:Infections caused by HCoVs are common and nowadays can cause lower respiratorytract infections. When combined with other medical conditions, such asneurologic or cardiologic disease, ICU care are possible.

ESPID-0314
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MYCOPLASMA PNEUMONIAE AS A CAUSE OF VULVAR ULCERS IN A NON SEXUALLY ACTIVE YOUNG GIRL

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[3]*First Paediatric Department, Athens University, Athens, Greece*

Background and aims: Acute genital ulcers rarely occur in non-sexually active girls. When present they pose a great diagnosticchallenge. *Mycoplasma pneumoniae* (MP) has rarely been linked to these ulcers in the literature.

Method: The case of a non-sexually active young girl with vulvar ulcers linked with MP infection is presented.

Results/case report:

This 10year old child three days before admission started to have fever, throat pain and mild cough. Later she developed intense pain and burn in the genital area and was admitted to hospital.

On admission she had fever, cough and O/E painful ulcers of variable depth and size with elevated violaceous borders located inside the labia majora. She did not have other problems such as oral ulcers, diarrhoea or abdominal pain.

She was initially managed with iv antibiotics and local care with antiseptics.

Four days after admission the lesions improved but the fever and cough persisted. A chest xray revealed Lt sided pneumonia. Azithromycin was added and 2 days later she became afebrile.

Cultures sent from the lesions were negative for bacteria. PCR in the tissue for HSV was also negative. Antibodies against HSV1 and HSV2, antinuclear antibodies, anti ds-DNA, ANCA-PR3, ANCA-MPO all negative. IgM antibodies to Mycoplasma was positive. PCR for MP in the nasopharyngeal secretions was positive and strongly positive in the sputum specimen.

Conclusions: Despite MP has rarely been linked with acute genital ulcers, in cases these ulcers coexist with fever and respiratory tract symptoms, MP should be considered in the differential diagnosis.

ESPID-0255
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

COMPLICATED PNEUMOCOCCAL PNEUMONIA IN PORTUGAL: ENHANCED ETHIOLOGICAL DIAGNOSIS AND SEROTYPE DISTRIBUTION

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Background and aims: *Streptococcus pneumoniae* is a major cause of pneumonia, including complicated cases, such as those associated with empyema or pleural effusion (PE). However, the etiology is frequently not established, given the low microbiological yield of the specimens by traditional methods. The aim of this study was to identify the serotypes of pneumococci in PE of children (< 18yrs) in Portugal using both cultural and PCR approaches.

Methods: The pediatric departments of 30 hospitals were asked to submit samples of all cases of complicated pneumonia with a suspected pneumococcal etiology. The serotype of the isolated pneumococci was determined by Quellung. Conventional (end-point) or real-time PCR (RT-PCR) analysis targeting the *lytA* and *cpsA* genes was performed for culture negative cases. Amplification of specific capsular genes by conventional PCR was used to identify the serotype in culture negative samples.

Results: A total of 105 complicated pneumonia cases were identified. Isolation of pneumococci was possible in 14 PE samples (13%). In the remaining 91 culture negative cases, pneumococci were identified in 70 samples (77%), of which 27 samples (30%) by both conventional and RT-PCR and in an additional 43 samples (47%) by RT-PCR only. The main capsular serotypes identified were serotypes 3 (n=22) and 1 (n=5).

Conclusion: RT-PCR offers a significant enhancement relative to conventional PCR and culture (51% of pneumococcal positive samples were identified by RT-PCR only). Serotypes 1 and 3 are the major causes of complicated pediatric pneumonia cases in Portugal (accounting for 70% of cases).

ESPID-0470
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

AN INTEGRATED APPROACH TO IDENTIFY RESPIRATORY VIRUSES AS THE SINGLE CAUSATIVE AGENT OF SEVERE ACUTE RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Introduction

Previously we showed that newly discovered viruses, like human bocavirus (HBoV), can cause severe acute respiratory tract infections (SARI) in previously healthy children. However, we found it difficult to assess the role of co-infections and therefore developed an integrated approach to exclude them.

Methods

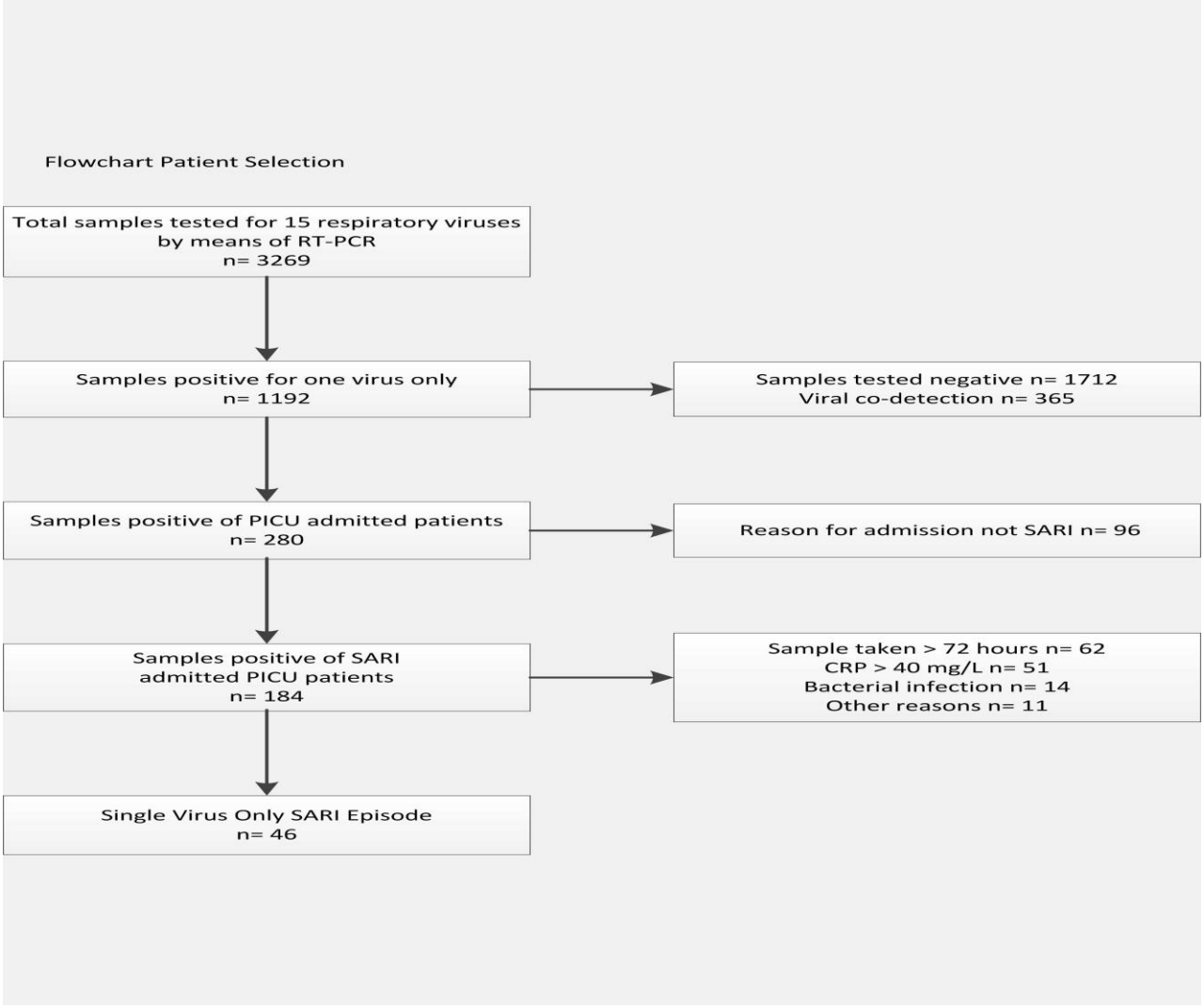
Retrospectively, during a 5-year period (2007-2012) samples were selected from our laboratory information system when RT-PCR was positive for any of the 15 respiratory viruses tested. A Single Virus Only SARI episode (SVOS) was defined when one virus was identified in a sample obtained ≤ 72 hours after Intensive Care (PICU) admission for SARI with CRP-levels ≤ 40 mg/L (≤ 24 hours) and (if available) in the absence of bacterial growth in blood, liquor and sputum. Median Ct-values were compared using the Mann-Whitney-U-test.

Results

In 3269 identified samples, 1192 tested positive for one virus only. From these, 184 were obtained during SARI related PICU admissions of 171 patients and 46 SVOSs were identified (see flowchart). Most SVOSs were caused by RSV and rhinovirus (both n=13; 28%), followed by HBoV (n=7; 15%), Influenza A virus (n=4; 9%), PIV1-3 [MdH1] (n=3; 6,5%), HCoVNL63 (n=2; 4%), PIV4, HCoVOC43, HMPV and adenovirus were found once (n=1; 2%). Only 12 SVOSs (27%) occurred in previously healthy patients. In 23 (50%) patients bacterial cultures were performed and CRP-levels were tested in all. Except for HBoV, Ct-values were not different between groups

Conclusion

This integrated approach shows that most respiratory viruses can be the single causative agent of SARI in children.



ESPID-0597
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ACUTE BRONCHIOLITIS: EXPERIENCE OF CARE SUPPORT IN HOSPITALIZATION AT HOME IN ROBERT DEBRE HOSPITAL (PARIS) BETWEEN 2012 AND 2014.

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Background and aims - Acute bronchiolitis (AB) is a leading cause of hospitalization of infants during winter. In Robert Debré hospital (Paris), since 2012, a plan called EPIVER has been developed and permitted selected children with AB to discharge with home oxygen therapy (HOT). The aim was to evaluate this care support.

Methods - We performed an observational study in this hospital, during 2 consecutive winters: 2012-2013 and 2013-2014.

Results - 471 patients were hospitalized for AB in the pediatric department, 141 were eligible for HOT and 54 patients had this support (11.5% of hospitalized patients). The mean age was 3.8 months (3 weeks to 13 months). The mean length of stay (LOS) in hospital before discharging home was 4.9 days (1 to 17). 73% of infants received HOT, 52% received nebulizations of hypertonic salty serum 3%. A mean of 5 visits of nursery per infant took place. Each infant was seen by a pediatrician. They all had respiratory physiotherapy. There was no call to urgent medical service and no hospitalization in reanimation. There were 2 readmissions for increase of respiratory distress and 2 consultations in an emergency department. The mean LOS for HOT was 6.6 days (1 to 33). The parents were globally satisfied at 98%.

Conclusions - Support by HOT for selected infants with AB is an interesting alternative to conventional hospitalization. It's a secure support and the parents were satisfied. An evaluation of the benefits of this support is necessary to estimate the costs and the impact on nosocomial infections.

ESPID-0331
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA AND PLEURAL EFFUSION HAVE HIGHER PROCALCITONIN SERUM LEVELS THAN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA WITHOUT PLEURAL EFFUSION

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Aims: We aimed to compare Procalcitonin(PCT) serum levels on admission between children with community-acquired pneumonia(CAP) with or without pleural effusion(PE).

Methods: In this prospective study conducted at the Emergency Room of the Federal University of Bahia Hospital, children aged under-5 years diagnosed with CAP admitted in a 21-month period were evaluated. On admission, clinical and radiological data were collected as well as biological samples to investigate etiological agents (11 viruses and 8 bacteria) and procalcitonin serum levels. All chest radiographs were read by a pediatric radiologist blinded to patient's clinical data. PCT concentration was measured by an immunoluminometric assay (LUMItest PCT, BRAHMS Diagnostica, Berlin, Germany, detection limit: 0.02 ng/mL).

Results: From 128 patients, PE was detected among 13(10.2%) cases. The median (IQR) PCT (ng/mL) on admission was 1.68 (1.19; 6.56) among those with PE and 0.69 (0.12; 2.53) among the others without PE (P=0.021; Mann Whitney U test). In the first group, sole viral (46.2%), atypical bacterial (7.7%), and typical bacterial (46.1%) infections were detected; 30.8% were pneumococcal (7.7% invasive disease all with positive blood culture) and 23.0% were mixed viral-bacterial infections. In the latter group, sole viral (47%), atypical bacterial (16.5%), and typical bacterial (36.5%) infections were detected; 26.1% were pneumococcal (7.8% invasive disease with positive blood culture [6.1%] and positive blood PCR [1.7%]) and 33.9% were mixed viral-bacterial infections.

Conclusion: PCT serum levels are higher among children with CAP and PE than in children with CAP without PE, even in cases with sole viral infection and PE.

ESPID-0904
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

IS RHINOVIRUS INFECTION ASSOCIATED WITH POOR CLINICAL OUTCOME IN HOSPITALISED CHILDREN?

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BACKGROUND AND AIMS

Human rhinovirus is commonly identified in children with acute respiratory infections (ARI) but data on their clinical severity are limited.

Objective: To compare clinical outcome of patients with ARI depending on the presence of rhinovirus in respiratory samples.

METHODS

Case-control study of children with ARI admitted to a tertiary paediatric hospital in which a multiviral PCR was requested from January 2012 to November 2014. Outcome measures: intensive care admission, length of hospital stay, respiratory requirements and death.

RESULTS

Sixty-four episodes were registered: 35 (54%) rhinovirus positive (R+), 19 of them coinfections, and 29 (46%) negative (R-). The median age was 14 months (IQR 2.75-62). Most frequent diseases were pneumonia (39.1%) and bronchiolitis (18.8%). In R+, lower respiratory tract infections were the most frequent diagnosis (17, 70.8%). Baseline characteristics, including underlying diseases, were similar between both groups. There were not any significant statistically differences in leucocytes count, protein-C-reactive, procalcitonin or radiological findings. There was an increased oxygen requirement in R- (96.6% versus 77.1%) although it wasn't statistically significant in multivariable regression (OR 0.14, CI 95% 0.02–1.23). In multivariable analysis adjusted for underlying conditions and age, children with R+ infections had decreased odds of PICU admission (OR 0.04, CI 95% 0.005–0.3) and need for mechanical ventilation (OR 0.09, CI 95% 0.02–0.4) compared to children with R-. Mortality was similar in both groups (6.9% vs 8.6%, OR 1.2, IC95% 0.2–8).

CONCLUSIONS

Unlike other previous studies have reported, in our series rhinovirus infection was not associated with worse clinical outcome.

ESPID-0976
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICAL IMPACT OF DIFFERENT TYPES AND SUBTYPES OF SEASONAL INFLUENZA VIRUSES IN CHILDREN.

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Background: There are few data available regarding differences in the clinical presentation of influenza virus infections in children. This study evaluates the signs , symptoms and the clinical course of laboratory-confirmed influenza infections in children attending an emergency room because of influenza-like illness.

Methods: we conducted a retrospective study from July2004-september2009 and a prospective one from November2009-march2014 in paediatric emergency room and wards at Donostia University Hospital. All cases of children<14years with influenza viral infection, confirmed microbiologically, were collected. Upon enrolment, systematics recordings were made of the patient´s demographic characteristics and medical history.

Results: Among the 929 children involved, 636 had influenza monoinfection (56seasonalAH_1, 181 pandemicAH_1N_1, 254AH_3 and 145B) Children infected with seasonalAH_1 and AH_3 were significantly younger than children infected with influenza pandemicAH_1N_1 or B (mean age 2,0±2,5 and 2,0±2,5years versus 4,2±4,5 and 4,1±3,8years p<0,001) There were not significant differences in clinical diagnosis except from fever without source and myositis associated significantly with AH_3 infection (p=0,02) and B infection (p<0,0001) respectively. Children with pandemicAH_1N_1 infection had higher hospitalization rates than those infected by the others subtypes (p=0,0213) but there were not differences regarding the percentage of admissions in PICU, the requirement of ventilatory support or the mean stay. The requirement of drug therapy and antibiotic use was similar in all the subtypes)

Conclusion: All subtypes had a similar clinical diagnosis and course. Despite higher hospitalization rate, children with influenza due to pandemicAH_1N_1 had uncomplicated illness and symptom severity and the risk of serious outcomes were similar to the other subtypes.

ESPID-0778
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICAL, ANALYTICAL, MICROBIOLOGICAL AND THERAPEUTIC FEATURES OF COMPLICATED COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN

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BACKGROUND AND AIMS:
The etiology of Complicated Community Acquired Pneumoniae (CCAP) remains poorly defined. We describe a cohort of patients with CCAP.
METHODS:

Retrospective, descriptive analysis of the patients below 15 years admitted to a tertiary care Hospital in Madrid diagnosed of CCAP, between june-2005 and march-2012. The data were obtained reviewing medical records. The microbiological study included blood cultures and atypical bacteria serology. TST and influenza or RSV antigens were performed at criteria of the attending physician. When thoracocentesis was done, culture and *Streptococcus pneumoniae* (Sp) antigen in pleural fluid were performed.

RESULTS:

We included 74 patients, 0,83 to 14 years (median 4), 58 % male. 74,3% had no underlying condition and 18,9% had episodic asthma. 66,2% had CRP ≥80 mg/L. 46% were hyponatremic. Thoracocentesis was done in 46%. They had simple parapneumonic effusion 59,5%, complicated paraneumonic effusion/empyema 20,3% and necrotizing pneumonia/abscess 20,2%. 43% had microbiological documentation: Sp in 19, *Streptococcus pyogenes* in 4, *Mycoplasma pneumoniae* (Mp) in 4, other typical bacteria in 2 and virus in 3. The median of days in antibiotics was 16 and the median long of stay 13 days. 33,8% had pleural drainage a median of 8 days. No patient died.
CONCLUSIONS:

1. CCAP remains an important cause of morbidity and prolonged admission.

2. Typical bacteria, mainly Sp, are the more frequent cause, but Mp and virus are also implicated.

3. Further etiological studies are needed. From april-2012 we have iniciated a prospective study about etiology of pediatric CAP, with an extensive microbiological workup.

ESPID-0848
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ETIOLOGY OF PARAPNEUMONIC EFFUSION IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA

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BACKGROUND AND AIMS:
Paraneumonic pleural effusion (PPE) is a frequent complication of Community-acquired pneumonia (CAP). We analyzed a cohort of in-patients diagnosed of CAP with (PPE) in two hospitals in Madrid.

METHODS:
Prospective evaluation of consecutive hospitalized children, from April-2012 through December-2014, diagnosed of CAP with PPE. An extensive microbiological workup was performed, including conventional methods (culture, serology) in blood and pleural fluid (PF), qualitative detection of *Streptococcus pneumoniae* (Sp) antigen from urine and PF samples and molecular techniques in blood and nasopharyngeal exudates.

RESULTS:
28 children, aged 17 to 158 months (median 60) were enrolled. Four children associated asthma exarcebation. 78.6% of the patients were classified in the WHO stage-I and 21.4%, in the stages-II/III. The radiographic image was unifocal in 82.1%. Natremia ≤135 mMol/L was found in the 28.6%. The increase of CPR was divided into groups: 39% revealed <40 mg/L; 21% were 40-80 mg/L and 39%, >80 mg/L. The procalcitonin level was ≤1 ng/mL in 63.6%. Thoracocentesis was performed in 7 patients. The pleural effusion was considered simple in 82.1% and complicated/empyema in 17.9%. A pathogen was identified in 96.4% of children. Bacterial strains (BS) were isolated in 25.9% (of which 85.7% were Sp); viruses in 70.4% and atypical bacteria (AB) were detected in 44.4%. There were co-infections: virus-BS in 14.8%, virus-virus in 14.8% and virus-AB in 22.2%.

CONCLUSIONS:

1. This study supports the changing profile of the etiology of CAP with PPE.
2. Viruses and AB, in addition to BS, must be considered as responsible of PPE in CAP.

ESPID-0595
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

COMPARING FIRST- AND SECOND-SEASON PALIVIZUMAB PROPHYLAXIS IN PATIENTS WITH HEMODYNAMICALLY SIGNIFICANT CONGENITAL HEART DISEASE (HSCHD) IN THE CARESS DATABASE (2005-2013)

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Background/Aims: Paediatric advisory guidelines recommend prophylaxis against respiratorysyncytial virus (RSV) for infants with HSCHD. However, current recommendations cast doubt as to whether prophylaxis is beneficial beyond 1year of age. To determine whether there are differences in RSV-related hospitalizations (RSVH) in HSCHD infants receiving palivizumab during the first versus second season in the Canadian Registry of palivizumab (CARESS) database.

Methods: CARESS is a prospective registry of infants who have received ≥1 dose of palivizumab at one of 32 sites across Canada during the 2005-2013 RSV seasons. Demographic data were collected at enrollment and respiratory-illness-related hospitalization events recorded monthly. Infants aged <24 months with HSCHD were recruited.

Results: 707(35.1%) of 2013 infants were prophylaxed during the second season (average age in months: 4.7 [first season] versus 14.7 [second season]). Baseline demographics for both seasons were similar. However, infants aged >1year had a more complicated neonatal course, with significantly longer neonatal lengths of stay(46.7 versus 25.6 days). 26 infants in the first year (RSVH rate: 2.26%) and 11 infants in the second year (RSVH rate: 2.09%) were hospitalized. Cox regression analysis showed no significant differences in hazards between infants in their first or second year of prophylaxis in the time to first RSVH.

Conclusions: Infants enrolled in the CARESS database in the second RSV season had a similar hazard of RSVH as those in the first year of life. These findings suggest that infants aged >1 year are equally at risk for RSVH and benefit from palivizumab prophylaxis.

ESPID-0261
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

COMPARATIVE STUDY OF HIGH DOSE ORAL AND PARENTRAL AMOXICILLIN-CLAVULANATE IN TREATMENT OF SEVERE PNEUMONIA IN CHILDREN UNDER FIVE

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Background & Aims:

WHO recommends treatment of severe pneumonia with hospitalization and intravenous antibiotics, which has its own disadvantages. Oral antibiotics are as effective as parentral antibiotics. We tested effectiveness and adverse effects of high dose oral, parentral and combined Amoxicillin- clavulanate in children with severe pneumonia.

Methods:

Children aged 3-60 months with WHO defined severe pneumonia were randomly allocated to three groups.

Group A: Oral treatment at home (7 days)

Group B: Parentral treatment at hospital (7 days)

Group C (Combined): Intravenous for 48 hours (In Hospital) and oral home (5 days)

Dosage: Amoxycillin 80 mg/kg/day in 3 divided doses.

Results:

Out of a total of 165 patients, 57 were randomized to group A, 55 to group B and 53 to group C. Complete clinical recovery was seen in 82.45%, 81.8% and 77.3% patients in group A, B and C respectively (P = 0.831). Risk differences analysis did not show significant difference between groups at 48 hrs & D_7 of treatment.

Diarrhea was the only side effect in oral group (P = 0.434)

On Multivariate analysis, female sex, fever at 48 hours and side effects were found to be independent predictors of treatment failure.

Conclusion:

Home based treatment with high dose oral Amoxicillin-clavulanate is equally effective and safe as parentral therapy in under five children with severe pneumonia.

Final Outcome	Group A (n=57)	Group B (n=55)	Group C (n=53)	Total (n=165)	P Value
Recovered	47 (82.45%)	45 (81.8%)	41 (77.3%)	133 (80.6%)	0.831
Treatment failure and Death	10 (17.54%)	9 (16.36%)	12 (22.6%)	31 (18.8%)	0.674
Left against medical advice	0	1(1.8%)	0	1 (0.6%)	0.366

ESPID-0071
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DIAGNOSTIC ACCURACY OF HUMAN METAPNEUMOVIRUS. SYSTEMATIC REVIEW

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Background: Respiratory viruses are common cause of disease. Specific etiology remains without identification at least at 50% of the cases. Human Metapneumovirus is an important agent in respiratory diseases in children. There are 4 diagnostic tools for human metapneumovirus: serologic, culture, PCR and antigens.

Objective: Identify diagnostic accuracy of PCR, culture, immunofluorescence and serologic tests for human metapneumovirus in pediatric patients.

Methods: Types of studies: Diagnostic accuracy papers. Search strategy: Keywords: Human Metapneumovirus, PCR, culture, immunofluorescence, serologic studies, antibodies, diagnostic test, diagnostic, diagnostic accuracy. We did search in data bases: Lilacs, Artemisa, Scielo, Pubmed, Embase.

Methodology Quality: All papers included were measured with Stard and Quadas scales. Results: 169 papers, 147 were dismissed because they were not diagnostic accuracy test or because they had incomplete data. We had culture against culture (one paper), immunofluorescence against culture (one paper), PCR against culture (four papers), immunofluorescence against PCR (fourteen papers) and PCR against PCR (2 papers).

Conclusion: The diagnostic test with the best diagnostic accuracy was culture. PCR is a useful diagnostic test but more studies are needed in order to get best evidence.

ESPID-0158
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

TRENDS OF INCIDENCE OF PERTUSSIS (WHOOPING COUGH) IN ARMENIA

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Background and aims

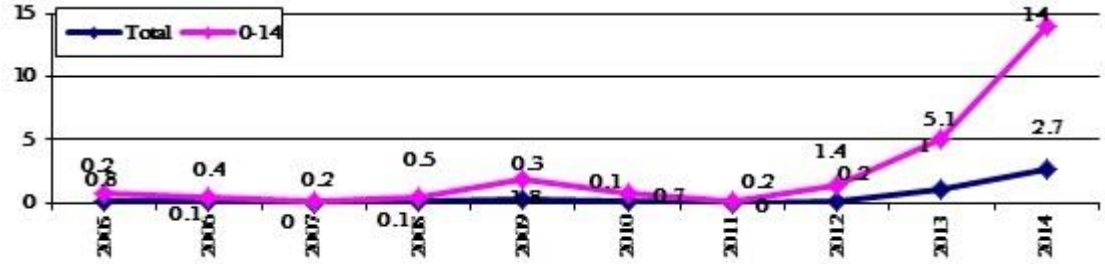
In the past pertussis (whooping cough) was a serious health challenge in many countries. However, the situation was changed dramatically after introduction of immunization, which contributed to the reduction of morbidity and mortality caused by whooping cough pathogen. This study aims to describe trends of incidence of whooping cough in Armenia during 2005-2014.

Methods

Monthly and annual reporting forms on vaccination coverage and disease, as well as epidemiological investigation cards are summarized during the study.

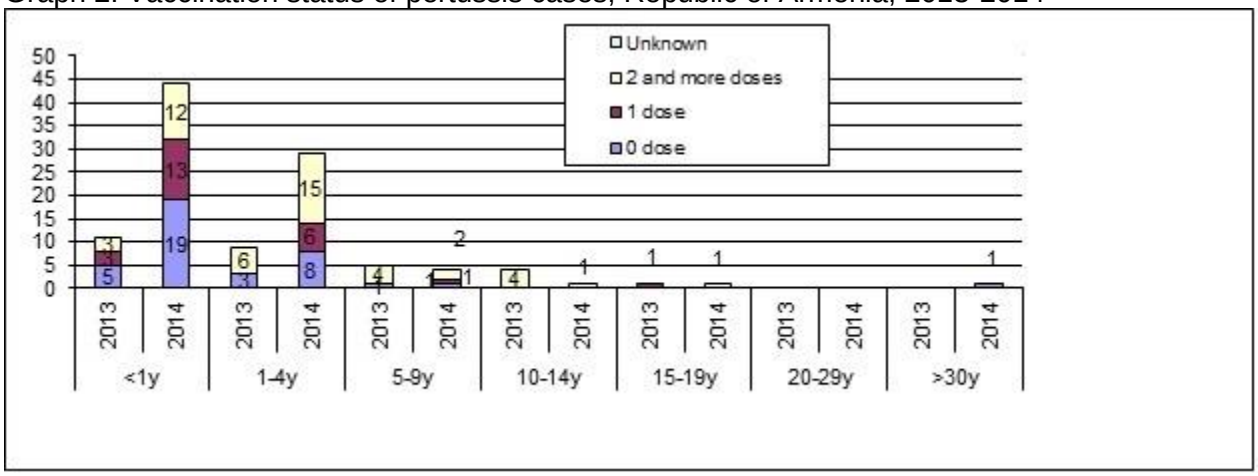
Results

In Armenia, basically single cases of pertussis were recorded during 2005-2012. In 2013- 2014 number of registered cases were increased, respectively 30 (1) and 81 (2.7), of which 97 and 99 percent of cases were among children under 14 years, including 2 fatal outcomes in infants (Graph 1).
Graph 1.Trends of incidence of pertussis in Republic of Armenia, 2005-2014



45% of patients among children <14 years in 2013 and 61% in 2014 were not vaccinated or received just one dose of whole cell containing pertussis vaccine (Graph 2).

Graph 2. Vaccination status of pertussis cases, Republic of Armenia, 2013-2014



Conclusions

Taking into account the high vaccination coverage in Armenia, increasing trends of disease incidence are a matter of discussion: the pathogen, most likely, has changed its biological specificity. Therefore, there is a need to control over the pathogen as an integral component of surveillance system.

ESPID-0111
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

FACTORS ASSOCIATED WITH PNEUMONIA AMONG THE OVERWEIGHT AND OBESE UNDER-FIVE CHILDREN IN AN URBAN HOSPITAL OF A DEVELOPING COUNTRY

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Background & aims: Pneumonia is one of the killer diseases in under-five children in developing countries. Though childhood obesity and overweight is not a common health problems in developing countries but it is emerging and often presented with infectious diseases like pneumonia. However, there is paucity of data in such conditions especially in developing countries. Thus, we sought to evaluate factors associated with pneumonia in childhood obesity and overweight.

Methods: In this retrospective chart analysis from electronic data base (SHEBA) of the Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), All admitted under-five children with pneumonia(11,274) in this hospital from January 2010 to June 2014 were enrolled. Children with obesity and overweight (BMI ≥ 2.00 SD) defined by WHO constituted cases (n=25) and randomly sleeted three fold age matched children from rest of the enrolled children (BMI of -1.99 SD to 1.99 SD) constituted controls (n=75). Demographic, clinical and laboratory data of the cases and the controls were compared.

Results: The overweight and obese pneumonic cases more often presented with a co-morbidity of diarrhea (72% vs. 29%, p= <0.001) and developed hypoxemia (28% vs. 7%, p= 0.009), however, other demographic and routine laboratory parameters including hemoglobin, white blood cell counts, serum electrolytes and microbiological tests were comparable among the groups.

Conclusions: Our data suggests that the pneumonia in overweight and obese children prone to be associated with diarrhea and often develop hypoxemia. However, future research with large sample size is imperative to consolidate or refute our observation.

ESPID-0579
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HOUSING ENVIRONMENT CONDITION EFFECTS ON CHILD MORBIDITY (ACUTE RESPIRATORY INFECTION AND DIARRHOEA) AMONG CHILDREN IN UGANDA

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Background and aims: Housing is significant factors for the health, and sub-standard housing condition is major public health issues. In developing countries, poor housing environmental conditions are associated with a high infant mortality and child morbidity (Acute respiratory infections and diarrhoea). Around 2 million children died every year due to acute respiratory infection that have not adequately accounted as other major child morbidities such as malnutrition. The present study examined the association of the household environment and child morbidity among children (under age five years) in Uganda.

Methods: The study used latest nationally representative Uganda Demographic Health Survey (UDHS-2011) which was conducted in 2011 year. The bivariate and multivariate analysis (multinomial regression analysis)has been used.

Results: The study found that the high prevalence of the Acute Respiratory Infection (ARI) (15%) and diarrhoea (23%) in the two weeks proceeding to survey in Uganda. The results from multinomial regression analysis study found that those household have used wood as cooking fuel, using shared toilet and not improved toilet, and household belongs to lower wealth, their children were significantly more likely to had ARI and diarrhoeal symptoms.

Conclusion: The present study has found the significant association of the poor household condition in the development of the ARI and diarrhoeal disease among children under age five years. Policy intervention should focus to provide proper cooking fuel and clean sanitation facility to each household and need for improvement of household condition belongs to the lower quintile to reduce the child morbidity in Uganda.

ESPID-0455
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

EMPYEMA DUE TO STREPTOCOCCUS PNEUMONIAE SEROTYPE 9V IN CHILD ALTHOUGH IMMUNIZED OF THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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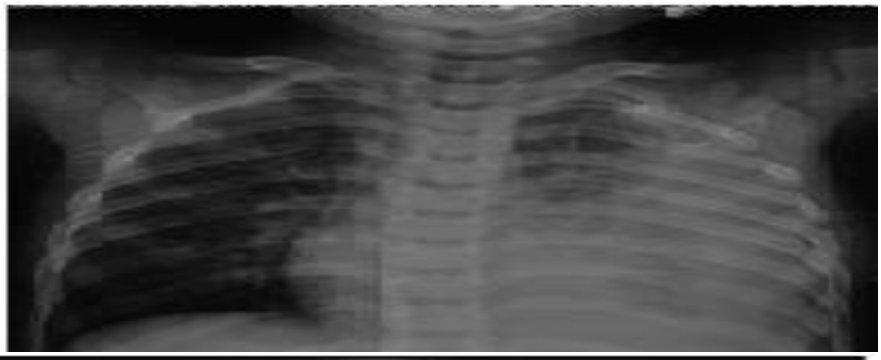
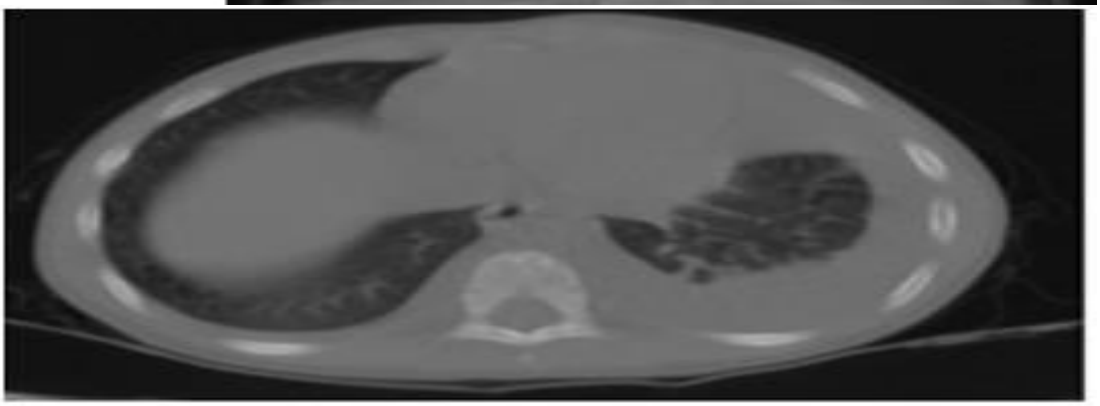
Introduction: Streptococcus pneumoniae is the most common identified cause of pneumonia with empyema. In this report, a pediatric case diagnosed with empyema due to Streptococcus pneumoniae serotype 9V with a history of pneumococcal vaccination is presented.

Case: A 2 years old male patient was admitted to the hospital with the complaints of fever and stomachache. On examination, he was irritable, pale and febrile; the heart rate was 120/min; respiratory rate was 58/min with intercostal recession along with diminished air entry on the left side. Diagnosis of left-sided pleural effusion was made and the same was confirmed on chest x-ray. Cell count of pleural fluid revealed a total of 10200 cells/mm^3, protein 3gm/dL and glucose 17mg/dL. Intercostal drain was placed and intravenous ampicilin sulbactam was initiated empirically. Gram stain of pleural fluid revealed Gram positive diplococci. Hemoglobin was 10.5gm%, total leukocyte count was 23,800/mm^3 platelet count was 343,900/mm^3 and C-reactive protein was 261mg/L. The pleural fluid culture and hemoculture of the patient yielded penicillin-susceptible pneumococci and the isolate was identified as serotype 9V by polymerase chain reaction. Patient's vaccination status, PCV-13 was done according to the Turkish national immunization schedule at 2, 4, 6, and 12 months of age. Our patient's serum level of specific IgG against 9V serotype was detected 220mg/L. The patient is doing well during follow up.

Conclusions: Although, PCV-13 seems to be the most protective against childhood pneumococcal empyema and IPD. There may be cases that do not functional although adequate respond to PCV-13 vaccination immunocompetant.





ESPID-0884
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

TREATMENT AND OUTCOME OF MILD OR MODERATE-TO-SEVERE INFLUENZA IN PRE-SCHOOL CHILDREN

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Background
Influenza in children usually presents as mild acute respiratory infection (ARI), but also may show a more severe course. We compared treatment and outcome in pre-school children with mild or moderate-to-severe influenza.

Methods
During January to April 2013, influenza was PCR-confirmed in 104 children 1-5 years of age presenting at paediatric practices with ARI. Moderate-to-severe disease was defined according to Jain et al. (NEJM, 2013): fever >39.0°C, or physician-confirmed acute otitis media (AOM), or lower respiratory tract illness (LRTI), or serious extra-pulmonary complication. In additional analyses, this definition was modified to fever ≥40.0°C instead of >39.0°C.

Results
Eighty-three (80%) children showed moderate-to-severe influenza (70 with fever >39.0°C, 11 with AOM, 20/4 with bronchitis/pneumonia, 4 with other complications). They had a higher CRP-value (p=0.002), received antipyretics more often (p=0.022) and required more additional practice visits (p=0.031) than children with mild influenza. Using the modified definition, 55 (53%) children were classified with moderate-to-severe disease; they showed a higher CRP-value (p=0.001), more additional practice visits (p<0.001), longer duration of disease (p=0.017), more days in bed (p<0.011), longer absenteeism from child care (p=0.026), and more frequent symptomatic treatment (mucolytics p=0.026, alpha-adrenergic nasal drops p=0.044). Regarding demographic characteristics, influenza type/subtype, viral co-infection, other treatment, and parent workdays lost, there was no significant difference in all analyses.

Conclusions
Moderate-to-severe influenza resulted in more frequent paediatric practice visits. Treatment and other outcomes were similar to mild influenza. However, they differed considerably when the definition of moderate-to-severe influenza by Jain et al. was modified to fever ≥40.0°C.

ESPID-0911
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

BRONCHIOLITIS-ASSOCIATED HOSPITALIZATIONS IN NEONATES AND INFANTS: AN 11-YEAR STUDY IN A TERTIARY CARE UNIT IN GREECE

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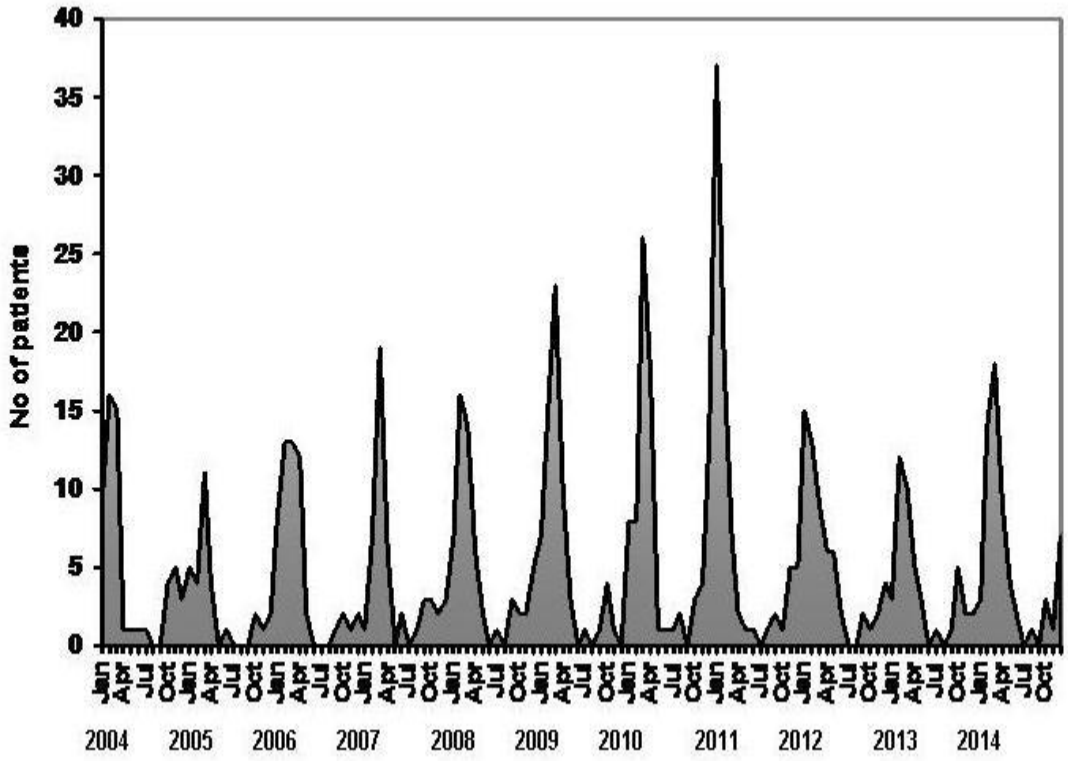
Background and aim: Bronchiolitis has been a common infection in children younger than 12 months. The aim of the present study was to investigate the epidemiology of bronchiolitis-associated hospitalizations in a tertiary care unit in Central Greece across an 11-year period.

Methods: The University General Hospital of Larissa (UGHL) serves as the academic, tertiary care referral center for the broader area of Central Greece. The medical records of children 0-11 months of age hospitalized at the UGHL for the first episode of bronchiolitis from January 2004 to December 2014 were reviewed.

Results: Across the study period, 642 children with bronchiolitis were hospitalized. Of these 642 infants, 450 (70.1%) were under 3 months of age, while 14.5% were premature (≤36 weeks of gestational age). The annual admission rate of bronchiolitis cases among hospitalized pediatric patients ranged from 162 to 408 cases per 10 000 hospital admissions, median=290 (χ^2 for trend *P*=0.2). Most of the bronchiolitis cases were hospitalized from January through April (Figure), while in 9 (81.8%) of the 11 years the peak of cases occurred in February or March. The proportion of the annual cases which were admitted was low in December (range 0% to 14.6%, median=6.4%), whereas it was high in the spring months March and April (range 11% to 53.2%, median=43.5%).



Conclusions: (1). Recent data from Greece indicate that there remains a significant burden of bronchiolitis cases. (2). In Central Greece, the bronchiolitis season has frequently a delayed onset and extends into the spring months March and April.

ESPID-0912
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CHANGES IN THE MANAGEMENT OF BRONCHIOLITIS IN A TERTIARY CARE UNIT IN GREECE (2004-2014)

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Background and aim: The management of hospitalized cases of bronchiolitis consists of measures to maintain appropriate oxygenation and hydration. The aim of the present study was to investigate whether there have been recent changes in the modalities used for the management of hospitalized cases of bronchiolitis.

Methods: The medical records of children 0-11 months of age hospitalized at the Neonatal Intensive Care Unit and the Department of Pediatrics of the University General Hospital of Larissa (UGHL) in Central Greece for the first episode of bronchiolitis from January 2004 to December 2014 were reviewed.

Results: Across the study period, 192 neonates and 450 infants (>30 days) were hospitalized. Signific**ant differences in the management of bronchiolitis according to the patient's age (Table 1) and changes in the used modalities (Table 2) were noted.**

Table 1. Management according to the patient's age

Index	≤30 days	31-60 days	>60 days
	n=192	n=162	n=288
Supplemental oxygen	123 (64.1%)	94 (58%)	128 (44.4%)
Duration of supplemental oxygen (days)	3.5±2.1	3.3±2.1	2.8±1.8
CPAP	56 (29.2%)	44 (27.2%)	27 (9.4%)
Duration of CPAP use (days)	2.9±2.2	2.4±1.8	2.1±1.5
Intubation	10 (5.2%)	7 (4.3%)	2 (0.7%)
Antibiotic use	81 (42.2%)	52 (32.1%)	60 (20.8%)
Duration of hospitalization (days)	8.0±3.9	7.0±4.1	5.7±3.6

Table 2. Management according to the study period

Modality	2004-2006	2007-2009	2010-2012	2013-2014	P
	n=141	n=171	n=224	n=106	
CPAP	0	16.9%	32.6%	20.7%	<0.001
Nebulized bronchodilators	96.5%	44.4%	10.7%	15.1%	<0.001

Nebulized steroids	86.5%	62.6%	4.5%	8.5%	<0.001
Steroids IV	48.9%	4.7%	0	2.8%	<0.001
Nebulized adrenaline	40.3%	52.6%	15.6%	21.7%	<0.001
Nebulized hypertonic saline	0	0.6%	4.5%	26.4%	<0.001
Antibiotics during hospitalization	52.5%	24.6%	25.9%	17.9%	<0.001

Conclusions: Recently, in the management of bronchiolitis at the UGHL, there has been a significant: (1) increase in the use of CPAP and (2) decrease in the use of nebulized bronchodilators and steroids, as well as of antimicrobial therapy.

ESPID-0856
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MANAGEMENT OF GROUP A STREPTOCOCCAL PHARYNGITIS IN CHILDREN AGED UNDER 15 WITHIN WORCESTERSHIRE ACUTE HOSPITAL 2006-2012

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Background and Aims:

The aim was to review the presentation and management, in those under 15 years, of Group A Streptococcus (GAS) at Worcester Royal Hospital (WRH), and to compare results over two, three years periods; according to the recommendations from Infectious Diseases Society of America (IDSA) 2012 guidelines.

Method:

All GAS positive throat swabs in those aged under 15 were obtained from the laboratories; over the two periods - May 2006-09 (n=23, 1 excluded), May 2009-12 (n=43). All 66 case notes were reviewed for demographics, symptomatology, antibiotic sensitivities, therapy and duration, with standards based on the IDSA Guidelines.

Results:

65 of 66 (98%) patients presented with features of GAS, most commonly tonsillopharyngeal inflammation and fever. 55 of 66 patients received antibiotics (83%), and an appropriate choice of antibiotic was given in all cases (33 cases (60%) receiving the primary agent of choice Penicillin V). Only 16 cases (29%) were treated for the recommended duration.

An increase in GAS incidence occurred between the two time periods. An increase was seen in use of the first choice treatment of Penicillin V from 39% to 56% of patients, and in receiving the correct 10 day duration from 6% to 41% of patients.

Conclusion:

Overall patients with clinical features of GAS were appropriately diagnosed with a throat swab. They were treated with appropriate antibiotics as per given sensitivities and the IDSA Guidelines, however the duration was usually shorter than the recommended 10 days. Concluding that further education with appropriate management is required.

ESPID-0063
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MYCOPLASMA PNEUMONIAE PNEUMONIA: CLINICAL, LABORATORY AND RADIOGRAPHIC FEATURES IN 18 CHILDREN, HOSPITALIZED WITH CAP.

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BACKGROUND: Mycoplasma pneumoniae is a common pathogen causing CAP in children. The difficulties to make the diagnosis based on clinical and radiographic signs often leads to inappropriate antibiotic therapy and treatment failure.

AIM: To characterize the clinical, laboratory and radiographic features of M. pneumoniae pneumonia in hospitalized children and to find signs, which make the diagnosis more likely.

METHODS: We present 18 children, between 5 and 15 years old (mean 9.5y) with serologic proven Mycoplasma pneumonia, admitted to the clinic from October 2013 to September 2014.

RESULTS: Most cases are in summer and early fall. There is rise in September 2014 with 30% from all patients, included in the study and 60% from all children with CAP treated in the clinic this month. High fever (72.2%) and dry, irritant cough (55.5%) usually leads to the doctor. Two atopic children (11.1%) present with severe dyspnea. Chest auscultation shows scattered or localized rales in 72.2%. Elevated ESR (88.9%) without leukocytosis is the typical finding in the blood picture. One child has coinfection with S. aureus. The radiographic manifestations are very heterogeneous. The most common chest X-ray abnormality is interstitial infiltrate (72.2%). Bilateral involvement occurs in 16.7% of cases. Pleural reaction is detected in 3 patients (16.7%). All children are treated successfully with Clarithromycin.

CONCLUSION: Although there is no sign, characteristic only for Mycoplasma pneumonia, school age, high fever, elevated ESR with normal leukocyte count and interstitial lung abnormalities are suggestive. Children with atopy are prone to severe bronchial obstruction.

ESPID-0056
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DIFFERENCES IN CLINICAL AND LABORATORY CHARACTERISTICS BETWEEN MONOINFECTIONS AND COINFECTIONS IN PRESCHOOL CHILDREN WITH VIRAL LOWER RESPIRATORY TRACT INFECTIONS

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Background and aims: Clinical pictures of different viral causes of lower respiratory tract infections (LRTI) are not well characterized and the effect of multiple concomitant viral infections on clinical characteristics is unclear. The aim of our study was to compare the clinical and laboratory characteristics between monoinfections and coinfections in preschool children with viral LRTI.
Methods: We included 198 preschool children, hospitalized because of viral LRTI. Multiplex polymerase chain reaction assay from nasopharyngeal swab was used for the detection of 10 most common respiratory viruses - influenza A and B, RSV, adenovirus, metapneumovirus, bocavirus, rhinovirus, coronavirus, enterovirus and parainfluenza.
Results: Results are presented in Table 1.
Table 1. Comparison of characteristics between monoinfections and coinfections.

Characteristic	Monoinfections N= 131	Coinfections N= 67	p value
Duration of hospitalisation, mean in days	5.2	4.3	0.06
Clinical, no (%)			
Pneumonia	39 (29.8)	19 (28.4)	0.87
Wheezing	70 (53.4)	41 (61.2)	0.36
Fever	64 (48.9)	39 (58.2)	0.32
Pharyngitis	75 (57.3)	22 (32.8)	≤0.01
Need for supplemental oxygen	55 (42.0)	21 (31.3)	0.17
CRP (mg/l), mean	28.2	34.6	0.34
WBC (x10^9/l), mean	14.4	15.3	0.32

Conclusions: Except for the marginal longer duration of hospitalization and higher incidence of pharyngitis in monoinfections, we found no significant differences between the both groups. Interestingly, coinfections added nothing to the severity of clinical picture of LRTI. These findings could be a consequence of prolonged shedding of some viruses, especially rhinoviruses. Further studies are needed to evaluate the clinical characteristics of particular combinations of viruses causing

LRTI

ESPID-0921
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MYCOPLASMA PNEUMONIAE AS AN ETIOLOGICAL AGENT IN COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN: CLINICAL, RADIOLOGICAL AND LABORATORY FEATURES

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Background and aims:

Mycoplasma pneumoniae (Mp) is a causative agent of Community-acquired pneumonia (CAP) in children. Our aim is to assess the prevalence and describe the clinical-radiographic-analytical features in hospitalized children with CAP caused by Mp.

Methods:

A prospective, observational study in children without underlying condition or with episodic asthma, admitted with CAP radiographically confirmed, to two hospitals in Madrid, between April-2012 through December-2014. Mp infection was defined by seroconversion and/or positive PCR in nasopharyngeal exudates.

Results:

Pneumonia caused by Mp was diagnosed in 16% (17/108) of the CAP cases; median of age 60 months (19-158). A half of the patients were under 5 years of age. Unilateral radiographic infiltrate was found in 16/17 patients (94.1%) and pleural effusion in 8/17 patients (47%). CRP values were >80 mg/L in only 5 cases (31%). All children had natremia ≥136 mMol/L and plasma albumin ≥3 g/L. The patients became afebrile in a median of 1 day (0-5). Four children (23.5%) need oxygen-therapy for a median of 1 day (1-8). We found that 6/17 infections (35.3%) were caused only for Mp, whereas 10 patients had association between Mp and viruses and a case had co-infection of Mp, virus and *Streptococcus pneumoniae*.

Conclusions:

1. Clinical, radiological or laboratory findings to distinguish CAP caused by Mp are lacking.
2. We have observed nonspecific laboratory exams.
3. The radiographic picture is usually unilateral and pleural effusion is frequent.
4. Mp CAP is usually associated to viral co-infection.
5. MP CAP is common in children under 5 years.

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ESPID-0958
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HYPONATREMIA IN HOSPITALIZED CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

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BACKGROUND AND AIMS:

The respiratory infections produce both, salt and water depletion as water retention due to inappropriate ADH secretion, leading both to hyponatremia. We analyzed the data of children with community-acquired pneumonia (CAP) with hyponatremia.

METHODS:
Prospective study evaluating clinical-laboratory and microbiological features of in-patients with CAP, in two hospitals in Madrid, from april-2012 to december-2014. An univariant analysis through X^2 was performed.

RESULTS:
Serum sodium ≤135 mMol/L was present in 41/108 (37,9%). 15/32 had urinary sodium <20 mMol/L and 10/32 >80. Median age was 30 months (2-194), 73,1% were male. Median CPR was 91 mg/L (1-442) and median procalcitonin was 1,18 ng/mL (0,02-36). The median for the days of IV antibiotics was 6 (1-18) and for the duration of fever 1 (1-14). The median for the hospital stay was 6 days (2-30). Viruses were documented in 32/36 patients, *Mycoplasma pneumoniae* in 5/36 and *Streptococcus pneumoniae* in 10/32 with 16/32 mixed infections.
Hyponatremia was associated to male gender [p= 0,005, RR 1.5 (CI95%1.1-2.1)], CRP >60 mg/L [p=0,023, RR 1,7 (CI95%1.0-2.8)], procalcitonin>0,5 ng/mL [p=0,03, RR 2,4 (1,3-4,5)] and longer IV antibiotics (p=0,038). No association was found with the hospital stay or days of fever.

CONCLUSIONS:

1. Hyponatremia is a common finding in hospitalized children with CAP.
2. Hyponatremia is often associated to hypovolemia, but inadequate ADH secretion is also a concern.
3. Hyponatremia is associated with male gender, higher CPR, higher procalcitonin and more days of IV antibiotherapy.
4. Hyponatremia could be considered as marker of severity and of inflammation.

ESPID-0732
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PECULIARITIES OF CAP IN HOSPITALIZED CHILDREN IN LATVIA.

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Background and aim: CAP remains to be a frequent cause of morbidity and mortality worldwide. Incidence is highest among children aged < 5 years. The aim is to find out peculiarities of CAP in children treated at University Children's Hospital.

Materials and methods: A descriptive cross-sectional study covers children with CAP from month to 18 years (10.2013.-02.2014.) The laboratory data were obtained using standardized methods.

Results: 117 children with CAP were analyzed from whom 70,1%(82) were aged 3 month - 5 years. Median: age - 34 months, duration of hospitalization - 6 days. 27,4%(32) were serologically positive to *M.pneumoniae* (65,6%(21) were 3 months to 5 years). Radiologically right side pneumonia - 50,4%(59), 8,5%(10)- bilateral pneumonia, 9,4%(11) no radiological changes have been found. CAP patients were diagnosed for: 100%(117) -cough 71,8%(84) – fever, 45,3%(53) – tachypnoea, 47%(55) - chest retractions, 14,5%(17) - SIRS positive. In 58.1%(68) CAP was mild, 35.9%(42) – moderate, 6%(7) - severe. Leucocytosis was found in 32,5% (38). 32,5% (n=38) of cases CRP > 50 mg/L. 79.5%(93) were vaccinated according to the NIP. Antimicrobial therapy (AB) didn't match CAP treatment guidelines in 49,6% cases. Inadequate AB treatment - 14,5%(17), inappropriate dosage - 28,2%(33).

Conclusions: No differences from literature were detected in clinical and laboratory features. Preventive measures were used only in 79.5%. In 49,6% therapy prescribed were not according to guidelines. Study underlines possibility of *M.pneumoniae* importance in children younger than 5 years.

Study supported by Latvia SRP 5.6.2.

ESPID-0906
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RETROSPECTIVE EVIDENCE OF THE ACHROMOBACTER XYLOSOXIDANS NOSOCOMIAL TRANSMISSION.

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Background and aims. The number of *A. xylosoxidans* cases in the healthcare units, not only in CF patients, was increased last years. The aim of this research was to analyze the diversity of this pathogen in the CF patients' respiratory tract.

Methods. Bacterial identification and genotyping were performed by amplification and sequencing of *16S rDNA, gltB* genes for *A. xylosoxidans*, MLST protocols for *Bcc*, *P. aeruginosa*, DLST – for *S. aureus*. Analysis of sequences was made by ClustalW2 and BLAST programs.

Results. The samples of the sputum, aspirate or/and strains of 240 CF patients were analyzed during two-three years period of time. 20.8% of the patients were infected by *Achromobacter spp.* All these patients demonstrated the intensification of respiratory symptomatology, the increasing of the number of chronic purulent bronchitis worsening, rapid degradation of the pulmonary function. In cases of the chronic colonization the eradication of this pathogen was practically impossible. Most of the CF patients' respiratory tract was colonized by *A. xylosoxidans* with 20 different *gltB* gene alleles. *A. xylosoxidans* with allele 1 and 2 had together prevalence 56%. The most frequently found pathogen was *A. xylosoxidans* with allele 2 (36%). Only one patient with *A. xylosoxidans* allele 2 was not hospitalized in special children healthcare unit. In this group the patients of 1996 and 1997 year of birth have predominated.

Conclusions. Apparently an outbreak of *A. xylosoxidans* had place in the last 1990 in the children hospital, so *A. xylosoxidans* with allele 2 have spread between CF patients.

ESPID-1020
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RHINOVIRUS C IS NOT ASSOCIATED WITH WHEEZING OR SEVERE DISEASE IN AN UNSELECTED BIRTH COHORT FROM THE NETHERLANDS.

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Background

Human rhinovirus (HRV) is a frequent pathogen in young children, eliciting symptoms ranging from common colds to wheezing illnesses and lower respiratory tract infections. The recently identified HRV-C seems to be associated with wheezing, asthma exacerbations and more severe disease, but results vary. We studied the prevalence and severity of infection with HRV in the unselected EUROPA birth cohort.

Methods

Children with acute respiratory symptoms entered the symptomatic arm of the cohort and were compared to asymptomatic children. Severity of wheezing and other respiratory symptoms were registered and respiratory viruses were evaluated using throat and nasopharyngeal swabs on first presentation and after symptomatic recovery (wheezing children). HRV genotyping was performed on HRV-PCR positive samples.

Results

HRV was the most prevalent respiratory virus and was found in 58/140 (41%) symptomatic children, in 24/96 (26%) control children and in 19/74 (25%) symptomatic wheezing children after recovery (p

Conclusion

In an unselected birth cohort from the Netherlands, HRV was the most prevalent respiratory virus. Our results suggest that HRV-C is not associated with more severe disease or wheezing in young children in the general population.

ESPID-0452
UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HUMAN BOCAVIRUS 1 INFECTION MARKERS IN CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT DISEASE IN LATVIA

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Background and aims

Respiratory infections due to HBoV1 are systemic and can be diagnosed serologically. Viremia is an excellent marker of acute HBoV1 infection.
Our aim was to identify the presence of HBoV1 DNA and determine HBoV1-specific IgM and IgG class antibodies in hospitalized children less than five years of age with acute lower respiratory tract infection (LRTI) in Latvia.

Materials and Methods

37 children hospitalized from October 2013 to February 2014 who fulfilled the LRTI WHO criteria and had fever were enrolled in this investigation. The mean age of the patients was 22.4 months (range 2-50). A blood sample, nasopharyngeal aspirate (NPA) and stool sample was obtained on admission. 37 whole blood samples, 33 NPAs and 24 stool samples underwent HBoV1 NS1-PCR. HBoV1 serology was done with ELISA using recombinant virus-like particles as antigen and blocking reagent.

Results

HBoV1 DNA was detected in 2/37 (5.4%) whole blood, in 5/33 (15.2%) NPAs and in 5/24 (20.8%) stool samples. In 3 patients HBoV1 DNA was found in two sample types simultaneously. The median age of the 9 HBoV1 DNA-positive children was 31.8 months (range 15-50). On admission all HBoV1 DNA positive patients had cough and fever, 6/9 had difficulty breathing, 2/9 had tachypnea and 5/9 crackles on auscultation. 7/9 HBoV1 DNA positive patients and 26 (70.3%) in total were HBoV1-IgG positive. In 3 PCR-positive patients HBoV1-IgM class antibodies were found.

Conclusion

In this study we confirm both acute and past HBoV1 infection among children with LRTI in Latvia using NS1-PCR and serology.

ESPID-0701
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

EVALUATION OF THE FIRST MEASLES, MUMPS AND RUBELLA (MMR) VACCINATION: ARE VACCINATION RATES SUFFICIENT?

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Background and Aims

MMR vaccination is very effective at reducing rates of measles, mumps and rubella. [1,2,3] The first dose should be given at 12 -13 months, the second at 40 months. [4]

Dr Wakefields' study (discredited) proposed a link between autism and the MMR vaccination resulting in a significant drop in uptake. [5] Consequences of this are ongoing, resulting in disease outbreak. [6] The World Health Organisation (WHO) aim to achieve vaccination coverage >95% to eliminate MMR by 2015.[7] This audit investigates the current MMR uptake in a primary care setting.

Methods

Retrospective audit investigating first MMR vaccine uptake, in children aged 13 -24 months (September 2014.) Data was collected using System One database. Information regarding patient demographics, age and uptake of vaccination were recorded.

Results

Of the 50 infants 60% were male, 40% female. 41/50 had received their first MMR (82%), leaving 18% unvaccinated. Average age of vaccination was 14 months.

Of the 9 who were unvaccinated; 1 parent refused all immunisations, 1 child was lost to follow up, 1 child was from a vulnerable family and failed contact was reported for the last.

Conclusion

At the time of the study, almost one in five (18%) children were unvaccinated. At present, vaccination rates fall below the WHO's target - 95%.[7] Methods to improve uptake include; contacting families and checking patients' records when they attend the surgery.

Low vaccination rates should not be ignored so future outbreaks of these very infectious disease and possible fatalities can be prevented. [4]

ESPID-0224
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

DIFFERENTIAL IMPACT OF PCV AND ROTAVIRUS VACCINE ON EMERGENCY-ROOM VISITS AND HOSPITALIZATION RATES IN CHILDREN

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Background: The introduction of rotavirus vaccine (RVV) and PCV7/PCV13 to the Israeli national immunization plan (NIP) resulted in a substantial reduction of rotavirus gastroenteritis (RVGE) and alveolar pneumonia, respectively, in children

Methods: Our center serves a captive population of ~30,000 children

Results: RVGE, alveolar pneumonia and LRI rates in outpatients significantly decreased by 80%, 76% and 19%, respectively, while non-RVGE gastroenteritis did not decrease significantly. In hospitalized children the decrease in disease rates was 66%, 36%, 29% and 26%, respectively (all p**Table 1)**. Overall PER visit and hospitalization rates were reduced by 6% and 19%, respectively.

Conclusions: Our data suggest that both RVV and PCV substantially contributed to the reduction in medical service use with emphasis on hospitalization. However, the study also suggests that in the immediate post-vaccine introduction RVV contribution

surpassed that of PCVs.

Table 1. Rates per 1,000 and incidence rate ratios (IRRs) of RVGE, non-RVGE GE, alveolar pneumonia and LRI pediatric Emergency Room (PER) visits and hospitalization in children <2 years old in southern Israel, April 2006–March 2013

	Outpatient PER visit					Inpatients				
	Apr 06 - Mar 08	Apr 08 - Mar 11	Apr 11 - Mar 12	Apr 12 - Mar 13	*IRR (95% CI)	Apr 06 - Mar 08	Apr 08 - Mar 11	Apr 11 - Mar 12	Apr 12 - Mar 13	*IRR (95% CI)
RVGE	9.7	6.1	2.4	1.9	**0.20 (0.15-0.25)**	8.8	10.6	4.3	2.9	**0.34 (0.27-0.42)**
Alveolar pneumonia	7.9	5.2	2.8	1.9	**0.24 (0.19-0.31)**	14.9	16.0	9.5	9.5	**0.64 (0.56-0.73)**
LRI	40.3	54.3	33.1	32.3	**0.81 (0.75-0.87)**	59.4	58.6	48.5	41.6	**0.71 (0.67-0.75)**
Non-RVGE GE	43.7	37.9	31.8	41.0	0.94 (0.88-1.00)	36.7	29.0	25.9	27.2	**0.74 (0.69-0.81)**
All visits**	360.7	349.9	305.8	330.8	**0.94 (0.92-0.96)**	282.2	261.4	235.4	216.2	**0.81 (0.79-0.83)**

* IRR (95% CI) is calculated for comparison of the 4th and the 1st periods

** IRR (95% CI) is calculated for the rate of ER and hospitalized children out of the entire region population

ESPID-0330
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

CONCOMITANT ADMINISTRATION OF A FULLY LIQUID, READY-TO-USE HEXAVALENT VACCINE DTAP-IPV-HB-HIB WITH A MENINGOCOCCAL SEROGROUP C VACCINE IN INFANTS.

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Background and aim: To study the immune response to all antigens included in this hexavalent vaccine when co-administered with MenC vaccine.

Methods: Phase III, open-label, randomised, multi-center study (HXM01C) in Finland. 350 infants primed at 2-3-4 months with hexavalent vaccine (Hexyon/Hexaxim/Hexacima). 175 infants had MenC vaccine (NeisVac-C) co-administered at 2-4 months. Routine vaccination of all infants with Prevenar 13 and RotaTeq. Non inferiority of hepatitis B response assessed one month post third dose of hexavalent vaccine. Acceptability of Men C response assessed one month after second dose of MenC vaccine. Antibody response to all antigens post third dose of hexavalent vaccine and hexavalent safety profile described.

Results:

Primary Objective: non inferiority for Hep B response post dose 3 / acceptability for MenC response post dose 2				
Primary Series (3-dose Hexavalent / 2-dose MenC) **Per Protocol Population**	**Hexavalent + MenC** **N=162**	**Hexavalent without MenC** **N=160**	**Seroprotection Rate Difference**	**Conclusion**
Anti-HBs ≥ 10 mIU/mL	156 (**97.5%**)	149 (**96.1%**)	1.37%	Non-inferiority met (1)
[95% CI] (≥ 10 mIU/mL)	[93.7;99.3]	[91.8;98.6]	[**-2.92** ; 5.95]	
(1) Group 1 seroprotection rate is considered as non-inferior to Group 2 seroprotection rate if the lower bound of the 95% CI of the difference is greater than -10%				
Anti-MenC ≥ 8 (1/dil) (rSBA)	162 (**100%**)	NA	NA	Acceptability met (2)
[95% CI] (≥ 8 [1/dil])	[**97.7**;100]	NA	NA	
(2) Seroprotection rate is considered as acceptable if the lower bound of the 95% CI is greater than the pre-specified acceptability threshold: 90%.				

Post-dose 3 Ab response to all Hexavalent vaccine antigens (Per Protocol Population)	**Hexavalent + MenC - N=162**	**Hexavalent without MenC - N=160**
Anti-PRP (% ≥0.15 µg/mL) [95% CI]	98.1% [94.6;99.6]	94.3% [89.5;97.4]
Anti-D (% ≥0.01 IU/mL) [95% CI]	100% [97.7;100]	99.4% [96.5;100]
Anti-T (% ≥0.01 IU/mL) [95% CI]	100% [97.7;100]	100% [97.7;100]
Anti-PT (% Vaccine response §) [95% CI]	98.7% [95.4;99.8]	100% [97.6;100]
Anti-FHA (% Vaccine response §) [95% CI]	99.4% [96.4;100]	100% [97.6;100]
Anti-IPV1 (%≥8 (1/dil) [95% CI]	100% [97.7;100]	98.7% [95.3;99.8]
Anti-IPV2 (% ≥8 (1/dil) [95% CI]	100% [97.7;100]	100% [97.6;100]
Anti-IPV3 (% ≥8 (1/dil) [95% CI]	100% [97.7;100]	99.3% [96.4;100]
§ Vaccine response: If pre-vaccination antibody concentration <8 EU/mL, then the post-vaccination antibody concentration should be ≥8 EU/mL. Otherwise, post-vaccination antibody concentration should be ≥ pre-immunisation level		

Safety profile was similar in both groups. Only one related SAE: fever ≤39.5°C in concomitant group.

Conclusions: Co-administration Hexavalent with Men C demonstrated as non-inferior in terms of seroprotection rate for hepatitis B post third dose. Acceptability of MenC seroprotection rate demonstrated post second dose. Good immune response to Hexavalent antigens when MenC co-administered. All vaccines were well tolerated. Hexavalent safety profile consistent with established product profile. Study funded by Sanofi Pasteur MSD.

ESPID-0505
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

PREFERENCES OF HEALTHCARE PROFESSIONALS REGARDING PEDIATRIC HEXAVALENT VACCINE DEVICES IN GERMANY. A DISCRETE CHOICE EXPERIMENT STUDY.

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Background and aims

Improvements of vaccine delivery devices can save time, reduce potential of incorrect handling / mishandlings and therefore be beneficial to health care providers (HCPs). This study was designed to understand the value that HCPs place on features of hexavalent vaccine devices in Germany.

Methods

A standardised survey methodology called a discrete choice experiment (DCE) was developed[1]. Literature review and qualitative interviews with HCPs were used to identify 5 key attributes of vaccine devices: type of device, years of experience with the device, preparation time, risk of mishandlings and administering incomplete content. 150 pediatricians and 150 nurses in Germany completed the DCE survey which presented participants with hypothetical pairs of devices. A conditional logistic regression model predicted which attributes participants preferred. The study was approved by US Salus IRB (A2348/0027).

Results

Analysis of the survey data showed that all identified attributes were significantly important ($p<0.01$). Probability of administering incomplete content was the most important attribute for both groups; Odds Ratio were 3.62, and 3.95 respectively for pediatricians and nurses. Significantly high value was placed by nurses and pediatricians on a pre-filled syringe (compared to one requiring reconstitution) and on years of experience with a device respectively ($p<0.01$). Pediatricians more than nurses valued devices which took less time to prepare ($p<0.01$).

Conclusions

This study shows the importance of improvements of vaccine delivery devices for HCPs. These factors may influence decisions in vaccination practices.

[1]Ryan M (2004) Discrete choice experiments in healthcare. BMJ. Feb 14, 2004; 328(7436): 360–361.

ESPID-0733
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

BCG ADVERSE EVENT ASSOCIATED WITH TRANSIENT LYMPHOPENIA IN INFANTS

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Background and aims: In countries where tuberculosis is highly prevalent, the early administration of BCG prevents disseminated tuberculosis, which has its highest incidence in the first year of life. However, this vaccination strategy allows that infants with a primary immunodeficiency disease not yet manifested and/or diagnosed receive a vaccine with live attenuated mycobacteria, risking the development of BCG adverse events (BCG-AE). The aim of this study was to assess lymphocyte subsets in infants with BCG-AE. **Methods:** From 2009 to 2011, 91 infants with localized BCG-AE were evaluated. They were tested for lymphocyte subsets (CD4+T, CD8+T, B and NK cells) by flow cytometry during BCG-AE follow-up. The study was approved by the Ethics Committee and all parents gave written informed consent. **Results:** Six out of 91 children (6.6%) had lymphopenia: three with low CD4+T (one, also low neutrophils), two with low CD8+T and one with low B cells. None had severe combined immunodeficiency disease diagnosed. None of them were HIV-exposed or had chronic granulomatous disease. All six infants had moderate to severe infectious episodes, but all of them had BCG healing after isoniazid treatment for a median period of 6 months (range,3-9). Two had genetic syndromes diagnosed. Table shows clinical and laboratorial data. After repeated reevaluations, all six children reached normal lymphocyte subset values between 18 and 52 months of age. **Conclusions:** Transient lymphopenia (either idiopathic or secondary) is associated with some cases of BCG-AE and should be part of differential diagnosis of immunodeficiency

conditions associated with vaccine adverse events.

Age at BCG-AE (mo)	BCG-AE	Reduced lymphocyte subset	Age at lab evaluation (mo)	Cells/mm³ (reference value)	Other clinical manifestations
3	suppurative lymphadenitis	CD4+ T cells	18 32 37 52	**732 (>957)** **540 (>786)** **666 (>786)** 986 (>786)	-Urinary tract infection and neonatal sepsis -Bronchopneumonia and bronchospasm -Pneumonia -Recurrent sinusitis and otitis media
3	suppurative lymphadenitis	CD4+ T cells	9 10 17 28	**614 (>1360)** **389 (>1360)** 2013 (>957) 1719 (>786)	-Pneumonia, diarrhea and sepsis with hospital admission -Pneumonia -Recurrent otitis media
2	suppurative lymphadenitis	CD4+ T cells/ neutrophils	3.7 8 26	**1161/730 (>1360/1500)** **1108/750 (>1360/1500)** 1213/1380 (>786/1500)	-Bacteremia after surgical drainage of lymph node -Perianal abscess -Renal lithiasis
1	suppurative lymphadenitis	CD8+ T cells	7 9 31 35	**359 (>559)** **357 (>559)** 455 (>452) 626 (>452)	-Podocki-Schaffer Syndrome (congenital bilateral cataracts, multiple CNS abnormalities and interartrial communication) -Recurrent bacterial infections, some with hospital admission
3	injection-site abscess	CD8+ T cells	7 35	**495 (>559)** 599 (>452)	-Chromosome 17p13.3 deletion syndrome -Neurodevelopmental delay -Pneumonia, anaphilaxys, stomatitis
3	enlarged lymph node>3 cm	B cells	6 10 18	**810 (>888)** **853 (>888)** 1993 (>649)	-Neonatal hospital admission for 25 days due to jaundice and poor weight gain -Recurrent moniliasis without improvement with nistatin

ESPID-0959
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

PNEUMOCOCCAL CARRIAGE AND IMPACT OF PNEUMOCOCCAL VACCINATION IN THE FIRST YEARS OF LIFE IN CHILDREN WITH ASTHMA

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Background and aims: *Streptococcus pneumoniae* (*Sp*) carriage is a prerequisite for the development of pneumococcal infection. Pneumococcal conjugate vaccines (PCVs) modify the carriage, reducing the risk of disease. Asthma favors pneumococcal infections. However, in pediatrics, PCV booster doses are recommended only in children with severe asthma receiving high dose corticosteroids. Knowledge of *Sp* carriage in asthmatic older children and impact of PCVs administered in the first year of life could permit to evaluate persistence of protection and need for further PCV administration.

Methods: Children aged 6-17 years with stable asthma regularly followed in 5 pediatric centers were enrolled. An oropharyngeal swab was obtained from each subject together with information regarding pneumococcal vaccination status. Swabs were tested for the autolysin-A (*LytA*) and wzg (*cpsA*) genes of *Sp* with real-time PCR. The positive samples were serotyped for the identification of PCV13 serotypes.

Results: A total of 423 asthmatic children (44.8% 6-9 years, 36.8% 10-14 years, 18.4% ≥ 15 years) was enrolled. Carriage was evidenced in 52.8%, 43.5% and 22.5% of the subjects included in the 3 age groups ($p<0.05$), respectively, and was independent of previous vaccination with PCV7. Even in vaccinated subjects colonization was mainly due to serotypes included in PCV13.

Conclusions: Asthmatic children older than 5 years who have received PCV in the first year of life are frequently colonized by *Sp*. Moreover, results indicate that duration of protection against carriage wanes with time, suggesting the need for systematic PCV booster doses during the school period in asthmatic children.

ESPID-0837
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

PS-SPECIFIC B MEMORY CELLS (MBC) INDUCED BY THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN HIV INFECTED ADULTS

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Background and aim:
Pneumococcal Invasive Disease is a major cause of morbidity and mortality in HIV infected adults. MBCs have been associated with the maintenance of immunological memory. We aim to enumerate PCV13-induced MBCs in HIV patients and explore the role of CD4 count on the establishment of immunological memory.

Methods:
Forty HIV-infected(27-57years) adults on ART with undetectable viral load received 1 PCV13. Blood samples were collected pre- and 1month post PCV13 for phenotypic analysis of PS3 and PS14-specific MBCs with flow cytometry and IgG-antibody measurement against PS 19A,3,14,18,9V with ELISA.

Results:
An overall increase in Resting([RM]PS+CD19+CD10-CD27+CD21+) MBCs was found and more profoundly in IgG(PS+CD19+CD10-CD27+CD21+IgM-) MBCs (7.5%vs15.6% p=0.02 for PS14, 5.4%vs8.9% p>0.05 for PS3). In contrast, a decrease in RM IgM(PS+CD19+CD10-CD27+CD21+IgM+) MBCs was observed (6.8%vs3.5% p<0.001 for PS14, 5.4% vs2.9%,p=0.04 for PS3). IgG MBCs post vaccination were significantly correlated with IgM MBCs at baseline(r=0.790,p=0.0003 for PS14, r=0.625,p=0.009 for PS3). Post-PCV13 antibody levels were associated with IgG MBC count pre-vaccination (r=0.538,p=0.03 for PS14, r=0.8246,p<0.0001 for PS3). Antibody levels against PS3 did not rise from baseline in patients with CD4 counts<400 cells/μl and IgM MBCs in this group were lower pre and post-PCV13 than in patients with CD4≥400cells/μl.

Conclusions:

Immunization with PCV13 results in the enrichment of the resting memory pool in HIV infected adults. However, the IgM MBC compartment was not replenished. PS specific MBC counts at baseline affected the magnitude of the immune response to

vaccination. CD4 counts <400 cells/μl were associated with impaired cellular and humoral response.

ESPID-0491
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

VACCINATION AGAINST MEASLES OVER TIME AMONG CHILDREN IN THE SLOVAKIA

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Background and aim:

In Slovakia vaccination against measles was introduced in 1969. At present we use trivalent vaccine (measles, mumps and rubella), first dose is recommended for children aged 15–18 months and second dose for 10 year olds. The aim of this work was to analyse vaccination coverage in the children population.

Methods:

Retrospective review of vaccination coverage of measles reported since 2000 to 2014. We analyse vaccination status of 24-months-old children according to age-group from 1998 to 2012 (MCV1) and 10-years-old children according to age-group from 1990 to 2004 (MCV1). The epidemiological data were obtained from the Epidemiological Information System of the Slovak Republic, data about vaccination from the regular controls in the Slovakia.

Results:

The vaccination against measles began on 1969 with monovalent vaccine, the vaccination against mumps began on 1987 with bivalent vaccine (measles, mumps) and from 1992 we used trivalent vaccines (MMR). Our analysis showed the positive impact of vaccination against measles on the epidemiological situation in Slovakia. Since 1999 measles has been eliminated, only imported cases were reported in our country. The vaccination coverage was at the highest level (98-99%) in the long-term. In the last children cohort (born in 2011and 2012) 96.6% and 94.1% vaccination coverage was noticed.

Conclusions:

Our analysis showed the positive impact of vaccination against measles on the epidemiological situation in Slovakia and influence of risk factors on our vaccination coverage. Our presentation was supported by the Slovak Research and Development Agency under No. APVV-0096-12 (EPIBIOMAT).

ESPID-0655
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

COMPARISON WITH IMMUNOGENICITY AND SAFETY OF THREE HEPATITIS A VACCINES IN CHILDREN

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Aims: Several kinds of hepatitis A virus vaccines have been licensed since 1997 in Korea. However, there were no head to head comparison studies for immunogenicity and safety among these vaccines in Korean children. Therefore, we conducted this clinical study.
Methods: Subjects were randomized to be vaccinated with either Avaxim™, Epaxal® or Havrix® on day 1 and after 6months in healthy children of 12 to 18 months of age. Then, total anti-HAV titers were measured by enzyme immunoassay (Elecsys® Anti-HAV [Roche Diagnostics GmbH, Mannheim, Germany]). And we also observed any adverse events on each dose of vaccinations.
Results: Total 107 cases we reenrolled, however, 103 cases were available to detect the immunogenicity. After the 2nd dose, all subjects demonstrated 100% seroprotection with all vaccines and the geometric mean titers of Avaxim™ (n=36), Epaxal® (n=30) and Havrix® (n=37) were 6,182, 1,871, and 2,759 IU/L, respectively. Most solicited reactions occurred within 4 days of vaccination, resolved within 3 days and were mild. Severe solicited events occurred after 0% of doses in Avaxim™, 6.1% in Epaxal® and 5.4% in Havrix®. All severe solicited events were not related to vaccination. No withdrawals occurred because of adverse events.
Conclusions: All three types of hepatitis A virus vaccines using in Korea are highly immunogenic and safe.

ESPID-0526
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

ANTI-MEASLES ANTIBODY LEVELS IN COMMERCIALLY AVAILABLE IMMUNOGLOBULIN PRODUCTS IN KOREA

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Background and Aims

Recently, as measles infection is rare in Korea, the anti-measles antibody level from the blood donors is expected lower than those of previous decades. This study was aimed to know the anti-measles antibody titer in the Korean immunoglobulin (IG) products and to suggest the protective dose of those products in pre- or post-exposure prophylaxis against measles.

Methods

We analyzed 16 lots of 2 intravenous immunoglobulin (IVIG) products and 2 lots of a single intramuscular immunoglobulin (IMIG) product commercially available in Korea. Plaque reduction neutralization (PRN) test was used to measure the anti-measles titer of the products. The measured geometric mean titer (GMT) was calculated into actual administration dose in current Korean IG dosage guidelines.

Results

The PRN GMTs of antibody against measles of the IVIG products ranged from 4.8 to 14.3 IU/mL (38.4 – 114.4 IU/kg when administered at the dose of 400 mg/kg) (**Table**). The PRN GMTs of 2 lots of the IMIG product were 10.9 and 15.8 IU/mL (2.7 and 4.0 IU/kg when administered at the dose of 0.25 mL/kg), respectively.

Conclusion

In this study, the IG levels of currently available IVIG products in Korea are suggested to be sufficient to prevent measles infection at the recommended dose of 400 mg/kg. The current guideline dose of 0.25 mg/kg of IMIG products, however, was not expected to be protective and is needed to be amended.

Table. Plaque Reduction Neutralization Titer Against Measles in Korean IVIG Products

Product	Lot	PRN GMT (IU/mL)	Dose* (IU/kg)
A	1	9.4	75.2
	2	9.6	76.8
	3	8.2	65.6
	4	10.4	83.2
	5	14.0	112.0
	6	6.6	52.8
	7	6.0	48.0
	8	7.4	59.2
	9	8.0	64.0
	10	4.8	38.4
B	1	9.3	74.4
	2	11.3	90.4
	3	6.6	52.8
	4	10.4	83.2
	5	14.3	114.4
	6	9.9	79.2

*Administration dose of intravenous immunoglobulin product at 400 mg/kg

IVIG, intravenous immunoglobulin; PRN, plaque reduction neutralization; GMT, geometric mean titer

ESPID-0925
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

NUMBER AND CHARACTERISTICS OF INTUSSUSCEPTION CASES FOLLOWING ROTAVIRUS VACCINATION REPORTED TO THE EUDRAVIGILANCE DATABASE 2006 - 2014

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Background and aims Observational studies in Australia and US indicate that rotavirus vaccines carry an increased risk of intussusception (IS) up to six additional cases per 100,000 infants. The number and characteristics of cases spontaneously reported 2006-2014 was searched for in the EU EudraVigilance database.

Methods IS reports submitted until 1 July 2014, where RV1 or RV5 were reported as a suspect or interacting medicinal product, were collected and analysed. Vaccine doses distributed was requested from manufacturers. Informed consent waived.

Results 296 reports were identified. Cases by product, gender, dose number and time to onset are presented.

	RV1		**RV5**	
	2-dose schedule		**3-dose schedule**	
Distributed doses	9.7 million		7.9 million	
	n	**%**	**n**	**%**
Number of reports	198	100	98	100
Distribution by gender				

Male	119	60.1	63	64.2
Female	62	31.3	35	35.8
Unspecified	17	8.6	-	-
Distribution by dose				
1	174	87.9	92	94
2	24	12.1	6	6
3			-	-
Distribution by time to onset (days)				
1-7	112	56.6	47	48.0
8-14	12	6.1	9	9.2
15-21	6	3.0	7	7.1
>21	34	17.2	24	24.5
	n	**days (±SD)**	**n**	**days (±SD)**
Mean age at administration by dose				
1	110	91.5 ±33	76 ±43	95 ±43
2	13	108 ±22	93 ±20	93 ±20
3	-		-	

Conclusions Spontaneous reports in EudraVigilance had information on vaccine used and dose number. Details on age at vaccination and time to onset of symptoms were not always available. Reporting can be improved. Another limitation is the lack of denominator in EU for incidence calculations.

ESPID-0377
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IMMUNOGENICITY OF MENINGOCOCCAL C AND DTAP-IPV-HIB VACCINES IN PREMATURE INFANTS

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INTRODUCTION & AIMS

Premature infants represent 7% of all births in the UK and have higher rates of vaccine preventable infections. National recommendations for vaccine schedules focus predominantly on term infants. We aimed to assess the immunogenicity of the UK immunisation schedule in premature infants as part of a vaccine trial.

METHODS

210 infants (*Haemophilus influenzae* type b; Pediacel®, Sanofi Pasteur MSD) vaccine at 2, 3 and 4 months of age and meningococcal C conjugate vaccine (Menjugate®, Novartis) at 2 and 3 months alongside 3 different PCV13 vaccine schedules. At 12 months of age participants received MMR, PCV13 and Hib-MenC-

TT (Menitorix®, GSK) vaccines. Antibody concentrations were measured before and one month after primary and booster vaccinations.

RESULTS

The median birth gestation was 29^{+6} weeks (range 23^{+2}-34^{+6}). Seroprotection rates at each time point are shown in table 1. Younger gestation was associated with lower antibody concentrations at baseline and following primary vaccination for meningococcal C and diphtheria. There was no effect of chronic lung disease, growth restriction or the receipt of blood products, antenatal or postnatal steroids on vaccine responses.

	Before primary vaccination		After primary vaccination		Before booster vaccination		After booster vaccination	
	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)
Hib	50/191	26 (20-32)	131/175	75 (68-82)	93/178	52 (45-60)	183/185	99 (97-100)
Meningococcal C	13/192	7 (4-11)	173/ 177	98 (95-100)	50/166	30 (23-38)	170/173	98 (94-99)
Diphtheria	36/190	19 (14-25)	173/175	99 (97-100)	132/178	74 (67-80)	178/185	98 (95-100)
Tetanus	118/190	62 (55-69)	173/175	99 (97-100)	157/178	88 (82-92)	183/185	99 (96-100)

Table 1: Percentage of infants with protective antibody concentrations / titres. Correlates of protection: Hib IgG ≥0.15µg/ml, MenC SBA ≥1/8, diphtheria IgG ≥0.1IU/ml, tetanus IgG IgG ≥0.1IU/ml.

CONCLUSION

Premature infants respond well to this schedule regardless of their co-morbidities. The low rates of Hib and meningococcal C seroprotection at 12 months of age highlight the importance of timely booster doses; further reductions in the number of priming doses may increase the period of susceptibility to these vaccine preventable infections.

ESPID-0184
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

EVALUATION OF OPSONOPHAGOCYTIC KILLING ACTIVITY OF NEW PNEUMOCOCCAL STANDARD REFERENCE SERUM, 007SP

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Background

A new human pneumococcal standard reference serum, 007sp, is available as a standard serum for the evaluation of anti-pneumococcal antibody. It was produced by U.S. Food and Drug Administration after collecting from 278 volunteers, 4 and 8 weeks after immunization with the 23-valent pneumococcal polysaccharide vaccine. Antibody concentrations in 007sp were established using the WHO reference ELISA by five independent laboratories. However, the opsonic titers (index) in 007sp were not established yet. This study was performed to determine the opsonic titers to several pneumococcal serotypes in 007sp.

Method

Functional antibody opsonic titers were measured by multiplexed opsonophagocytic killing assay (MOPA) for 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F). These assays were repeated 36 times for each serotype on different days.

Results

The mean opsonophagocytic killing titers and standard deviations are summarized in table 1. The interassay coefficient of variation for each serotype ranged from 13 to 48%.

Conclusion

A multi-laboratory OPA study is currently being performed to assign OPA titers in 007sp including Ewha Center for Vaccine Evaluation and Study. This study will be helpful for the evaluation of new pneumococcal vaccines.

ESPID-0672
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

SEQUENCING ANALYSIS OF THE ANTIGENS INCLUDED IN THE FOUR-COMPONENT VACCINE AGAINST B MENINGOCOCCUS IN THE CZECH MENINGOCOCCAL ISOLATES IN 2007-2013

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Background and aims: Study of the antigens included in the newly registered four-component vaccine against meningococcus B (MenB vaccine) and assessment of the potential of the vaccine for use in the Czech Republic.

Methods: Czech isolates of *Neisseria meningitidis* were screened for four antigens: fHbp (factor H binding protein), NHBA (Neisseria heparin binding antigen), NadA (neisserial adhesin A), and PorA P1.4 outer membrane protein. A total of 304 *N. meningitidis* isolates from 2007-2013 were included in the study: 262 isolates from invasive meningococcal disease (IMD) and 42 isolates from healthy carriers.

Results: The gene encoding the fHbp peptide was detected in all study isolates from both IMD cases and healthy carriers. The presence of the nhba gene encoding the NHBA peptide was revealed in all study isolates from both IMD cases and healthy carriers. The presence of the nadA gene encoding the NadA peptide was only found in 26.6% of serogroup B isolates from IMD cases in comparison to 40.7% of non-B isolates from IMD cases. As few as 4.8% of isolates from healthy carriers harboured the nadA gene. The PorA P1.4 protein was only detected in two serogroup B isolates from IMD cases and in none of the isolates from healthy carriers.

Conclusions: The four-component MenB vaccine has proven suitable for use in the Czech Republic.

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ESPID-0060
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

CHILDREN WITH BREAKTHROUGH VARICELLA INFECTION REQUIRING HOSPITALIZATION IN TURKEY (VARICOMP STUDY 2008-2013)

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Introduction: Varicella in previously immunized individuals, known as “breakthrough varicella”. While the majority of breakthrough cases are mild, some may be more severe, requiring hospitalization in previously healthy children or children with an underlying condition.

Methods: The VARICOMP Study is a multi-center study (served 50% of the pediatric population), conducted to provide epidemiological data on hospitalization for varicella infections among children in Turkey between 2008-2018. We aimed to evaluate breakthrough varicella infection requiring hospitalization before the use routine use of varicella vaccine between 2008-2013.

Results: Between 2008-2013, 1939 children were hospitalized due to varicella infection, 36 children (20 boys, 16 girls, mean age 68.0+37.6 months, all received single dose live varicella vaccine, 61.1% previously healthy children) with breakthrough varicella infection requiring hospitalization. The median time elapsed since vaccination was approximately 5 years. Neurological complications, mainly

encephalitis/meningitis, were the most common reason for hospitalization in previously healthy children. The median length of hospital stay was 8 days. Acyclovir was administered to 83.3% of children (median 8 days), antibiotics to 70.6% of children. One child with leukemia died due to secondary bacterial infections and sepsis.

Conclusion: Breakthrough varicella requiring hospitalization is not rare in Turkey in the pre-vaccine era, is mainly observed in previously healthy children at 5 years after a single-dose varicella vaccine. Our further surveillance since 2013, in the same settings could evaluate the effectiveness of national immunization with single-dose varicella vaccine at 12 months of age. A two-dose varicella vaccine policy may be needed to provide improved protection.

ESPID-0890
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

AN UPDATE OF THE COST-EFFECTIVENESS OF INFANT PNEUMOCOCCAL VACCINATION IN THE UNITED KINGDOM

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Background and aims: In the light of new evidence regarding efficacy against vaccine and cross-reactive serotypes (STs), the cost-effectiveness of the 10-valent pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) is evaluated versus the 13-valent Pneumococcal Conjugated Vaccine (PCV-13) for infant vaccination in the United Kingdom using the model published by Knerer, G. et al, J Med Econ, 2012.

Methods: Using, in accordance with expert panel, the efficacy estimates below (see Table1) and estimates for pneumonia similar for both vaccines, the model estimates impact of vaccination on invasive pneumococcal disease (IPD), pneumonia and acute otitis media (AOM) in terms of cases, resource use, costs and quality-adjusted life years (QALY).

Results: The model estimates a similar reduction in IPD and pneumonia for both vaccines and for PHiD-CV fewer general practitioner (GP) consultations and tympanostomy tube placements (TTP) related to highly prevalent AOM. With parity pricing, the Incremental Cost-Effectiveness Ratio (ICER) per QALY gained for PHiD-CV vs. PCV-13 is -£ 9,288 (dominant) reflecting both cost savings (-£ 2,595,939) and health benefits (279 QALY).

Conclusions: Parity priced PHiD-CV offers both cost savings and health benefits compared to PCV-13 due to fewer cases of AOM/TPP. Perspectives of the model are

instrumental in informing policy makers and decision making by payer jurisdictions.

IPD	PHiD-CV	PCV-13	References
Common STs 1,4,5,6B,7F,9V,14,18C,19F,23F	0.947	0.947	Whitney, C.G., et al. Lancet, 2006. Andrews NJ, et al. Lancet Infect Dis, 2014.
ST 3	0	0	Andrews NJ, et al. Lancet Infect Dis, 2014.
ST 6A	0.76	0.947	Vesikari, T., et al. Pediatr Infect Dis J, 2009. (PHiD-CV and PCV-7 similar antibody responses to 6A) Whitney, C.G., et al. Lancet, 2006. Andrews NJ, et al. Lancet Infect Dis, 2014.
ST 19A	0.500	0.947	Conservative estimates based on immunogenicity/expert opinion for PHiD-CV Whitney, C.G., et al. Lancet, 2006. Miller, E., et al. Vaccine, 2011. Andrews NJ, et al. Lancet Infect Dis, 2014.
AOM			
Common STs plus 3, 6A/C, 19A	0.57	0.64	Saez-Llorens, X., et al. Paper presented at ISAAR, 2013.
Non-vaccine STs* (* ST/pathogen replacement)	-0.33	-0.33	Eskola, J., et al. N Engl J Med, 2001.
NTHi	0.21	-0.11*	Saez-Llorens, X., et al. Paper presented at ISAAR, 2013. Jokinen, J., Palmu, A.A. and T. Kilpi, Clin Infect Dis, 2012.
Myringotomy	0.49	0.30	Extrapolated from: Fireman, B., et al. Pediatr Infect Dis J, 2003. (PCV-7)

ESPID-0359
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

THE QUANTIFICATION OF ANTI-BORDETELLA PERTUSSIS IGA ANTIBODIES IN BREAST MILK: A BELGIAN-ISRAELI COLLABORATION.

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- Background

Some countries recommend vaccination of pregnant women against pertussis to protect young infants against whooping cough. As breast milk of vaccinated women contains pertussis antibodies, lactation can offer an additional benefit. The University of Antwerp protocol for processing anti-PT IgA in breast milk was adopted in an Israeli study. Comparability of results of both laboratories was checked.

- Methods

A commercially available anti-PT IgA immunoassay (Euroimmun®) was performed in both laboratories using 16 breast milk samples of Israeli mothers who received Boostrix® during pregnancy.

Sample preparation consisted of centrifugation, 10 minutes at 1000x g followed by 30 minutes at 10,000x g.

- Results

The coded breast milk samples were analyzed in Belgium in a blinded manner. The results indicate that the protocol is replicable in other laboratory facilities. The additional 1:10 dilution to the manufacturer's 1:101 dilution recommendation, yielded results within the standard curve for 15 of the 16 samples.

- Conclusions

We report a successful international comparison of anti-PT sIgA antibodies measurement in breast milk using an optimized in-house sample preparation combined with a commercial ELISA. Different dilutions of breast milk samples should be performed as a function of the time elapsed between delivery and sample

collection. To ensure that at least one result is within the standard range,samples up to 14 days postpartum could be diluted 1:101 and 1:10; and from thereon preferably at 1:10. The adaptation of the lower dilution might enable quantification of even exceedingly low levels of breast milk anti-PT IgA.

ESPID-0772
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

VACCINATION STATUS OF GERMAN MEDICAL STUDENTS AGAINST VACCINE-PREVENTABLE INFECTIOUS DISEASES (VPID) FROM 2004 TO 2014

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Introduction

We investigated the vaccination status of German medical students against VPID at Wuerzburg University.

Method

Between 2004 and 2014 vaccine records of third-year medical students (mean: 126 per semester) were reviewed in an obligatory immunisation course. A complete vaccination status was defined as: a booster dose of tetanus, diphtheria and pertussis vaccine in the previous 10 years, two doses of measles, mumps, rubella (MMR) and varicella (VZV) vaccine (or a history of VZV infection) and at least three doses of hepatitis B vaccine.

Results

In all 1636 medical students (median age 23.5 years), overall vaccination status was incomplete in 66.6% for pertussis, 42.5% for rubella, 40.3% for mumps, 37.5% for measles, 17.2% for diphtheria, 16.4% for hepatitis B, 14.2% for tetanus; 3.1% of the students were still susceptible for varicella. The percentage of unvaccinated students decreased from 2004 to 2014: for pertussis from 82.8% to 35.5%, for rubella from 65.6% to 13.8%, for mumps from 60.1% to 9.2%, for measles from 55.5% to 9.2%, for diphtheria from 17.2% to 13.2%, for hepatitis B from 23.4% to 4.6%, for tetanus from 13.3% to 10.5%; the proportion of varicella-susceptible students decreased from 3.1% to 1.3%.

Conclusion

The decrease of susceptible students may reflect changes in vaccination recommendations.
However, a considerable part of German medical students still lack important

vaccinations. Medical school based programs should be used to detect and close this gap of immunity in this group of future health care workers.

ESPID-0851
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

QUALITY OF LIFE IMPACTS FROM ROTAVIRUS GASTROENTERITIS ON CHILDREN AND THEIR FAMILIES IN THE UK

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Aims
Rotavirus vaccines (RV) are safe and effective but demand significant investment of healthcare resource. In countries with low mortality due to rotavirus, a key component to assessing cost-effectiveness is quantifying the Quality of Life (QoL) lost due to rotavirus acute gastroenteritis (RVAGE). UK RV cost-effectiveness calculations used estimates from Canadian primary-care of 5.8 Quality Adjusted Life Years (QALY) lost per thousand family units.

Methods
Families with children less than six years old with gastroenteritis were recruited from attendees to Bristol Children's Hospital Emergency Department. Children's QoL was assessed at presentation using Health Utilities Index 2 (HUI2) with visual analogue scale(VAS). The effect of the child's illness on the QoL of up to two adult caregivers was assessed using EQ-5D-5L. Stools were tested for viral causes of gastroenteritis. Families completed a daily symptom diary to assess time to recovery and within-family transmission.

Results
127 families consented to take part, 79(61%) had rotavirus as the cause of illness. At attendance median paediatric QoL with RVAGE was 77%(HUI2) and 45%(VAS). Primary / secondary caregiver's QoL 76%/84% (EQ5D) or 80%/85% (VAS). The median number of QALYs lost due to RVAGE was 3.0(IQR 1.5-4.5) per thousand children and 8.3(IQR 4.0- 9.4) per thousand family units.

In 29% of RVAGE families at least one other member developed a secondary case of gastroenteritis. For working parents, 63% missed a median of 2.3 days' work(IQR 1.4-3.6).

Conclusions
QoL loss associated with RVAGE presenting to Paediatric Emergency departments is substantially higher than estimates used in UK cost-effectiveness calculations.

ESPID-0180
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

INDIRECT EFFECT AFTER PNEUMOCOCCAL CONJUGATE VACCINE INTRODUCTION ON ANTIMICROBIAL USE IN A HOSPITAL, JAPAN, 2008-2013

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Background and aims:In 2010 PCV7 was introduced in Japan, and invasive pneumococcal diseases such as meningitis, sepsis, and pneumonia have been decreasing. As a result, there is a possibility that decision for the antimicrobial prescription of pediatrician is changed.Our study was aimed to investigate indirect effect of pneumococcal conjugate vaccine for antimicrobial usage of the community-acquired pneumonia (CAP).

Methods:We retrospectively investigated clinical records of CAP inpatient (n=616) during six years (PrePCV7 (Pre), 2008-09; Transient PCV7 (Tr), 2010-11; Post PCV7 (Po), 2012-13) in Tokyo Rinkai hospital. We determined the antimicrobial usage rate and types of antimicrobial ratio before/after admissions. Differences were analyzed by chi square test.

Results:The antimicrobial usage rate in the outpatient significantly decreased in periods (Tr: 16.7% reduction / Po: 34.8% reduction; $p<0.05$). The antimicrobial agent which was administered are as follows (Pr: Penicillin(Pn) 7.0%, Cephalosporine(Ceph) 32.8%, Macroride(Mac) 52.3%, Quinolone(Qu) 0%. Po: Pn 4.3%, Ceph 31.4%, Mac 41.4%, Qu 11.4%). The macrolide was decreased and the quinolone was increased significantly ($p<0.05$). The antimicrobial usage rate in the inpatient was not different significantly (Tr: 1.7% increase / Po: 7.6% reduction). The penicillin was used frequently in the inpatient (Pr: Pn 70.6%, Ceph 2.7%, Mac 14.7%, Qu 0% / Po: Pn 76.7%, Ceph 4.0%, Mac 11.3%, Qu 4.0%).

Conclusion:PCV7 contributes the decrease of the antimicrobial usage rate in outpatient for an indirect effect and it leads to Antimicrobial Stewardship. We could treat CAP by penicillin in most inpatients, thus it is important to enlighten narrow antimicrobial choice in the outpatients.

ESPID-0272
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

USE OF ROUTINE LABORATORY DATA FOR SURVEILLANCE OF ROTAVIRUS VACCINE EFFICACY AND POTENTIAL FOR IDENTIFICATION OF VACCINE ESCAPE PHENOMENA

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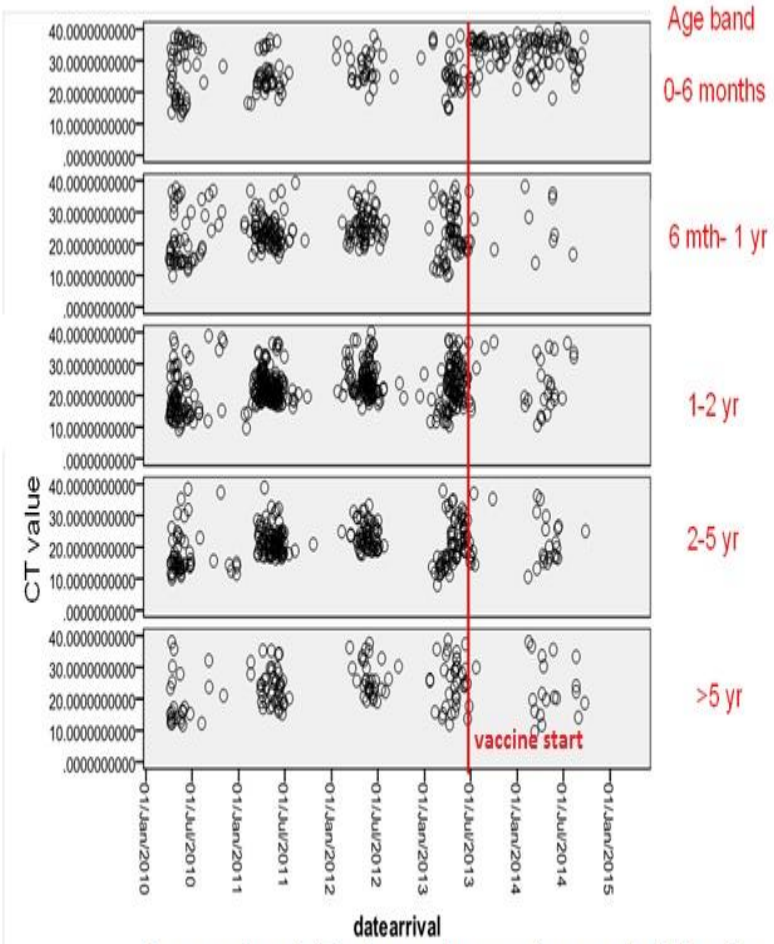
Background and aims: Rotaviruses are the commonest cause of severe diarrhoea in children worldwide. From 1st July 2013, live rotavirus vaccine was introduced in Northern Ireland. Assessing the efficacy of vaccination and identifying vaccine escape phenomena using laboratory data are problematic as standard real-time PCR assays detect both vaccine and wild-type virus. We hypothesised that using cycle threshold (CT) values (a semi-quantitative measure of viral load) at a population level might usefully help discriminate between vaccine and wild-type virus and allow better understanding of the effect of the vaccine on rotavirus infections and provide a mechanism for early recognition of vaccine escape phenomena.

Methods: We used scatter plots of CT value for all positive rotavirus results against time for a 5 year period.

Results: Comparing periods before and after the introduction of vaccine statistically significant effects were observed. An increase in detections and a rise in CT values in <6months age group was seen, consistent with vaccine detection. There was a dramatic reduction in the number of detections in the 6month – 1 year age group with unchanged mean CT value suggesting a real reduction in rotavirus disease.

Conclusions: Using simple scatter plots we were able to visualise success of vaccine in the target age group at a population level. We suggest that this method provides a basis for recognition of virus escape phenomenon and provides a mechanism for selection of laboratory specimens for sequence based virus

characterisation.



Scatter plot of CT value against specimen arrival date for each age band

ESPID-0256
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASE IN PORTUGAL AFTER 10 YEARS OF PNEUMOCOCCAL CONJUGATE VACCINE USE

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Background and aims. Conjugate pneumococcal vaccines first become available in 2001 with the introduction of PCV7 followed by PCV10 and PCV13 in mid-2009 and early-2010, respectively. Soon after their introduction changes in the serotypes causing invasive pneumococcal disease (IPD) were observed. This study aimed at documenting the recent changes in the serotypes causing IPD.

Methods: Between July 2012 and June 2014 a total of 141 cases of pediatric (<18 yrs) IPD were reported. Among these, 113 isolates were available for serotyping and antimicrobial susceptibility testing. The remaining 28 culture negative samples were positive by PCR for pneumococcal specific genes.

Results: Serotype identification was possible in 131 samples. Among these a clear increase of serotypes not included in any PCV formulation (Non-PCV) was observed representing 41% of the serotypes identified. Serotypes 15B/C (n=10), 10A (n=8) and 24F (n=7) were the most frequent Non-PCV serotypes. PCV7 serotypes still accounted for 24% of the IPD cases in the pediatric setting while the additional serotypes included in PCV10 and PCV13 represented 17% and 18%, respectively. Among the vaccine serotypes, serotypes 3 (n=20), 1 (n=16) and 14 (n=11) are still important causes of IPD in Portugal.

Conclusions: PCV13 serotypes remain major causes of IPD, highlighting the potential role of enhanced vaccination in reducing pediatric IPD in Portugal. The number of cases caused by PCV7 serotypes remained stable but that of PCV13 serotypes declined. The number of IPD cases caused Non-PCV was increasing in the study period.

ESPID-0708
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

OVERALL AND HERD EFFECT OF MENINGOCOCCAL C CONJUGATE VACCINE AFTER 3 YEARS OF VACCINATION INTO ROUTINE IMMUNIZATION IN BRAZIL

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BACKGROUND AND AIMS: Routine immunization with meningococcal C conjugate vaccine/Men-C began in Brazil in Nov/2010 administered at 3, 5 and 12 months of age. We assessed the effectiveness of Men-C on meningococcal disease (MD).
METHODS: We used individual data from the national surveillance system for notifiable diseases (SINAN), and from the national reference laboratory (Adolfo Lutz Institute/IAL) for the years 2008-2013. Record linkage was performed within each database to clean duplicate records and in between the databases to include cases and/or laboratory details not notified to SINAN but reported to IAL. An interrupted time-series analysis was conducted to estimate rates of MD in the post-vaccination period, based on rates from pre-vaccination period, adjusting for seasonality and secular trends. The analysis excluded the year after vaccine introduction. The outcomes were all MD, confirmed MD (CMD), and serogroup C MD (SCMD) rates. The effectiveness was estimated as the percentage change of observed and predicted cumulative post-vaccination rates with respective 95%CI and p-value. Vaccine coverage was estimated as >95% for the years 2012-2013.
RESULTS: Men-C vaccination reduced significantly MD, CMD and SCMD rates for age-groups targeted for vaccination (Table). Protective effect was found for MD in unvaccinated individuals of 5-9 years of age.
CONCLUSION: After 3 years of vaccination with Men-C in Brazil high impact was observed on SCMD, and herd effect for MD. Continuous monitoring of SCMD is essential to evaluate the need for a catch-up or booster dose in older children.

Table. Effectiveness of Men-C on rates of meningococcal disease in Brazil: an interrupted time series analysis, 2008-2013.

Meningococcal disease	Age-group	Probable vaccination schedule	Vaccine effectiveness		
			%	95% CI	p-valu
All cases	0-2 mo	none	1.2	-113.5; 115.9	0.924
	3-11 mo	2+0	50.3	31.6; 69.0	0.000
	12-23 mo	2+1	60.3	34.7; 86.0	0.000
	2-4 y	mixed	39.7	12.4; 67.1	0.000
	5-9 y	none	15.9	4.2; 27.6	0.019
	10-17 y	none	14.0	-30.1; 58.0	0.129
	18-39 y	none	10.5	-19.2; 40.3	0.101
	= 40 y	none	-9.3	-51.4; 32.8	0.395
Confirmed cases	0-2 mo	none	-16.1	-150.5; 118.3	0.320
	3-11mo	2+0	53.1	26.5; 79.6	0.000
	12-23mo	2+1	64.5	37.6; 91.5	0.000
	2-4 y	mixed	39.5	26.0; 53.0	0.000
	5-9 y	none	13.2	-28.0; 54.4	0.097
	10-17 y	none	14.2	-30.7; 59.0	0.140
	18-39 y	none	9.4	-25.5; 44.2	0.216
	= 40 y	none	-7.9	-61.2; 45.5	0.470
Serogroup C cases	0-2 mo	none	13.1	-174.1; 200.3	0.504
	3-11mo	2+0	80.0	60.9; 99.2	0.000
	12-23mo	2+1	89.9	74.8; 105.0	0.000
	2-4 y	mixed	53.4	39.3; 67.5	0.000
	5-9 y	none	11.5	-48.4; 71.3	0.237
	10-17 y	none	10.7	-32.3; 53.7	0.286
	18-39 y	none	7.3	-32.9; 47.6	0.379
	= 40 y	none	-16.7	-75.4; 42.0	0.279

Laboratory confirmation include the following specific methods: Gram stain showing gram-negative diplococcic, culture and antigen detection methods. The latter comprise latex, contraimmuno-electrophoresis, enzyme-linked immunosorbent assay, polymerase chain reaction or immunofluorescence tests.

ESPID-0717
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

SINGLE-DOSE VARICELLA VACCINE EFFECTIVENESS IN BRAZIL: A MULTICENTER CASE-CONTROL STUDY

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BACKGROUND: Varicella zoster vaccine (VZV) was introduced into the Brazilian Immunization Program (NIP) in October/2013 as a single-dose using the tetravalent measles, mumps, rubella, VZV (GSK) administered at 15 months of age. We evaluated the VZV effectiveness in a case-control study.

METHODS: A multicenter neighborhood matched case-control study (1:2) was conducted in São Paulo and Goiânia municipalities in Brazil. Suspected VZ cases were prospectively identified during Nov-Dec/2013 and Jul-Dec/2014 in healthcare units. Cases were defined as children with vesicular rash and fever, and therefore eligible to receive VZV vaccine at 15 months. Varicella case definition was based aon the detection of DNA VZV by PCR (94%) or by an epidemiological link with a varicella case (6%). Vaccination details were collected from immunization cards. We defined immunized children if ≥28 days had elapsed between vaccination and rash or interview. Vaccine effectiveness/VE was estimated as [1-odds ratio]*100.

RESULTS: 149 cases and 291 controls (aged 15-35 months) were enrolled. The proportion of immunized cases was lower than that of controls (16.8% and 45.4%). The median time since vaccination was longer in cases than controls (7.2 and 4.8 months). Immunized cases experienced less number of lesions (p=0.009) compared to non-immunized cases. After adjusting for confounders, VZV VE was 78.6% (95%CI:61.1-88.2) for any varicella severity and 86.5% (95%CI:70.2-94.1) for moderate/severe cases.

CONCLUSIONS: Single-dose VZV provided high protection against varicella disease in children targeted by the NIP, soon after the first year of vaccination. Further effectiveness data are needed to assess long-term protection with single dose.

ESPID-0808
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

OVERALL AND INDIRECT EFFECT OF PCV10 ON PNEUMONIA HOSPITALIZATIONS IN CHILDREN IN BRAZIL AFTER 3 YEARS OF VACCINATION

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Background and Aims: Routine infant immunization with 10-valent pneumococcal conjugate vaccine (PCV10) began in Brazil in March/2010 administered at 2, 4, 6 and 12 months of age. We assessed the direct and indirect effect of PCV10 on rates of pneumonia hospitalizations after 3 years of vaccination introduction.
Methods: We used data from the Brazilian Hospitalization System from 2005-2013. An interrupted time-series analysis was performed excluding the year 2010, and the H1N1 pandemic months of 2009. Pneumonia rates (ICD-10, J12-J18) were estimated for the post-vaccination period (2011-2013), based on rates from pre-vaccination period, adjusting for seasonality and secular trends using Holt-Winters method. Comparison groups were congenital malformation (Q00-Q99), non-respiratory causes (all except ICD-10 Chapter X), and all causes of hospitalization. Effectiveness of PCV10 was calculated as the percentage changes of observed and predicted rates for the post-vaccination period with respective 95%CI. The number of hospitalizations for pneumonia prevented by vaccination in the post-vaccine period was also estimated.

Results: Pneumonia hospitalization rates declined by 16.6% (p=0.016), 14.4% (p=0.024), 17.4% (p=0.001), 14.1% (p=0.000), 15.2% (p=0.000) 4.8% (p=0.141), respectively for the age-groups 2-23 months, 2-4 years, 5-9 years, 10-17 years, 18-39 years, and 40-64 years. For individuals ≥65 years of age, pneumonia rates increased by 9.9% (p=0.004) in the post-vaccination period. Nationally, 224,542 hospitalizations for pneumonia were avoided in the post-vaccination period.

Conclusion: After 3 years of PCV10 vaccination in Brazil a significant decline was observed for the targeted age-groups for vaccination besides a herd effect for unvaccinated children and adults

ESPID-0156
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

SEROTYPE DISTRIBUTION AND PENICILLIN RESISTANCE OF STREPTOCOCCUS PNEUMONIAE IN KUWAIT: A TEN-YEAR STUDY OF IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINES

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Background and Aims: The pneumococcal conjugate vaccine-7 (PCV-7) was introduced in Kuwait in August 2006 and PCV-13 in August 2010 for children less than 2 years. The study is done to evaluate the impact of PCV7 and PCV13 on serotype distribution and antimicrobial resistance of invasive *S.pneumoniae* isolates.

Methods: The study included all cases of invasive pneumococcal disease (IPD) divided into two periods. The pre vaccination period is from August 2003 to July 2006 and the post vaccination period is from August 2006 to July 2013. Serotyping and penicillin susceptibility testing are done using Quellung reaction and Etest, respectively.

Results: There are 63 invasive isolates, 25% from children ≤5 years, and 156 invasive isolates, 28% from children ≤5 years, in the pre and post vaccination periods, respectively. In the pre vaccination period, PCV-7 and PCV-13 vaccine coverage in all age groups and in children < 5 years is 50% and 70%, respectively. In the post vaccination period, the vaccine coverage in all age groups and in children <5 years is 21%, 29% for PCV-7 and 46% and 51% for PCV-13. The drop in vaccine serotypes and the increase in the non-vaccine serotypes during post vaccination period compared to pre vaccination period is statistically significant (*p* value 0.001). Penicillin resistance among *S.pneumoniae* isolates dropped from 67.9% in pre vaccination period to 46.2% in post vaccination period (*p* value 0.006)

Conclusion: After 7 years of PCV use in Kuwait, new emerging serotypes of *S.pneumoniae* are seen.

ESPID-0585
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IMPACT OF ROTAVIRUS VACCINATION DURING 5 YEARS AFTER ITS COMMERCIALIZATION

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BACKGROUND

Rotavirus is the most frequent etiology in hospitalized infants (younger than 2 years) with acute gastroenteritis (AGE). Rotavirus vaccine (RV), commercialized in Spain since 2006, is not included in official vaccination calendar. It is estimated that RV coverage has grown from 24% to 44% in 2009-2013.

AIMS

Describe the impact of RV in epidemic pattern.

METHODS

Retrospective description of infants discharged from a 2nd level hospital of Madrid with diagnosis of AGE. We compare two periods: pre-vaccine (2003-2006) and post-vaccine (2009-2013) commercialization, considering 2007-2008 as transitional. Rotavirus was diagnosed by specific antigen in stool.

RESULTS

471 patients were included (5% of total hospitalizations). No significant differences were seen: age (8.9 SD 6.1 vs 9.6 SD 6.7 months, p=0.1), length of stay (3.8 SD 2,4 vs 3.5 SD 2,3 days, p=0.3), gender (males: 55.8% vs 53.5%, p=0.7) and prematurity history (8.8% vs 9.7 %, p=0.7).

Proportion of AGE respected total admissions decrease 39% (from 6.1% to 4.7%, p=0.00001). Rotavirus was the etiology in 60.4% in the first period vs 38.8% in the second one (p=0.0001). This reduction was more prominent in 2009, 2010 and 2012 (21-32%).

50% of season rotavirus AGE occurred from November to January in pre-vaccine period, and from December to February in post-vaccine period.

CONCLUSIONS

Rotavirus vaccination has decreased significantly admissions for AGE in infants (total and by rotavirus), in an irregular pattern.

No significant changes in epidemiological characteristics are seen. A shift in epidemic peak has been observed between both periods.

ESPID-0777
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IMPACT OF THE FIRST YEAR OF A NATIONAL ROTAVIRUS VACCINATION PROGRAMME IN SCOTLAND

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Background and aims
Rotavirus is a highly infectious virus and the leading cause of gastroenteritis in children worldwide. Rotavirus is a seasonal infection, peaking between January and April, resulting in additional pressure on healthcare facilities. In 2013, a national rotavirus immunisation was introduced in the UK. Efforts are now focused on monitoring the impact on the burden of disease.

Methods
Surveillance systems have been established by Health Protection Scotland (HPS) to supplement existent monitoring of laboratory confirmed cases.

Results
There has been a marked reduction in laboratory confirmed rotavirus samples in both the vaccine cohorts and unvaccinated older children, suggestive of an indirect impact. Data on hospital admissions and attendances at Accident & Emergency departments, of infants with gastroenteritis has shown a similar reduction across the seasonal peak. This pattern was also seen in community settings with General Practitioner consultation rates for vomiting, diarrhoea and gastrointestinal illness in young children. Calls to the National Health Service telephone helpline, NHS24 also showed a statistically significant reduction in calls for diarrhoea and for vomiting across the seasonal peak.

Conclusions
Initial indications were that the national rotavirus immunisation programme has had an immediate and pronounced impact on rotavirus infection in Scotland; however a recent report provided evidence that 2014 had exceptionally low levels of circulating rotavirus infection even in countries without rotavirus immunisation. Therefore, epidemiology of rotavirus infection in Scotland in the first year following the introduction of the vaccine will be presented along with some preliminary data available from 2015.

ESPID-0831
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

CAN SEROPREVALENCE EVALUATION BE USED TO MEASURE THE IMPACT OF LIVE ATTENUATED INFLUENZA VACCINATION IN CHILDREN IN SCOTLAND?

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Background and aim

Annual seroprevalence evaluation was undertaken in Scotland to determine influenza susceptibility in the paediatric population following the 12/13 and 13/14 influenza seasons. Following the first phase (October 2013) of the influenza vaccination programme in children in Scotland, we explored the option of using this evaluation method to measure the impact of a live attenuated influenza vaccine (LAIV) on influenza susceptibility in children.

Method

Anonymised residual blood samples were collected by regional laboratories in Scotland during the influenza inter-season periods (n=467). Samples were tested using a haemaglutinin inhibition assay (1:40 dilution) to determine sero-positivity levels against vaccine related Influenza A and B strains. Retrospective linkage was undertaken to allow stratification of sero-positivity rates by vaccination status.

Results

The sero-positivity rate for the influenza vaccine related strains tested was 76.7% (95% CI 74.9-78.5). Higher sero-positivity rates were seen in LAIV vaccinated children compared to unvaccinated children but this did not reach statistical significance e.g. sero-positivity rates for Influenza A H1N1 2009 and H3N2 in LAIV vaccinated children aged 1-4 years (n=45, 18.8%, 95% CI 8.9-35.3 and 43.8 95% CI 28.2-60.7, respectively) were higher than unvaccinated children (n=422, 13.9%, 95% CI 9.1-19.9 and 28.6%, 95% CI 22.0-36.2, respectively).

Conclusion

Differences in the level of influenza immunity (using seroprevalence as a proxy) in children vaccinated with LAIV compared to unvaccinated children is of interest and will be further evaluated. The full impact of the LAIV programme in children in Scotland will only become evident over multiple influenza seasons.

ESPID-0761
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

ANAPHYLAXIS FOLLOWING IMMUNIZATION OF CHILDREN AND ADOLESCENTS IN GERMANY

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Background and objective. Anaphylaxis is a life-threatening event. The aim of this study was to estimate in Germany the annual frequency of anaphylaxis within 48 hours following immunization in individuals under 18 leading to hospitalization.

Methods. Clinicians were asked to notify all patients with suspected anaphylaxis within 48 hours following vaccination from June 2008 through May 2010 to the German surveillance unit for rare pediatric diseases (ESPED). The ESPED reports as well as all AEFI (adverse events following immunization) reports of suspected anaphylaxis in minors received by the German Federal Institute of Vaccines and Biomedicines (PEI) in the observational period were classified according to the Brighton Collaboration Case Definition (BCCD) for anaphylaxis AEFI. Only hospitalized cases of anaphylaxis within 48 hours following immunization fulfilling BCCD level 1–3 criteria were eligible. Estimates for the annual frequency were calculated by using capture–recapture methods.

Results. A total of 22 reports were eligible of which 3 were sent exclusively to ESPED, 13 to the PEI, and 6 were found in both sources.
The annual frequency of anaphylaxis within 48 hours following immunization with a non-pandemic vaccine was estimated to be 8.2 (95% CI: 7.2–13.2).
As to AS03 adjuvanted A/H1N1 pandemic influenza vaccine, the total frequency of anaphylactic reactions was estimated to be 11.0 (95% CI: 8.5–26.2) which translates into an incidence of 11.8 (95% CI: 9.2–28.2) per 1,000,000 doses administered.

Conclusion. This study confirms that anaphylaxis following immunization in children and adolescents is a rare event and provides the first estimates for Germany.

ESPID-0990
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

SAFETY AND IMMUNOGENICITY OF A TWO-DOSE SCHEDULE OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE IN RUSSIAN CHILDREN AGED 9 TO 23 MONTHS

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Background: Polysaccharide serogroup A, A+C, and ACWY meningococcal vaccines are currently available in the Russian Federation, but at enrollment, no quadrivalent meningococcal conjugate vaccine (MenACWY-D) had been licensed. A 2-dose MenACWY-D series with doses administered 3 to 6 months apart could fit into the Russian Federation immunization schedule. We studied MenACWY-D in a Russian/Indian open-label, single-arm, descriptive study. This abstract represents an interim report of results from the 4 Russian centers.

Methods: Study entry enrolled 100 participants from 9 to 17 months of age, and 98 completed a 2-dose series of MenACWY-D. Blood samples were collected pre-Dose 1 and 1-month post-Dose 2. Immunogenicity was measured via human complement serum bactericidal assay. Safety was assessed for all participants: solicited systemic and local reactions were registered through 7 days postvaccination, SAEs were reported during the entire study period.

Results: Participants (59% were girls) achieved robust immune responses 1 month after the second vaccination as measured by the % achieving ≥1:8 1/dil (Full Analysis Set): A (99.0%), C (92.9%), Y (93.9%), W (98%). The geometric mean titer ratios were 25.9 (A), 24.8 (C), 24.1 (Y), 40.4 (W). MenACWY-D was well tolerated. One SAE was reported, and it was not related to vaccination.

Conclusion: A MenACWY-D 2-dose series demonstrated a good immunogenicity and safety profile The results are in line with those found in other studies of MenACWY-D in this population, and the data suggest MenACWY-D could be considered for Russian vaccination programs. Study funding: Sanofi Pasteur (NCT01890759).

ESPID-0463
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

QUALITY OF IMMUNE RESPONSE TO HEPATITIS B VIRUS VACCINE IN CHILDREN WITH TYPE I DIABETES MELLITUS

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AIMS: To investigate the quality of the immune response to hepatitis B virus (HBV) vaccine in children with type 1 diabetes mellitus (DM1) in comparison with a population of healthy controls.

MATERIAL AND METHODS: This is a prospective, observational study in which 109 children with DM1 (median age 12.05 years) and 346 healthy controls (median age 8,75 years) have participated. All patients had been completed vaccinated of HBV vaccine in the first year of life. Antibody titers were measured by ELISA.

RESULTS:

1.-A statistically significant relationship was found, by logistic regression, between anti-HBs titers and age of serological investigation in the control group (coefficient -0.12, p value= 0.000).

2.-The percentage of non-responders to HBV vaccine (anti-HBs < 10 mUI/mL) was statistically significant higher (p=0.04) between children with DM1 than in controls (71.6% versus 60.7%).

3.-The percentage of children with undetectable titers of anti-HBs was higher in the group of DM1 than in the control one (14.68% versus 8.38%). The difference is in the limit of statistic significance (p=0.054).

CONCLUSIONS:

1.-Anti-HBs titers decreased with time. When evaluating serological response to HBV vaccine, time elapsed since vaccination should be consider.

2.-The response to HBV vaccine in children with DM1 seems to be worse than that of the healthy population. However there are necessary more studies with younger patients to confirm this finding.

ESPID-0540
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IS THE IMMUNOPHENOTYPE OF INTRAEPITHELIAL LYMPHOCYTES RELATED TO HEPATITIS B VIRUS VACCINE RESPONSE IN CHILDREN WITH CELIAC DISEASE?.

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BACKGROUND AND AIMS: To analyze if there is a relationship between the number of intraepithelial lymphocytes (IEL), gamma delta lymphocytes (γδ) and CD3- lymphocytes (CD3-) and the quality of the immune response to hepatitis B virus (HBV) vaccine in children with celiac disease (CD). This possible relationship has never been studied before.

MATERIAL AND METHODS: The phenotype of intraepithelial lymphocytes was studied by flow cytometry in jejunum specimens form 168 children with CD. Anti-HBs titers were measured by ELISA. The relationship between the number of IEL, γδ and CD3- with anti-HBs titers was analyzed by Spearman correlation.

RESULTS: are summarized in table 1

Table 1: Spearman coefficient and statistic signification between the number of IEL, γδ and CD3- with anti-HBS titers (measured in mUI/mL).

	ANTI-HBS TITERS
LIE	Spearman coefficient= -0.1874 p= 0.0280
γδ	Spearman coefficient= -0.018 p= 0.82
CD3-	Spearman coefficient= 0.1938 p= 0.0167

There is a statistic relationship between the number of IEL and CD3- with anti-HBs titers. In the first case the coefficient indicates that anti-HBs titers are lower in patients with more number of IEL. In the second case the titers are lower in the CD patients with fewest number of CD3-.

CONCLUSIONS:

Changes of intraepithelial lymphocytes towards a more inflammatory profile are associated with a worse immunological response to HBV vaccine.

ESPID-0839
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

HOUSEHOLD SOURCES OF PERTUSSIS INFECTION: CONTRIBUTING TO THE DEBATE OVER THE BEST IMMUNIZATION STRATEGIES TO PROTECT YOUNG INFANTS

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Despite high vaccination rates have led to a dramatic decrease in incidence and mortality, resurgence of pertussis has been reported in Western countries. Shift of cases from school-age children to adolescents, adults and infants in their first years of life occurs, and mortality rates in infants are still sustained. Different vaccination strategies have been explored, including neonatal immunization, additional booster to adolescents and adults, vaccination of childcare workers, pregnant women and household contacts ('cocoon"). We weighed the contribution of close contacts in transmitting pertussis to infants.

Data linkage between mandatory notifications and hospital registrations for pertussis was performed to obtain cases throughout 2001-2014 in Puglia region, Italy. We retrieved those <12mo of age with the same family-name as at least another pertussis case. The serial interval for pertussis was set to range 10-35 days. We referred to secondary cases <12mo if the duration between their times of symptom onset and that of other cases in the household was within serial interval. Coprimary transmission was considered when household members were infected in less than 10 days.

Forty/530 pertussis cases <12mo had the same surname as at least another case (twenty <3mo). Six were secondary cases (two <3mo) of six primary ones (age: 0-9y), 19 were coprimary cases (twelve <3mo) and 15 showed serial interval >35 days (37-181).

Close household contacts (siblings or paternal-cousins) accounted for 15% transmission to infants. Prevention of pertussis requires simultaneous use of more than one vaccination strategy aimed at maintaining high coverage and avoiding waning immunity.

ESPID-0903
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

PRELIMINARY SAFETY OF CUBAN HEPTAVALENT CONJUGATE PNEUMOCOCCAL VACCINE IN PHASE I CLINICAL TRIAL IN INFANTS OF 7- 11 MONTHS OLD.

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A new heptavalent conjugate vaccine containing the seven serotypes of S.pneumoniae more frequently associated with most invasive serotypes worldwide has been designed in Cuba. The candidate vaccine (PCV7-TT) contains 2µg of each capsular polysaccharide 1,5,14,18C,19Fand 23F and 4µg of 6B, conjugated to tetanus toxoid (TT) and aluminium phosphate as adjuvant.The safety of the vaccine in healthy adults and 4-5 years old children, were showed in 2012 and 2013,respectively. Our study its a phase 1 , parallel,controlled and double blind clinical trial designed to assess the safety of PCV-7 in 30 infants of 7 months old. Infants were randomized to receive three doses of PCV7-TT (n=20) or Synflorix (n=10) following the schedule 2p+1. Each child was followed for 3 hours after the vaccination for immediate adverse events. During the next 30 days the child s parents recorded any adverse events in a diary, and they received medical visits at 7, 21and 30 days after immunizations .Same procedure was done after each dose.Blood samples were obtained 30 days after 2nd and 3th dose of vaccination for immunological evaluation. No serious adverse events were reported using PCV 7-TT. The adverse events reported were comparable between both vaccines; local indurations and eythema were the most frequents.PCV 7-TT shows a good safety profile. Once demonstrate the general safety profile of PCV7 in infants of 7 months, we will develop phase I-II clinical trial in infants of 2-6 months of age during the 1st quarter of 2015.

ESPID-0344
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

VARICELLA INFECTIONS AT THE POPULATION IN BITOLA IN THE PERIOD BETWEEN 2012-2014

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Varicella is a highly contagious disease caused by the varicella zoster virus (VZV). In the absence of vaccination, this infection is acquired mainly in childhood.

Objectives: To show the prevalence of varicella infections at the population in municipality of Bitola from year 2012 to 2014, who were registered at the Center for Public Health.

Methods: The retrospective, epidemiological study included respondents aged from 0 to over 60 years in the period from year 2012 to 2014, who were diagnosed with varicella infection. It was confirmed by clinical and laboratory examinations.

Results: During the period of 3 years in Center for Public Health, Bitola were registered a total number of 1637 cases, confirmed with a diagnosis of varicella infection, (general rate of morbidity=149.4/10000), 52.17% male and 47.89% female. In relation to age, varicella infections were more common in children from 0 to 6 years old (rate of morbidity=520.6/10000), living in an urban environment (rate of morbidity=64.5/10000) with the highest incidence in the winter months from November to January.

Conclusion: The prevalence of varicella infections at the population in municipality of Bitola, was from 500-600 cases per year, more common among children, male, aged 0 to 6 years old. Vaccination against this disease, in our country, is not implemented yet. Full implementation of the routine varicella vaccination program should result in further reductions in varicella incidence.

ESPID-0590
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

COMPARING DETECTION RATES BY Q-PCR OF UPPER RESPIRATORY BACTERIA IN NASOPHARYNGEAL (NP) AND SALIVA (SV) SAMPLES IN PRE-SCHOOL CHILDREN

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BACKGROUND AND AIMS: Oro and NP swabs are frequently used to detect colonising bacteria in vaccine effectiveness studies, but require trained staff and are not well tolerated by children, especially when done repeatedly. Sv sampling is much easier. Previous studies have reported high rates of pneumococcal detection in Sv but direct comparison has not been reported in young children.

METHODS: In March 2014, children (4m-6y) attending nurseries had simultaneous NP and SV samples collected. After storage at -80°C and DNA extraction, samples underwent single gene quantitative PCR for *S. pneumoniae* (Sp)(lytA), *H. influenzae* (Hi)(hdp), *M. catarrhalis* (Mc)(ompJ), *S. pyogenes* (GAS)(ntpC) and *S. aureus* (Sa)(nuc). Ct values of ≤35 were considered positive and densities converted into CFU/mL using previously established standard curves.

RESULTS: Rates and density of detection are in table

n=114	**NP (%)**	**SV (%)**	**NP SV + +/ + - /- +**	**Median NP Log_{10}CFU/mL**	**Median SV Log_{10}CFU/mL**
Sp	73 (64)	64 (56)	55/18/9	3.22	1.47
Hi	103 (90)	94 (83)	87/16/7	3.54	1.98
Mc	90 (78)	51 (45)	50/40/1	3.66	1.92
GAS	9 (8)	25 (22)	5/4/20	1.86	2.16
Sa	14 (12)	8 (7)	4/10/4	3.49	2.30

CONCLUSIONS: These upper respiratory bacteria can all be detected in saliva by qPCR but, apart from GAS for which the opposite is true, with somewhat reduced sensitivity and at 16-57 fold lower density than by NP swab. Since saliva collection is much easier, it may be a useful approach in some carriage studies.

Work supported by an investigator-led project grant from Pfizer

ESPID-0065
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IMMUNOGENICITY AND SAFETY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE VERSUS 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN HEALTHY INFANTS IN CHINA

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Background and Aims: Safety and immunogenicity of 13-valent pneumococcal conjugate vaccine (PCV13) was compared with currently licensed 7-valent PCV (PCV7) in Chinese infants.

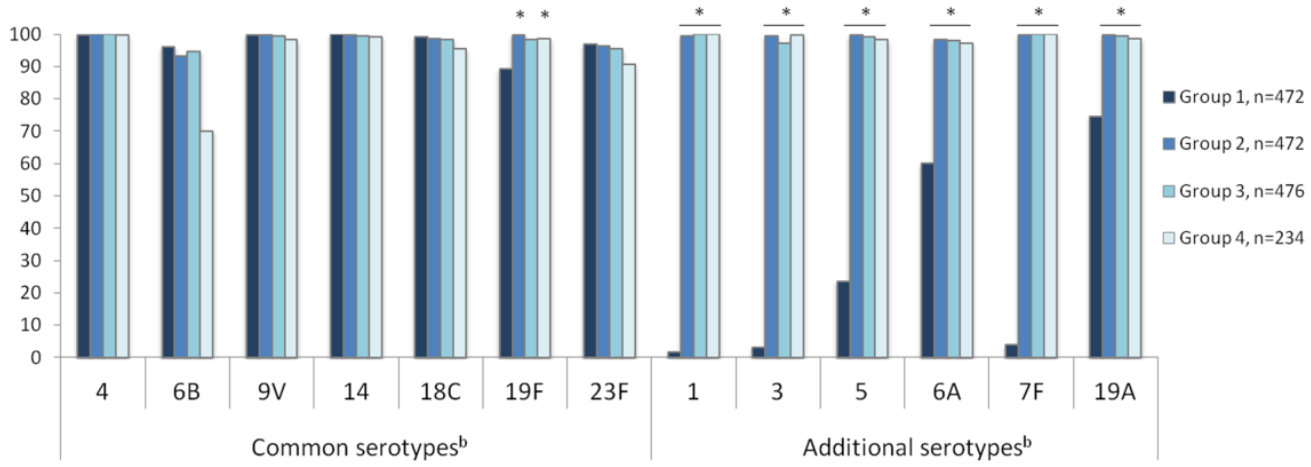
Methods: Healthy infants 2 months of age were randomized (n=1654) to receive PCV7 (Group 1, n=472) or PCV13 (Group 2, n=472) at 3, 4, and 5 months (double-blind); PCV13 (Group 3, n=476) at 2, 4, and 6 months, or PCV13 (Group 4, n=234) at 3 and 5 months. Serotype-specific IgG concentrations were measured 1 month after the last dose. Local reactions, systemic events, and adverse events were assessed after vaccination.

Results: After 3 doses of PCV13 (Groups 2 and 3), the percentage of subjects with IgG ≥0.35 µg/mL to the 7 common serotypes was noninferior to PCV7 (Group 1**;** **Figure**). The percentage of seroresponders in Group 4 was similar, except serotype 6B, which was significantly lower. The percentage of responders to the 6 additional serotypes was statistically significantly higher in PCV13 than PCV7 recipients. PCV13 and PCV7 were well tolerated. Local and systemic reactions were mild in severity and generally similar across groups, except irritability was slightly higher after dose 1 in Group 3. Adverse events were consistent with common childhood illnesses; no related serious adverse events were reported.

Conclusions: Immune responses after 3 doses of PCV13 were noninferior to PCV7 for the 7 common serotypes. PCV13 recipients had significantly higher immune responses to the 6 additional serotypes, suggesting additional protection against

pneumococcal disease compared with PCV7.

Figure: Proportion of Subjects Achieving Serotype-Specific IgG Concentrations ≥0.35 µg/mL Compared to Group 1[a]



a. Noninferiority criterion was met for PCV7 serotypes in Groups 2 and 3 if the lower limit of the 97.5% CI for the difference in proportion of responders (PCV13 - PCV7 reference) was greater than -10%.
b. Reference value is the corresponding proportion in the PCV7 group (Group 1).

ESPID-0673
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

PERSISTENCE OF IMMUNITY FOLLOWING IMMUNISATION WITH A LICENSED CAPSULAR GROUP B MENINGOCOCCAL VACCINE IN THREE DIFFERENT TODDLER SCHEDULES.

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Background

The capsular group B meningococcal vaccine (4CMenB) is licensed for use in children at 12 to 24 months of age as 2 doses given 2 months apart, with a booster dose given 12 to 24 months later. This study provides the first data on the persistence to 4 years of age of human complement serum bactericidal titres (hSBA) following such 2-dose ‘toddler’ schedules, and the immunogenicity of a booster dose given at this time.

Methods

hSBA titres were determined in 4 year old children previously immunised with 4CMenB at 12 and 14, 18 and 20 or 24 and 26 months of age and compared to those from age matched 4CMenB-naive controls. hSBA titres against four reference strains (H44/76, 5/99, NZ98/254, M10713 to evaluate responses to fHbp, NadA, PorA and NHBA respectively) were studied at baseline and 30 days post booster.

Results

Participant numbers were: 206 (vaccine naïve), 96 (4CMenB, 12/14 months), 11 (4CMenB, 18/20) and 11 (4CMenB, 24/26). At baseline, the proportions of participants (comparing the vaccinated arms with the control arm) achieving hSBA titres ≥ 1:5 were: 9-11% vs 0% for H44/76; 84-100% vs 4% for 5/99; 2-20% vs 1% for NZ98/254 and 59-60% vs 60% for M10713. After a dose of 4CMenB in previously

immunised children the proportions achieving hSBA titres ≥ 1:5 were 100% (H44/76, 5/99), 70-96% (NZ98/254) and 93-100% (M10713).

Conclusion

The observed waning of hSBA titres following 2 doses of 4CMenB at age 12 to 24 months supports the use of a booster dose.

ESPID-0744
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

SINGLE-DOSE SAFETY AND TOLERABILITY OF A 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN HEALTHY INDIAN ADULTS: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND PHASE-1 STUDY

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Background and Aims: Serum Institute of India has developed a low-cost 10-valent pneumococcal conjugate vaccine (SIILPCV10) incorporating the most prevalent developing-world serotypes. This first-in-human study aimed to evaluate and compare the safety and tolerability of SIILPCV10 with Pneumovax®23 (MSD).

Methods: 34 healthy Indian adults (24M/10F), aged 18-30 years, were randomized (1:1) to receive a single intramuscular dose of either SIILPCV10 or Pneumovax®23. Occurrence, severity, and relationship of solicited and unsolicited adverse events (AEs) were monitored through 7 and 28 days post-vaccination, respectively, including baseline/Day-7 lab-work.

Results: 30 participants (SIILPCV10: 13/17 vs. Pneumovax®23: 17/17) experienced at least 1 solicited AE, most occurring within 2-3 days post-vaccination, SIILPCV10 vs. Pneumovax®23 being; Local: 13/17 vs. 16/17; Systemic: 6/17 vs. 11/17. Local solicited AEs were mostly grades 1 or 2, systemic mostly grade 1. 6 SIILPCV10 vs 10 Pneumovax®23 participants had grade 2, and one participant in each group had grade 3 solicited AEs. Pain, tenderness (local); headache, myalgia/arthralgia (systemic) were the common solicited AEs. Incidence of unsolicited AEs was comparable between the groups, all being grade 1, except one grade 2 event (Pneumovax®23: URTI). One participant from each group had post-vaccination grade 1 injection-arm paraesthesia, which resolved spontaneously (same day). Changes in laboratory variables (haematology/biochemistry, organ-function) were unremarkable in both groups, one Pneumovax®23 participant having grade 1 raised liver enzymes (re-tested normal on Day-28). No deaths, other SAEs, or AEs leading to participant withdrawal were reported.

Conclusion: SIILPCV10 was well-tolerated, its safety profile comparable with Pneumovax®23 in healthy Indian adults.

ESPID-0319
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

LOCAL REACTIONS AND HISTOPHATHOLOGICAL CHANGES AFTER INJECTION OF A NEWLY DEVELOPED GCC TDAP VACCINE IN MICE

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BACKGROUND: Acellular pertussis vaccine contained diphtheria and tetanus toxoid (DTaP, Tdap) are widely used. aP vaccine is safer than whole cell pertussis vaccine and has fewer adverse effects, but local reactions are still reported. Pathophysiological mechanism of these reactions is controversial. To clarify the cause of local reactions and confirm the local reaction levels of Tdap vaccine, we conducted studies using the murine model.

AIM: To confirm the local reactions and serial histophatological changes of GCC Tdap vaccines(newly developed by Green Cross corporation in Korea) after administration in a murine model, and to find out local adverse events before human clinical phase I study.

METHODS: 5 weeks old 12 female mice was enrolled in each group. One quarter of human dose Tdap vaccine was subcutaneously injected on abdomen, and we observed local reactions and histopathological change at injection site at 24h, 48h, 7 days, and 14 days. Same methods were conducted in negative control group(injected physiologic saline) and positive control group(injected Boostrix®).

RESULTS: All mice of study and positive control group showed indurations at injection sites. Histophathologically, we observed leukocytes(neutrophils and eosinophils) invasion. These dramatic changes persisted until 7 days and simultaneously peripheral fibrosis had begun. Those reactions were markedly attenuated on 14 days. There were no difference between those two group.

CONCLUSIONS: Histopathological changes suggest that local reactions are caused by inflammatory and allergic responses. Also, we find out that local reactions are tolerable. This study will be useful for studies focusing on local reactions of aP contained vaccines.

ESPID-0115
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINATION PROGRAM ON NASOPHARYNGEAL CARRIAGE, SEROTYPE DISTRIBUTION AND ANTIMICROBIAL RESISTANCE OF STREPTOCOCCUS PNEUMONIAE AMONG CHILDREN IN TURKEY

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In this study we determined nasopharyngeal carriage, serotype distrubition and antimicrobial resistance of *S. pneumoniae* in healthy children, in Istanbul, Turkey after introduction of pneumococcal conjugate vaccine (PCV) in to the national immunization programme. A total of 2165 children, aged 0-18 years were enrolled in the study between September 2011 to September 2013. The mean age was 76±56 months and 1139 (53%) of participants were female . The overall nasopharyngeal pneumococcal colonization rate was 6.4% (139/2165). We found children vaccinated at least single dose PCV had a significantly lower odds of colonization by a vaccine serotype compared with non-vaccinated children. [OR:0.61 (95% CI=0.41-0.91), p=0.01]. Of the 133 isolates, 26 different serotypes were identified, among them the most common 5 isolates were serotype 6A/B/C (17.2%), serotype 19F (13.5%), serotype 23F (10.5%), serotype 9V/A (7.5%), serotype 12F (4.5%), serotype 15A/F (4.5%), serotype 22F/A (4.5%). Seventeen (12.7%) isolates were non-typeable. Among the isolates 60% of them were non-susceptible (NS) to penicillin (oral), 6% of them NS to parenteral penicillin and 13% of them NS to ceftriaxone (parenteral for meningitis). Moreover, 44% of isolates were NS to eritromycine and 31% of them were NS to clindomycine. We found that macrolid resistance were efflux type in 16 isolates (m. phenotype), were constitutive (cMLSB) in 41 isolates and were inducible (iMLSB) resistance pattern in 1 isolates. We shown that pneumococcal conjugate vaccination programme decreased nasopharyngeal carriage rate in children with respect to pre-vaccination period in Turkey.

ESPID-0173
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

SAFETY AND IMMUNOGENICITY OF GENETICALLY DETOXIFIED ACELLULAR PERTUSSIS BOOSTER VACCINES, WITH OR WITHOUT TETANUS AND DIPHTHERIA TOXOIDS, IN ADULTS

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Background: Despite widespread availability and high coverage of primary/booster tetanus (T), diphtheria (d), and acellular pertussis (aP) vaccinations, pertussis (whooping cough) has resurged in developed countries. It is suggested that current Tdap vaccines induce immunity that may not be long-lasting or efficacious against circulating strains. To identify a next generation aP booster vaccine (with/without Td) that could provide long-lasting protection and improved immunity relative to licensed Tdap vaccines, this Phase I study assessed the safety and immunogenicity of investigational aP and Tdap vaccines, containing a genetically detoxified pertussis toxoid, as compared to a licensed Tdap vaccine.

Methods: 420 healthy adults aged 18–40 years were randomized into 1 of 10 vaccine groups: 3 investigational aP, 6 investigational Tdap and 1 Tdap comparator. Antibody responses to pertussis antigens [pertussis toxoid (PT), filamentous hemagglutinin (FHA) and pertactin (PRN)] were assessed 30, 180 and 365 days post-vaccination.

Results: All investigational vaccines were well tolerated with no safety concerns identified. Thirty days post-vaccination most antibody responses correlated with FHA/PRN content per dose. However, PT-specific antibody responses induced by the investigational aP and Tdap vaccines were similar or significantly better than the licensed comparator, despite lower antigen doses. Antibody persistence (180/365 days) was evident in all groups, although waning of PT- and PRN-specific antibodies was slower for the investigational vaccine groups, as compared to the licensed Tdap group.

Conclusion: The genetically detoxified PT antigen appears to elicit improved and long-lasting (at least 1 year) immune responses post-vaccination as compared to the licensed Tdap vaccine.

ESPID-0242
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

CONCOMITANT ADMINISTRATION OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE (MENACWY-CRM) WITH A PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN INFANTS

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Background: In infants, concomitant administration of quadrivalent meningococcal conjugate MenACWY-CRM vaccine (Novartis Vaccines) with 13-valent pneumococcal conjugate PCV13 vaccine (Pfizer) could potentially cause immunologic interference, since both vaccines contain the CRM_{197} carrier protein.

Methods: Overall 751 infants were randomized to receive 3 or 4 doses of MenACWY-CRM (2, 6, 12 or 2, 4, 6, 12 months of age) with PCV13+routine vaccinations (ACWY3 and ACWY4 groups, respectively) or PCV13+routine vaccinations only. Here we report on the immune responses to PCV13 antigens; immunological non-inferiority was evaluated at 7 and 13 months of age. At 7 months, prespecified noninferiority criteria were based on the percentage of subjects with anti-pneumococcal capsular IgG concentrations ≥0.35 µg/mL against each PCV13 serotype. At 13 months, prespecified noninferiority criteria were based on geometric mean concentrations of anti-pneumococcal capsular antibodies.

Results: At 7 months of age, noninferiority criteria were met for all PCV13 serotypes except for serotypes 3 and 5 in Group ACWY3 and 19A in Group ACWY4. At 13 months of age, noninferiority criteria were met for all PCV13 serotypes for both ACWY groups. MenACWY-CRM induced a robust immune response against serogroups ACWY (88-100%) at 13 months of age.

Conclusion: After completing the vaccination series, immune responses to all PCV13 antigens were noninferior in subjects receiving MenACWY+PCV13+routine vaccinations versus those receiving PCV13+routine vaccinations only. Immunological noninferiority was not established for all PCV13 serotypes at 7 months, although no serotype consistently failed to meet the criteria. This likely reflects insufficient power to test noninferiority, rather than vaccine interference.

ESPID-0254
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

IMMUNOGENICITY AND SAFETY OF A MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE IN HEALTHY ADOLESCENTS IN KOREA

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Background: Meningococcal serogroup B is a significant cause of septicemia and meningitis worldwide. This Phase 3 randomized, controlled study assessed the immunogenicity and safety of a multicomponent meningococcal serogroup B vaccine (4CMenB; Novartis Vaccines) in healthy Korean adolescents.

Methods: 264 adolescents (11-17 years-old) were randomized to receive two doses, one month apart, of 4CMenB or control vaccines [a placebo followed by one dose of MenACWY-CRM vaccine (Novartis Vaccines) one month apart]. Immunogenicity was evaluated by serum bactericidal assay with human complement (hSBA) against three serogroup B test strains specific for individual vaccine antigens (fHbp, NadA or PorA P1.4), or by enzyme-linked immunosorbent assay (ELISA) against the NHBA antigen. Solicited reactions and any adverse events (AEs) were assessed.

Results: One month post-second vaccination, 98%, 97%, and 97% of subjects in the 4CMenB group achieved hSBA titers ≥4 against the fHbp, NadA and PorA test strains, respectively, while percentages in the control group were comparable to baseline (27%, 16%, and 17%, respectively). Geometric mean ELISA concentrations (GMCs) against NHBA increased 52-fold relative to baseline in the 4CMenB group, while there was no substantial increase in GMCs in the control group. Frequencies of solicited reactions after any vaccination were higher in the 4CMenB group as compared to the control group, although most reactions were of short duration and mild to moderate intensity. There were no vaccine-related serious AEs.

Conclusions: Two doses of 4CMenB induced robust immune responses against the vaccine antigens and were well tolerated, with no safety concerns identified, in Korean adolescents.

ESPID-0854
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

THE ANTIBODY RESPONSE TO A 12-MONTH BOOSTER DOSE OF 13- OR 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINES

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Background UK children receive the 13-valent pneumococcal conjugate vaccine (PCV-13) at 2, 4 and 12 months of age. This randomised controlled trial assessed whether a 12-month booster dose of the 10-valent pneumococcal conjugate vaccine (PCV-10) generates a non-inferior immune response compared with PCV-13.

Methods 178 children who had previously been vaccinated with PCV-13 at 2 and 4 months were randomised 1:1 to receive a booster of either PCV-13 or PCV-10 at 12 months of age. Serum IgG concentrations and OPA titres were measured for PCV-13 serotypes before and at 1 and 12 months following vaccination. The primary objective was non-inferiority (10% level) of 1-month post-booster proportions of participants with IgG ≥0.35 mg/ml for PCV-10 serotypes.

Results For 8 out of the PCV-10 serotypes at least 97% of participants in both groups had IgG ≥0.35 mg/ml; inferior responses were seen for serotypes 5 and 9V in PCV-10 (74%, 88%) compared with PCV-13 recipients (96%, 99%). Secondary endpoints including geometric mean IgG concentrations and OPA titres showed similar or statistically superior post-booster responses in PCV-10 compared with PCV-13 recipients for serotypes 4, 18C and 19F, but significantly inferior responses to the other serotypes.

Conclusions A booster dose of PCV-10 induced IgG responses that were non-inferior to PCV-13 for 8 out of the PCV-10 serotypes. The statistically superior IgG responses seen for serotypes 4, 18C and 19F in PCV-10 compared with PCV-13 recipients may be explained by a higher antigen content and/or by conjugation to previously administered proteins (diphtheria and tetanus toxoid).

ESPID-0546
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

CLINICAL EXPERIENCE WITH THE MENINGOCOCCAL B VACCINE, BEXSERO®

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Background: Meningococcal disease remains an important cause of mortality and morbidity in children and young people. In most industrialized countries, serogroup B (MenB) strains are the commonest cause of disease; outbreaks occur unpredictably, particularly in high-risk populations such as university students. In 2013, Bexsero® (Novartis Vaccines and Diagnostics Srl, Italy) became the first broad-coverage vaccine against MenB and is now licensed in the European Union (EU), Australia, Canada, Chile, Uruguay and Brazil.

Methods: We review international clinical experience with Bexsero.

Results: Since 2013, over 640,000 doses of Bexsero have been distributed in 19 countries worldwide, including >430,000 in EU and >170,000 in Canada.

In 2014, a vaccination campaign was implemented in the Saguenay-Lac-Saint-Jean region of Québec, with 43,740 individuals (aged 2 months–20 years) receiving a first dose of Bexsero. Real-time active surveillance for adverse events (AEs) was performed. The most frequent reported AEs in the 7-day post-vaccination period were general malaise (56%) and local reactions (49%). Fever was most common in those aged <2 years. Notably, antipyretic prophylaxis reduced the probability of fever by 50%. No vaccine related hospitalizations were reported. 99% of responders intended to receive the second dose.

Bexsero has been used under an Investigational New Drug protocol during MenB outbreaks at the Universities of Princeton and California, Santa Barbara. Recently, a UK university offered the vaccine to approximately 4,000 first-year students.

Conclusion: Clinical experience with Bexsero is increasing rapidly in infants, adolescents and young adults. No unexpected safety concerns have arisen.

ESPID-0955
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

NASOPHARYNGEAL COLONIZATION AND ANTIBODY RESPONSE IN WARAO AMERINDIAN CHILDREN VACCINATED WITH THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE

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Background:

The 13-valent pneumococcal conjugate vaccin (PCV13) was included in the national vaccination program in Venezuela in 2014. However, the numerous Amerindian populations residing in Venezuela have little access to PCV due their remote living circumstances.

Methods:

Nasopharyngeal swabs and serum samples were collected before and seven weeks after vaccinating 415 PCV-naïve Warao children aged 6 weeks - 59 months with a primary series of PCV13 according to CDC-recommended age-related schedules (Table 1).

Results:

For all serotypes except for 6B, antibody responses were ≥0.35 ug/ml in ≥70% of the children. For serotype 6B, around 50% of children showed an antibody concentration ≥0.35 ug/ml. Serum levels were generally higher in younger children who received more vaccine doses.

Before vaccination, 70% of the children were colonized with *Streptococcus pneumoniae* of which 39% were vaccine-type (VT) pneumococci and 31% were non-VTs. After vaccination, 51% was colonized with *S. pneumoniae* of which 31% were VTs and 20% were non-VTs. Colonization rates of *Staphylococcus aureus* increased almost threefold following PCV13 vaccination.

Conclusions:

While the PCV13 vaccine appeared to be immunogenic in Warao Amerindian children, an early shift in nasopharyngeal carriage toward non-PCV13 serotypes was not observed. The impact of vaccination on pneumococcal carriage is likely dependent on the number of doses and it might take longer before effects are measurable.

Table 1. Vaccine schedule.

Age at first dose	Total number of doses (primary series)
6 weeks - 6 months	3
7 - 23 months	2
24 - 59 months	1

ESPID-0968
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

NUTRITIONAL STATUS INFLUENCES SALIVARY AND SERUM IMMUNE RESPONSES TO THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN WARAO AMERINDIAN CHILDREN FROM VENEZUELA

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Background:

Saliva is a more accessible sample than blood. We determined serum and salivary antibody titers following PCV13 vaccination of Warao children aged 6 weeks - 59 months to study whether saliva can be used as read-out for vaccine responses.

Furthermore, malnutrition leads to immunological alterations and may thus alter vaccination response. Because many Warao children are malnourished, we studied the influence of nutritional status on antibody levels.

Methods:

A total of 504 children were vaccinated with a primary series of PCV13 according to CDC-recommended age-related schedules. Serum and salivary samples pre-vaccination and a median of 47 days (IQR 45-48) post-vaccination were obtained from 411 children. A multivariate linear regression analysis was performed to assess the influence of nutritional status (weight-for-age and height-for-age Z scores) on antibody responses.

Results:

In both malnourished (40%) and well nourished (60%) children, salivary antibody levels correlate well with serum levels for all serotypes with coefficients varying from 0.29 for serotype 6B to 0.80 for serotypes 5, 6A and 23F (all $p<0.01$).

Surprisingly, lower Z scores indicating a poor nutritional status are associated with higher serum and salivary antibody levels (for respectively 5 and 10 out of 13 serotypes). We speculate that Th2 skewing in poorly nourished children could be the underlying immunological mechanism for the more abundant reaction to PCV13.

Conclusions:

Saliva might be useful as future surveillance tool for PCV vaccination studies. Additionally, immune responses following PCV13 vaccination of Amerindian children are affected by nutritional status. The underlying immunological mechanisms require further studies.

ESPID-0179
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

COMPARISON OF ORAL SUCROSE SOLUTION AND ORAL ROTAVIRUS VACCINE FOR REDUCING PAIN DURING INFANT VACCINE INJECTIONS

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Introduction and aims

Oral rotavirus vaccine contains sucrose. Sucrose solution administered prior to vaccine injection in infants has been demonstrated to reduce pain. Currently there are no recommendations regarding the order of administration of rotavirus vaccine relative to injectable vaccines administered at the same visit. If sucrose sweetened rotavirus vaccine can be shown to reduce vaccine-induced injection pain it's administration could be standardized to precede injectable vaccines. The aim of this study was to compare the analgesic effectiveness of rotavirus vaccine and sucrose solution.

Methods

Two and 4 month-old infants receiving two routine injectable vaccines concomitantly with rotavirus vaccine, at the same visit, were randomized to receive oral rotavirus vaccine (Rotarix™) before the injectable vaccines and sucrose (Tootsweet™) afterwards or sucrose before and rotavirus afterwards. Parents and clinicians, blinded to treatment allocation, assessed pain using a 0-10 point Numerical Rating Scale (NRS). Separately, blinded observers assessed pain from videotapes using the 0-10 point Modified Behavioural Pain Scale (MBPS).

Results

120 infants participated: 60 were randomized to rotavirus first. There were no differences between groups in infant characteristics, including; age, sex and weight ($p>0.05$). MBPS and clinician NRS scores did not differ between groups. Parent NRS score after the second injection and mean parent NRS score for both injections was lower in infants given rotavirus first; $p=0.046$ and $p=0.032$, respectively.

Conclusion

Rotavirus vaccine is effective in reducing injection-induced pain. Based on these findings, it is recommended that rotavirus vaccine be administered prior to injectable vaccines at 2 and 4 months of age.

ESPID-0514
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

ANTI-DIPHTHERIA AND ANTI-TETANUS ANTIBODIES LEVELS IN HEALTHY POLISH CHILDREN - POSTVACCINATION STATUS.

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Currently used vaccination programme in Poland recommends giving seven doses of tetaus-diphtheria vaccine before aduldhood. It is desiged to assure protection in the population in the 10-year period following the last booster.
In this study we evaluated the levels of antibodies to diphtheria and tetanus in healthy children after primary series of vaccinations.
A total of 85 serum samples were colected from individuals with ages ranging from 19 months to 5 years. Antibody concentrations were measured with an enzyme-linked immunosorbent assay.
In the analysed group there were 85 children, 49 boys and 36 girls, median age was 4.17.Median concentrations of specific antibodies were 1.23 IU/ml for anti-tetanus IgG and 0.9 IU/ml for anti-diphtheria IgG. There were no seronegative patients for dipteria (<0.1 IU/ml) or tetanus (<0.01IU/ml). No reliable protection against tetanus and diptheria was observed in 5 children (5.89%), 20 (23.5%) other had no reliable protection agianst diptheria with only basic protection against tetanus. Low levels of anti-diphtheria antibodies were observed more frequent than anti-tetanus ($p<0.001$). There were no children with low levels of anti-tetanus antibodies and preserved protection against diphtheria. High levels of anti-diphtheria antibodies (>1.0 IU/ml) were found in 12 children (14%), and in 17 (20%) against tetanus (>1.1IU/ml).
Results of this study reveal that in most cases diphtheria and tetanus (dT) vaccination are efficient between booster doses. Protection against diphtheria after the same number of doses is weaker than against tetanus. To maintain full protection children from the study group required further booster doses of Td vaccine.

ESPID-0909
VACCINE EFFICACY, EFFECTIVENESS, SAFETY AND MARKERS OF PROTECTIONS

THE IMPACT OF VACCINE COMMUNICATION ON VACCINE ACCEPTANCE IN GREECE: A QUALITATIVE STUDY

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BACKGROUND AND AIMS: Vaccine hesitancy is increasing worldwide. Widespread dissemination of misinformation may be one important factor but sociopolitical and culture factors may mediate this influence.

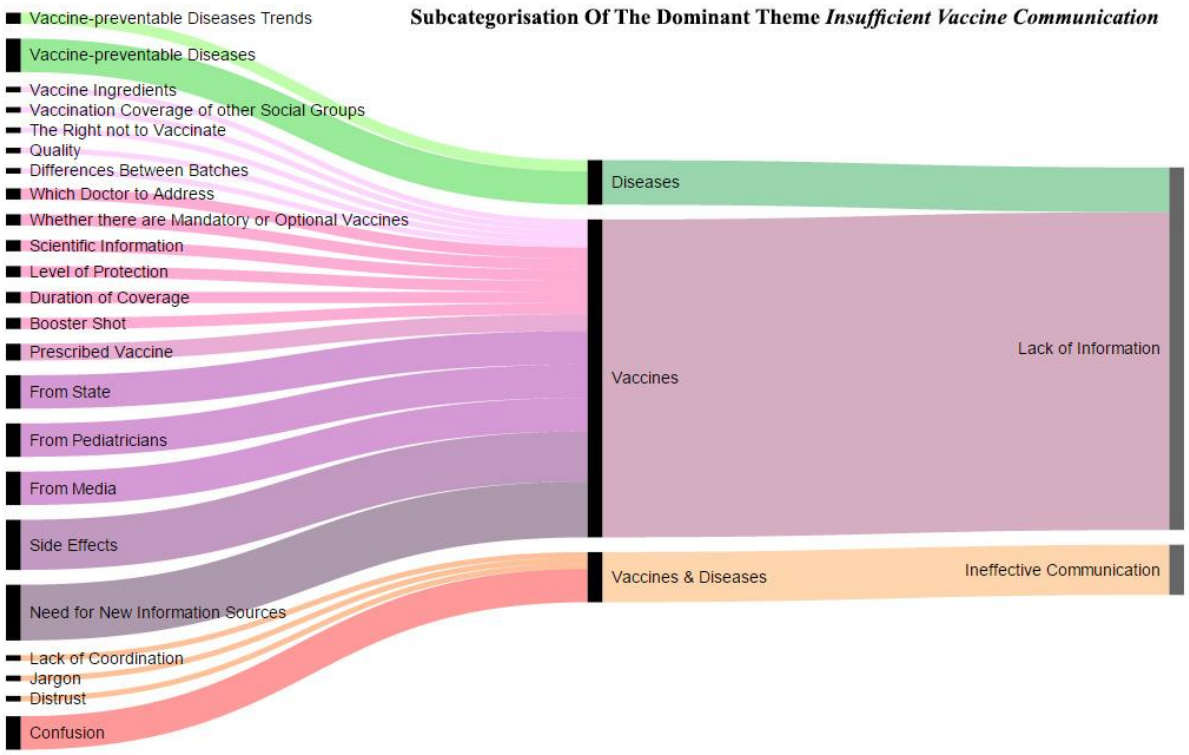
This qualitative study evaluates the impact of vaccine-related media coverage on vaccine acceptance among caregivers and immunization providers of young children and adolescents in Greece, an upper income country facing significant economic challenges.

METHODS: We conducted focus groups and semi-structured interviews in Greek with 88 caregivers and 32 pediatricians, homeopaths, public health officials and gynecologists in urban and semi-urban Athens. Data were transcribed and translated into English. Analysis for common themes followed using qualitative data analysis software (NVivo 10).

RESULTS: We identified 1.700 comments within 18 primary themes from focus groups. Pediatricians and caregivers reported high vaccine acceptance. Caregivers reported frequent exposure to negative information about vaccines from media sources, but this did not significantly affect their decision-making. Caregivers viewed vaccination as a shared decision with their pediatricians and viewed pediatricians as their primary source of vaccine information. However, both pediatricians and caregivers acknowledged that the medical community provided inconsistent messaging. A need for more accessible and reliable vaccine sources was expressed.

CONCLUSIONS: Vaccine acceptance is generally high in Athens. Efforts to strengthen the immunization program in Greece should focus on ensuring consistent communication from the medical community. Further research can identify the most effective implementation strategies for dissemination and proliferation of information

to caregivers and immunization providers.



ESPID-1070
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

VISCERAL LEISHMANIASIS INFANT IN ITS ATYPICAL AND SEVERE FORMS OF 108 CASES

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Kabylia,nowadays, remains the region most supplying Algeria in cases of Visceral Leishmaniasis (VL). Atypical and / or serious forms of recent observations are current, which goes against the development of screening tools (PCR, leucocytoconcentration), new therapeutic molecules (Ambisome) and prophylactic means undertaken. **Objectives**: analysis of the frequency and prognostic factors forms of atypical and severe LV.**Methods**:Prospective collection of 108 cases of atypical LV and / or severe from a series of 276 infant LV, gathered in 11 years (2000 to 2010).**Results**: Children aged 1 month and a half to 15 years, the average age was 6.45 +/-15.8 with a ratio of 1.57 Atypical forms are noted in 46.8% :Atypical: age (in less than 3months (5), and in more than 6 years (7); clinical signe absence of fever (6);No splenomegaly (5); Atypical visceral forms: frequency of gastro intestinal involvement (12) pulmonary form in less than1 year (8), form granulomatous liver (7).form neurology(2)and renal (1) Severe forms are noted in 53.2%. Predictive factors of gravity conditioned life threatening are marked with:The severity of the neuropathy <1000 (9); Anemia <5(4);Thrombocytopenia <50000 (11); The absence of inflammation (5); Undernutrition (10) ;A hemorrhagic syndrome(8);Thesetableshavesignificantlyconditionedprescription Fungizone (22) and Ambisome(5) as first-line treatment with supplements (97 antibiotics,TB (2,) corticosteroids, (7)immunosuppressive(4) depending on terrain and complications.Evolution marked by ten deaths .**Conclusion**: Despite the recent ways of diagnosis, treatment and prophylaxis initiated, the emergence of these frequent and recent forms of observation seem to be related to the state of immunosuppression of patients, even in parasite virulence.

ESPID-0757
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

SUBDURAL EMPYEMA DUE TO ACINETOBACTER JOHNSONII IN A FOURTEEN-YEAR-OLD-GIRL: A CASE-REPORT

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Background

Acinetobacter is an important pathogen of hospital acquired infections. Acinetobacter baumanii is the most prevalent species and has, rarely, also been associated with community acquired infections including meningitis. Other emerging species, like Acinetobacter johnsonii, have also rarely been associated with disease.

Case presentation

A fourteen-year-old girl with no previous medical history was admitted to another hospital with headache and fever. Biological work-up revealed an inflammatory syndrome (neutrophiles 14700/µL, CRP 330mg/L). A diagnosis of ethmoido-fronto-maxillar sinusitis was made on a cerebral CT-scan. A sinus washing was performed followed by large spectrum antibiotics. After three weeks of treatment, she was transferred to our pediatric center because of persisting symptoms. At arrival, her clinical examination was completely normal. She complained of unilateral headache, fever, phonophobia, photophobia and vomiting. A cerebral MRI showed a right pansinusitis, a large subdural collected empyema and frontal cranial vault osteitis. The empyema was quickly drained and Meropenem and Vancomycin were empirically started. Per-operative cultures showed massive growth of multiresistant Acinetobacter johnsonii. The girl showed a good clinical and radiological evolution, Meropenem was pursued for 6 weeks. Her close follow-up showed only a slight muscular left leg weakness.

Conclusion

Acitenobacter johnsonii is an emergent human pathogen that has rarely been associated with septicemia, endocarditis, abcess and urinary tract infections. To our knowledge, this is the first reported case of community-acquired cerebral empyema due to this pathogen. This report provides further evidence that this organism can cause life-threatening community-acquired infections.

ESPID-0538
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

HEPATOSPLENIC FORM CAT SCRATCH DISEASE IN CHILDREN

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Background and aims: Cat scratch disease (CSD) is a common benighn disease in children, caused mainly by *Bartonella henselae*. It is usually presents as prolonged fever and tender regional lymphadenopathy. However, atypical cases do occur in a minority of cases. The purpose of the present study is to evaluate the abnormal findings associated with hepatosplenic involment demonstrated by abdominal ultrasound in hospitalised children with CSD.

Methods: From January 2003 to July 2014, 135 cases of CSD were diagnosed in children. In 36 of them was performed ultrasound for diagnostic purpose.

Results: In 17 patients (47,2%) were observed abnormalities in liver (3), spleen (9) or both (5). The most common liver finding was slight enlargment without focal lesions (6 cases). Other findings were the presence of two hypoechoic cystic-like lesions, 1.3 and 2.2 cm each (one case) and enlargment of hylar lymph nodes (one patient). Abnormalities of spleen were enlargment without focal lesions (7 cases) and hypoechoic cystic-like lesions suggesting abscesses (7 patients). The number of focal lesions were one to four in 5 patients, ranged in diameter from 0.37 to 7 cm, and multiple in 2 cases, all these <6 mm. Mesenteric lymphadenopathy was revealed in 6/17 (35,3%) of children. The transaminase levels were normal. The clinical outcome was excellent in all patients. Re-examination was performed in 6 children after 2 months and the lesions were improved or completely resolved.

Conclusions: The CSD should be considered in case of hepatosplenic abnormalities in children, especially in cases with cystic-like lesions.

ESPID-0613
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

COMPARISON OF ROSE BENGAL AGGLUTINATION TEST AND ENZYME-LINKED-IMMUNOSORBENT ASSAY FOR DETECTION OF BRUCELLA ANTIBODIES IN CHILDREN WITH ACUTE BRUCELLOSIS

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Background and aims: Brucellosis is a zoonotic of public health priority in Greece. Given that symptoms and signs of brucellosis are nonspecific and culture yield of *Brucella spp* is time consuming, serological tests are necessary for diagnosis of disease. Our study was undertaken to evaluate Rose Bengal test (RBT) and enzyme-linked immuno-sorbent assay (ELISA) in the diagnosis of acute brucellosis.

Material and methods: From January 2003-December 2011, 1685 serum samples from children with a compatible clinical presentation for brucellosis were examined. All serum samples were subjected to RBT, while 783 samples were selected for detection of specific IgM/IgA/IgG antibodies by ELISA.

Results: Acute brucellosis was diagnosed in 32 children. Among these, 31 children demonstrated positive antibodies response by RBT, while in the single RBT negative patient, Elisa and blood cultures shown positive results. Among all 1653 patients without brucellosis, RBT results were negative, except for one child. Seropositivity for *Brucella spp* antibodies detected by Elisa was determined in 31 out of 32 children; *Brucella spp* antibodies were found as follows; IgM 96,9%, IgA 93,8% and IgG 87,5%. In the single Elisa negative patient, RBT and blood cultures were positive. Among 751 children without brucellosis, negative results were observed in 737 cases by Elisa (98,1%) and false positive in 14; IgM ten, IgA two and IgG three.

Conclusions: It is suggested that for an accurate diagnosis of brucellosis, a combination of RBT and Elisa should be performed, especially in case of RBT negative patients with a history suggesting this disease.

ESPID-0429
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

DENGUE SEVERITY ASSESSMENT AND PROGNOSTICATION

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Introduction: Dengue infection has become an international public health burden. Children need to be monitored closely and managed aggressively.

Aim: To develop a coding system for assessment of severity of dengue infection with simple clinical and laboratory parameters assessed at the onset of critical phase:

- Early identification of probable serious cases
- To reduce the hospital burden.
- To compare with WHO grading of Dengue.

Methods: An observational, descriptive and retrospective study conducted on 260 dengue cases confirmed by Dengue NS1Ag and or Dengue IgM MAC ELISA with or without IgG ELISA, admitted in a tertiary care hospital in Kolkata, India between July-November 2014. Patients between 1 month and 15 years of both sexes were included.

Results: Various clinical and laboratory variables were assessed. Variables with $p<0.05$ were considered significant .The significant variables include-abdominal pain, decreased urine output, bleeding episodes, capillary leak, hepatomegaly, rash ,serum alanine aminotransferase , albumin, cholesterol, platelet, and hematocrit.Rash showed inverse relation with severity. With the significant variables a coding system has been developed and patients were classified into 3 groups- mild, moderate and severe corroborating with WHO grading system.

Conclusion: With the significant parameters measured at the onset of the critical phase, a coding system was generated. This can serve as a guide to home or hospital management on the basis of severity . Our study when compared with the already existing WHO grading system correctly diagnoses 70% of the cases , over and under diagnosed were 15% each.

ESPID-0893
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

AN IMPORTED CASE OF HUMAN RABIES ENCEPHALITIS IN A 5-YEAR-OLD CHILD

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Background and aims – Most countries in the Western Hemisphere have succeeded in eliminating human rabies transmitted by dogs, including Brazil. However, close countries such as Bolivia and Haiti still represent the highest incidence rates in the Americas. We describe an imported case of human rabies from Bolivia, diagnosed in a quaternary care hospital in Sao Paulo.

Case description – a previously healthy 5-year-old child admitted to ER with fever, drowsiness and neurologic symptoms (ataxia, irritability, dysphagia, delirium, paresthesia, and modification of sleep–wake cycle) for 5 days. At admission Glasgow Coma Score was 13, there was serum leukocytosis with neutrophilia, head CT and CSF were normal. Intravenous ceftriaxone and acyclovir was initiated. After 48h the patient developed altered consciousness level and acute respiratory distress, which required intensive care and mechanical ventilation. A scar in the face was noted on the face and when asked the mother about its origin, she reported a previous bite of an unknown dog occurred 2 months before. Human rabies was assumed and nested RT-PCR in saliva, hair follicle and CSF, and serum neutralizing antibodies were collected for diagnosis. The Milwaukee-based Brazilian Human Rabies Treatment Protocol, which comprises intravenous amantadine, sapropterin, deep sedation with midazolam and ketamine was initiated 9 days after onset. After 36 days of treatment, persistent fever and coma the patient died.

Conclusion – human rabies must be considered in all acute neurologic disease of unknown etiology, especially when in immigrants from countries where rabies is endemic

ESPID-0618
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

CLINICAL, MICROBIOLOGICAL PROFILE AND COMPARISON OF ELISA-IGM WITH IFA IN RESOURCE LIMITED COUNTRIES FOR DIAGNOSIS OF RICKETTSIAL INFECTIONS IN CHILDREN

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Background and Aims

Rickettsial infections are endemic in many parts of India. Indirect fluorescent antibody(IFA) test is 'gold standard' diagnostic test. Clinical profile, causative species and therefore serology varies widely with geographical area. Due to unavailability, IFA is rarely used in India. We hypothesized that ELISA-IgM is a 'non-inferior low-cost alternative' to IFA for diagnosis and species identification.

Methods

This prospective study was conducted from Nov-2011to Oct-2012 in children aged upto 12 years admitted with clinical diagnosis of rickettsial infections in district level hospital from south India, where rickettsial infections are 'very endemic'. Details of demography, clinical course, complications and outcome were meticulously recorded. All were screened by Weil-Felix and ELISA-IgM test. Due to cost constraints and non-funded study; ten random patients were tested for IFA.

Results

Forty patients were enrolled consecutively. Mean(±SD) age was 3.2±2.66years. Common clinical features were; fever(100%), hepatosplenomegaly(100%), rash(97.5%), seizures(20%), altered consciousness(15%), lymphadenopathy(12.5%), and eschar(10%). Among organ dysfunctions; encephalitis(22.5%), respiratory failure(15%), myocarditis(12.5%), shock(5%) and renal failure(5%). Laboratory abnormalities were; Anemia(90%), thrombocytopenia(45%), elevated AST(100%), elevated ALT(75%) and CSF lymphocytic pleocytosis(27.5%). Weil-Felix test was positive in 31(77.5%) and ELISA-IgM: 38(95%). Of 10 random patients tested for IFA, all were positive and also by ELISA-IgM, whereas only 6(60%) by Weil-Felix test. *Rickettsia Conorii* was the species identified in all cases.

Conclusion

Rickettsia Conorii (causative agent of Indian tick typhus) was the primary species found. ELISA-IgM was as sensitive and specific as IFA and may be a 'non-inferior low-cost alternative' to IFA for diagnosis and species identification in resource limited set up.

ESPID-0270
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

EPIDEMIOLOGIC, DIAGNOSTIC, CLINICAL AND THERAPEUTIC ASPECTS OF BRUCELLA BACTEREMIA (BB) IN CHILDREN IN SOUTHERN ISRAEL: A 7-YEAR RETROSPECTIVE STUDY (2005-2011)

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Background: Data on the various aspects of brucellosis in children living in southern Israel are
missing.

Objectives: To study the epidemiological, microbiological, diagnostic, clinical, therapeutic and outcome features of brucellosis in children <19 years of age in southern Israel during 2005-2011.

Patients and Methods: The diagnosis was established according to a clinical presentation compatible with brucellosis + presence of BB.

Results: Of 252 patients hospitalized with a diagnosis of brucellosis, 128 (50.8%) had BB; *B. melitensis* grew in all cultures. All patients were of Moslem Bedouin ethnicity**.** Overall duration of symptoms before diagnosis was 10.1±10.9 days. Fever at diagnosis was recorded in <20% patients. The most frequent symptoms were arthralgia, weakness, gastrointestinal disturbances, myalgia and headache (61.7%, 32, 8%, 27.3%, 25.0% and 18.8%, respectively). The main clinical findings recorded included monoarthritis, hepatosplenomegaly, lymphadenopathy, heart murmur and skin rash (36.7%, 25%, 17.2%, 11.7 and 9.4%, respectively). Anemia, leukopenia, thrombocytopenia and pancytopenia were reported in 17.6%, 29.6%, 12.8 and 2.3% patients. Twenty-nine (30.5%) patients had serum agglutinin titers ≤1/160 (13, 13.7%, had titers<1/160). 27/29 (93%) patients aged 0-4 years were treated with gentamicin and trimethoprim-sulfamethoxazole and 77/128 (60.2%) patients received gentamicin and doxycycline.

Conclusions: 1. BB was diagnosed in >50% of the children with brucellosis; 2. Arthralgia, weakness and gastrointestinal complaints were the most commonly reported symptoms and monoarthritis, hepatosplenomegaly and lymphadenopathy were the most common clinical findings; 3. A considerable number of patients with BB had undetectable/low serum agglutinin titers, suggesting insufficient reliability on serology alone in the diagnosis of brucellosis.

ESPID-1083
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

If a magician is a friend of you and you have a lymph node: please, search for Francisella

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Background: Tularemia is an emerging disease in Spain. There was 3 outbreaks in 1997-2013 (See Table). Source of infection is usually handling with rabbits or rodents. Other possibilities include fly bites, inhalation exposure or contaminated water, even handling crayfish. Francisella tularensis; a cocobacillus very resistant under extreme conditions cause the disease.

Methods: A 6 year-old girl, with five days of fever was admitted to the hospital by enlarged and painful inguinal lymphadenopathy receiving oral ceftibuten for S. aureus urinary infection. She had casual contact with diferent pets. In four days lymph nodes grew to 7 cm (See figure) accompanied by red and crusted buttocks lesions and vaginal discharge. She started therapy with cloxacillin, cefotaxim and clindamycin.

Results: Vaginal discharge culture: Haemophilus spp. Blood Culture (-). PPD: (-). Serology: CMV, VEB, HHV-1, HHV-2, HHV-6, HHV-8, VIH, Bartonella, Parvovirus, Toxoplasma, Brucella and Chlamydiophila: negatives. Francisella Tularensis: (+) dilution 1:8192. Lymph node biopsy: Pathological findings consistent with necrotizing granulomas. PCR: (+) to Francisella Tularensis holoartica Streptomycin treatment was ordered for ten days with complete clinical recovery. In a new interrogation the girl recognized a close contact with a rabbit owned by a magician that became ill and died two weeks before. Unfortunately we have not animal necroscopy

Conclusions: 1. Considere rare pathogens for painful lymph node infection refractory to treatment. 2. Biopsy with culture or molecular techniques confirm the suspected diagnosis. 3. A correct clinical history is essential for proper diagnosis. 4. Treatment of choice is aminoglycosides. It´s also possible use oral fluorquinolones

ESPID-0326
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

PECULIARITIES OF CHILDREN CAMPYLOBACTER CAUSED DIARRHEA IN KAUNAS, LITHUANIA, 2014

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Aim and background. *Campylobacter* is the predominant etiological agent of children diarrhea in Lithuania during last few years. The aim of this study was to estimate the clinical aspects of *Campylobacter* caused diarrhea in children hospitalised between January and September in 2014.

Method. A retrospective study of 60 cases *Campylobacter* caused diarrhea in children hospitalized in Kaunas Clinical Hospital.

Results. *Campylobacter* caused diarrhea was diagnosed in 32 girls and 28 boys from 1 month to 17 years old. 58.3% of the patients were younger than 3 years of age. 93.3% of children had fever (mean 38.83±0.8ºC for 2.85±1.3d), 43.3% - had vomiting. Diarrhea episodes were in range from 3 till 21 per day (average 10.24±4.06). Hemocolitis was seen in 65% of cases starting in average on 2.45±1.6 days and more frequently observed in younger children (Spearman's Rho -0.353, p=0.006). The mean duration of hospitalization was 3.69±1.75 days. Species identification of 31 available isolates revealed that *C.jejuni* was the dominant species (90.3%) followed by *C.coli* (9.7%). Rotavirus Ag was found in stool of 7 patients from 39 examined, no other enteropatogens were indentified. CRP mean was 52.1± 40.9 mg/l (range 2.8-221.2 mg/l), the mean WBC count was 12.5 $x10^9$/l (range 3.6-27.1 $x10^9$/l), elevated WBC count (> 9 $x10^9$/l) was found in 70% of cases. Antibacterial treatment was given to 28 (48.3%) patients.

Conclusions. 1. Species identification revealed that *C.jejuni* was the dominant species in analyzed cases. 2. Hemocolitis presented in 65% of cases and was more frequent in younger children.

ESPID-0328
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

EPIDEMIOLOGY OF KAWASAKI DISEASE IN GERMANY: A PROSPECTIVE, POPULATION-BASED STUDY

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Background and Aims: National estimates of Kawasaki Disease (KD) incidence often do not include incomplete cases diagnosed on laboratory or echocardiographic criteria, and/or they rely on retrospective case reports and data registries where underreporting is a problem. We describe the epidemiology of KD in children in Germany while addressing these issues.

Methods: We conducted prospective nationwide KD surveillance (2011-2012) in children aged <5 years through the hospital-based German Pediatric Surveillance Unit *(ESPED).* We accounted for underreporting in two German states by applying capture–recapture methodology (CRC) using hospital discharge records with KD ICD-10 code (i.e., M30.3). KD diagnoses were classified as "complete" and"incomplete" according to the American Heart Association 2004 criteria.

Results: Incidence of KD, corrected for underreporting, was 7.2/100,000 in children aged< 5 years in Germany. Underreporting to ESPED was estimated at 37%-44%. Overall, 315 validated KD cases were reported. The male-to-female ratio was 1.5:1. Of the 64 (20%) incomplete cases, 58% (37/64) were detected through echocardiographic findings and 42% (27/64) through laboratory criteria alone. Incomplete cases tended to be younger than complete cases (1.2 vs. 2.0 years, p<0.001) and had more coronary aneurysms (43% vs 11%, p=0.001).

Conclusions: A substantial number of incomplete KD cases were diagnosed based on laboratory and echocardiographic criteria only, particularly in infants <1 year of age – an age group known to have an increased risk of developing coronary aneurysms. In addition, we found a high rate of underreporting to the national Pediatric Surveillance Unit. Development of better diagnostic tests remains a priority.

ESPID-0350
ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

CLINICAL EPIDEMIOLOGY OF 182 CHILDREN WITH MEASLES IN CHILDREN'S HOSPITAL OF FUDAN UNIVERSITY IN 2012

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Objective The aim of this study is to investigate the main factors that influence measles morbidity and to know the genotype of measles virus, so as to provide evidence for scientific decision making to further control the prevalence of measles.

Methods Analyzing the clinical epidemiology of the patients with diagnosed measles and hospitalized in Children's Hospital of Fudan University in 2012. Gene sequencing of measles virus had been done at the same time.

Results 182 patients were enrolled with 125 males and 57 females. No allopatric virus strain was found. Clinical feature: ① 146 patients were under the age of 1 (80.22%). ② All the patients had fever and obvious rash (100%). 8 patients had rash before fever (4.40%), 17 patients had atypical rash (9.34%). 159 patients received sputum culture detection and there were 60 cases with positive results (37.74%). The dominant cultured bacteria were Pneumonia Streptococcus (9.43%), Haemophilus Influenza (9.43%), Catarrhus Branhamella (4.40%). ③ Many patients had complications. There were 98 cases of Pneumonia (53.85%), 38 cases of Bronchitis (20.88%), 80 cases of laryngitis (43.96%), 109 patients with Diarrhea (59.90%), 12 cases with myocardial damage (6.59%), 4 patients with hepatic function damage (2.20%), and no patient had Encephalitis. ④Among the patients, only 11 had received Measles Vaccine vaccination before (7.24%). Additionally, there were 145 floating population among all 182 patients (79.67%).

Conclusions The results indicated that we should strengthen immunization in infants and try to improve vaccination coverage rate in floating population, so as to prevent measles outbreak.

ESPID-0064
Unallocated Posters

UNREASONABLE USE OF ANTIBIOTIC THERAPY IN ACUTE RESPIRATORY VIRAL INFECTION

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INTRODUCTION: The important issue for Central Kazakhstan is unjustified antibiotic prescribing for acute respiratory infections (ARVI) in children.
MATERIALS: We retrospectively studied 100 medical histories of outpatient children in two clinics. The selection of medical histories of child was blinded method. Inclusion criterias were verified diagnosis of ARVI in children aged 0 to 3 years. We registered 41 of cases of ARVI with mild course of the disease and 59 of cases with moderate course of ARVI. The clinical picture of ARVI manifested by rhinitis, pharyngitis, laryngitis, bronchitis and intoxication syndrome.
RESULTS: Analysis of history of the childreen showed that 13 of the children of the first year of life, 12 children of the 2nd year of life, and 11 of the children 3 years of ages were prescribed antimicrobials. It can be noted that this category of children who are unnecessarily prescribed antibiotics, had a risk of negative consequences of irrational antibiotic therapy. However, according to the study, there has been a reasonable assignment of antibiotic therapy due to stratification of bacterial infection in 6 children; 2 children due to recurrent otitis history and under unfavorable premorbid background (2-3 degree malnutrition, rickets subacute grade 2) a child under the age of 6 months.
CONCLUSION: Analysis of treatment showed that the fear of complications in children with AVRI is one of the main reason that physicians prescribe antibacterial agents in the outpatient setting. Therefore, identifying inappropriate antibiotic treatment at ARVI, requires further measures for its prevention in childhood.

ESPID-0101
Unallocated Posters

MANAGEMENT OF SEVERE ACUTE MALNUTRITION IN UNDER FIVE SUDANESE CHILDREN ADMITTED TO A RURAL HOSPITAL IN KHARTOUM, SUDAN.

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Problem statement: Infection and malnutrition are the main causes of high under five mortality in Sudan. One third (31%) of children under the age of five years are moderately or severely underweight (<-2 Z score, weight for age). The level of global acute malnutrition (14.8% - < 2 Z score, weight for height) is just below internationally recognized standards for indicating a nutrition emergency.

The WHO provided guidelines for management of PEM at a hospital level by two dietary formulae F75 and F100. A local formulae with cheap available constituents is proposed and evaluated. These are Gezira Initial Formula (GIF) and Gezira Maintenance Formula (GMF).

Methods: It is a prospective observational study in which all Under-five children with weight for height under 70% of the WHO standard for Wt/Ht were included.

Results: The number of children studied was 293. 66 children (22.5%) were admitted initially to the Intensive Care Unit to receive initial treatment for hypothermia (6%), severe dehydration (8%), pneumonia (6%) and Xerophthalmia (2%). 287 (72.5%) children showed improvement by either reaching or approaching the WHO expected Wt/Ht, 10.4% of children (n=41) died and 68 children escaped before being officially discharged (17.2%). The mean duration of stay in hospital was 18 days with a range of 12-44 days. The mean increase in weight per day was 7gm/day with average of 5-19 grams/day. The mortality rate fell to 10% compared with the mortality rate of 33% before Gezira Formulae Introductory.

ESPID-0522
Unallocated Posters

CYTOMEGALOVIRUS INFECTION IN CHILDREN AFTER BONE MARROW TRANSPLANTATION: RISK FACTORS, CLINICAL ASPECTS AND OUTCOMES

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Introduction: Cytomegalovirus (CMV) infection remains the most common and potentially severe viral complication in patients given HSCT.

Materials and methods: This study was a retrospective analysis of clinical, laboratory and outcome data of all pediatric patients underwent BMT, at King Faisal Specialist Hospital and Research Centre (KFSH&RC)-Jeddah, Saudi Arabia, from July 2005 to June 2014.

Results: Out of 95 cases, males were 63 (66.3%) and females were 32 (33.7%). Majority of patients have hematological malignancy (n=31; 32.6%) followed by nonmalignant disorder (n=30, 31.5%), solid tumors (n=19, 20%) and HLH (n=5; 5.3%). CMV reactivation was observed in 29 patients (29/95; 30.5%) within 100 day of post BMT. Out of them majority were asymptomatic (n=21; 77.8) and remaining (n=9 ; 22.2%) had clinical manifestation/organ involvement (Liver, Skin, GIT and CNS).

Age less than 5 year (p= 0.043), AML (p=0.019), patients with positive pre-transplant CMV status (p=0.007), conditioning regimen containing ATG ($p < 0.041$), allogeneic BMT ($p < 0.027$) lymphopenia < 300/mm ^{3} (p=0.049) were identified as risk factors associated with development CMV reactivation in post BMT pediatric patients. A total of 36 (37.9%) patients developed GVHD and overall 27 (28.4%) patients were expired. Both outcome variables were statistically significant GVHD (OR: 5.4; 95% CI: 2.42-12.18) and mortality rate (OR: 8.1; 95% CI: 2.51-25.61) in patients with CMV reactivation versus no CMV reactivation respectively.

Conclusion: Young age, AML, positive pre-transplant CMV status, ATG containing conditioning regimen, allogeneic BMT and lymphopenia were identifiable factors associated with development CMV reactivation in post BMT pediatric patients.

ESPID-0008
Unallocated Posters

A NOVEL ETHIOLOGICAL AGENT OF KERION CELSI IN A CHILD

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Tinea capitis is a fungal infection of the scalp caused by dermatophytes. Kerion celsi (KC) is known as the inflammatory type of tinea capitis which is a hypersensitivity reaction of the body to fungal agents. Differential diagnosis with bacterial pyoderma, abscess may avoid unnecessary and inappropriate surgical drainage. Although *Trichosporon* species are the causative agents of cutaneous infections, there is no KC case associated with *Trichosporon asteroides* in the literature.
A previously healthy 10-year-old boy was admitted to our hospital with complaints of swelling, discharge and pain behind of the right ear. Initial physical examination revealed a painful, yellow colored purulent discharge and hair loss at 3x2 cm area on the scalp behind the right ear. There also was a mobile, painful palpable

lymphadenopathy in the postauricular region (Fig. 1). The skin lesion was consistent with KC and the swab culture from patient's lesion was sent to the laboratory for bacterial and fungal cultivation. *Trichosporon* colonies were detected on Sabouraud Dextrose Agar SDA plates. The sequence of our case isolate was 99 % identical to that of AB018017, AF075513 thus, molecular product was identified as*Trichosporon asteroides*. Fluconazole (10 mg/kg/day) was initiated and ketoconazole shampoo was given two days a week. At the end of the 8th week, the lesion was found to be significantly resolved and new hair formation was observed on the lesion (Fig. 2) and the treatment was stopped.

Herein, we report a ten year-old boy who had KC related to *Trichosporon asteroides* and successfully treated with fluconazole.

ESPID-0013
Unallocated Posters

UNUSUAL COMBINATION OF COMPLICATIONS IN A CHILD WITH ROTAVIRUS GASTROENTERITIS

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Rotavirus may cause life-threatening complications in untreated patients during the course of gastroenteritis. Electrolyte imbalance, bacteremia and sepsis are the most common complications of Rotavirus gastroenteritis (RG). It is believed that translocation of intestinal microorganisms due to intestinal epithelium dysfunction is the underlying mechanism of bacteremia in RG. Although gram negative bacteremia has been stated as a complication in RG, *Staphylococcus aureus* bacteremia and endocarditis have not been reported in the previous literature. A 22 month-old child was admitted with complaints of fever, diarrhea and dehydration to our clinic. He was diagnosed with RG which was complicated with *S. aureus* bacteremia, pyomyositis and endocarditis. We call attention to these complications in patients with prolonged or late onset fever during RG as rare complications on the course of disease.

ESPID-0014
Unallocated Posters

AN UNCOMMON PRIMARY PYOMYOSITIS AGENT IN AN INFANT: STREPTOCOCCUS PNEUMONIAE SEROTYPE 5

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Pyomyositis is an uncommon pyogenic infection of striated muscle tissue. While *Staphylococcus aureus* is main causative agent, *Streptococcus pneumoniae* rarely occurs in the etiology.

A 2.5 month-old girl was admitted to our hospital with complaints of fever and an inability to move her left leg. On initial physical examination, she had increased capillary refill and tachycardia with toxic appearance. Flexion-adduction and internal rotation posture, and warmth, tenderness and limitation of movement of the left hip joint were detected. The fluid replacement therapy was given to her immediately. After blood culture was taken, intravenous ceftriaxone (75 mg/kg/day) was initiated. Heterogeneous appearance on the left quadriceps muscle group was detected sonographically. And also pathologic signal change, contrast enhancement and myositis of left quadriceps muscle group were identified by magnetic resonance imaging. The blood culture was positive for *S. pneumoniae*.The pneumococcal serotype was typed as *S. pneumoniae* serotype-5 according to PCR assay. Fever resolved and limitation of abduction of the hip joint gradually improved at follow-up. Control sonographic findings and physical examination were completely normal at the end of first month of follow-up.

Herein, we present an infant with pyomyositis due to S. pneumoniae serotype 5. PM should be considered in the differential diagnosis of pain and restriction in movement of the hip joint in a child with toxic appearance. Moreover, PM should be kept in mind especially if a child with pneumococcal bacteremia has pain and limitation of hip joint on physical examination and patient should be evaluated with imaging techniques immediately.

ESPID-0195
Unallocated Posters

ECONOMIC CRISIS AND VACCINATION COVERAGE IN UNFUNDED VACCINES (ROTAVIRUS-PNEUMOCOCCAL). VALENCIAN COMMUNITY. YEARS 2008-2014

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Background and aim

Rotavirus (Ro) and pnemococcal vaccines (Pn) are not funded in children vaccination programme of Valencian Community (VC), saving for risk groups for Pn. These vaccines are recommended by pediatricians, and parents can acquire them without public funding. Economic crisis from 2011 could have an impact on vaccination coverage. The aim was to determine trends in unfunded childhood vaccines coverage rate (rotavirus and pneumococcal) in Valencian Community from 2008 to 2014.

Methods

A retrospective descriptive analysis of Ro and Pn vaccination coverage from 2008 to 2014 was done.

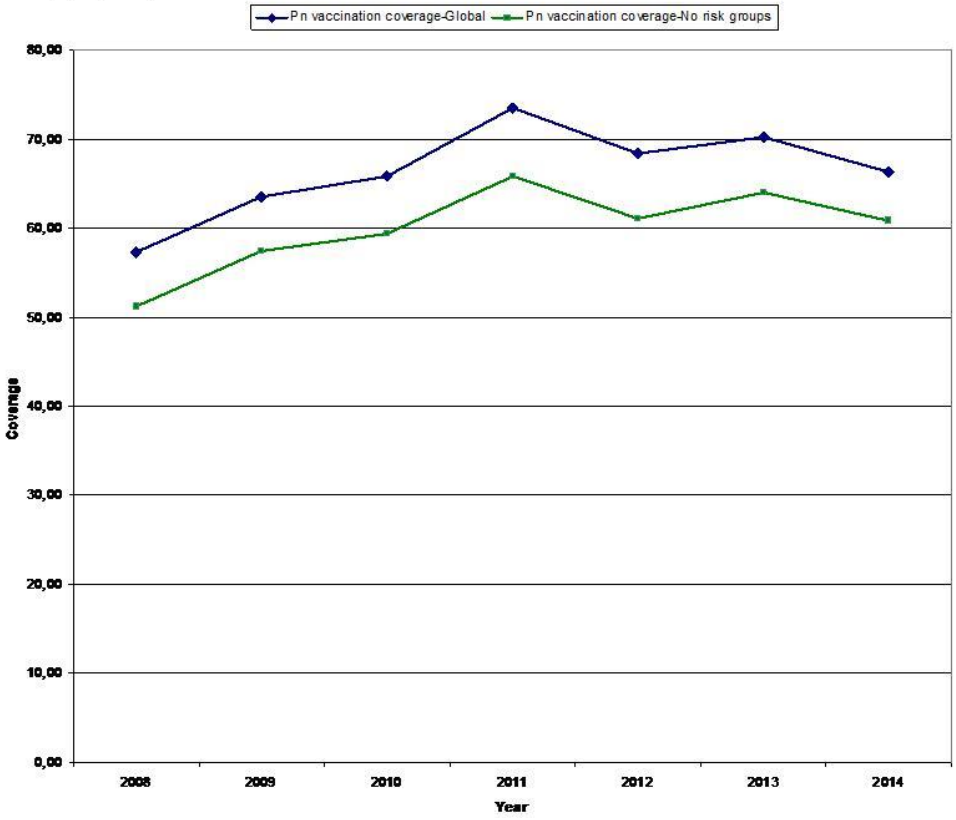
Vaccination data were obtained from Vaccination Immunization System (SIV) of VC. Age-specific coverage was obtained according demographic data from Population Information System (SIP).

Results

239,287 Pn vaccine doses were administered in children aged 1-2 years during the study period. The highest coverage was registered in 2011 (73.53% for children in

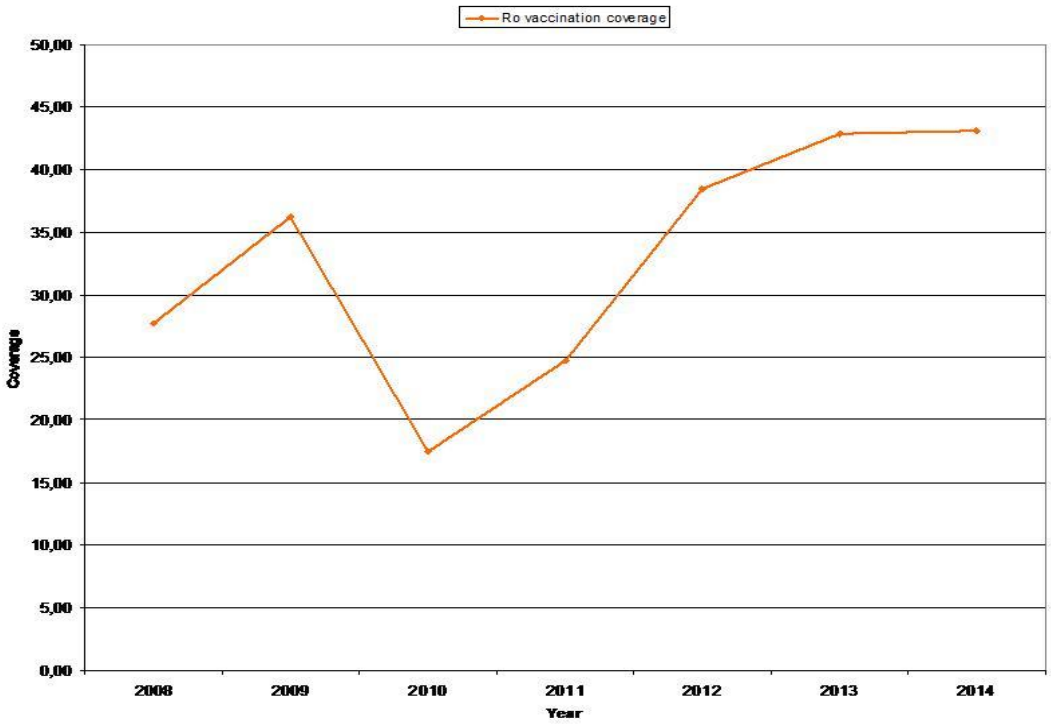
risk and non risk).Figure 1.

Figure 1. Trends in pneumococcal vaccination coverage (global and no risk groups) in Valencian Community (Spain). 2008-2014



345,768 doses of Ro vaccine were administered. The highest coverage of Ro vaccine in children aged less than 1 year was registered in 2014 (43.14%). Figure 2.

Figure 2. Trends in rotavirus vaccination coverage. Valencian Community (Spain). 2008-2014



Conclusions

According to the results, economic crisis has not highly affected vaccination coverage of unfunded vaccines, only a slight decrease of Pn vaccine coverage was observed from 2011 in children aged 1-2 years. Nevertheless, specific situations such us the vaccine shortage of the rotavirus vaccine have produce a decrease of the coverage in 2010 and 2011.

ESPID-0516
Unallocated Posters

ANALYSIS OF VACCINATION STATUS IN CHILDREN UNDER TWO YEARS OLD, HOSPITALIZED FOR PNEUMONIA FROM 2008 TO 2012 IN VALENCIAN COMMUNITY

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Background and aim

The replacement of the 7-valent pneumococcal conjugate vaccine (PCV7) by the 13-valent (PCV13) has led to improved protection against pneumococcal infection. The aim of the study was to analyze antipneumococcical vaccination status in children aged less than 2 years hospitalized for pneumonia (PnH).

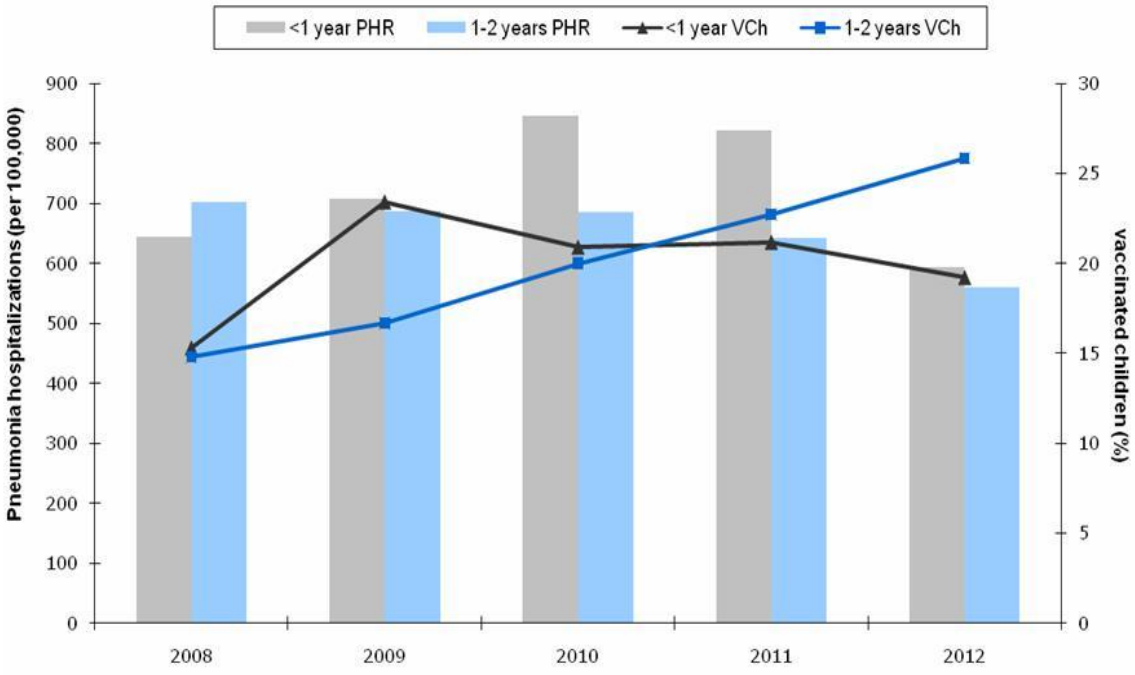
Methods

Minimal Basic Data Set (CMBD) from 2008 through 2012 was used to estimate the annual number of PnH (codes ICD-9-CM 480-486) among children aged <2 year. Annual age-specific hospitalization rates were obtained according demographic data from Population Information System (SIP). Databases of Vaccine Information System (SIV) and CMBD have been contrasted in order to find the percentage of vaccinated with different types of antipneumococcical vaccines between patients hospitalized for pneumonia of less than two years old, and compare it with the population vaccination coverage of these age groups.

Results

Analyzing the overall period of study, 19.6 % of hospitalizations of children under one year were given 3 doses of pneumococcal vaccine and 25.6 % of those 1-2 years 4 doses (Figure 1). From 2008 to 2010, approximately 95 % of vaccinated children had administered the PCV7.

Figure 1. Pneumonia Hospitalizations Rate (PHR) between children younger 1 year and children from 1 to 2 years old with standard antipneumococcical vaccination scheme (VCh)



Conclusions

From the year 2011, there is a direct relationship between the decrease in the rate of hospitalization for pneumonia and increased use of PCV13 and we have also observed a trend toward reduction hospitalizations in line with raised vaccination coverage during these last years.

ESPID-0519
Unallocated Posters

SURVEILLANCE OF ADVERSE EVENTS FOLLOWING HUMAN PAPILLOMAVIRUS IMMUNIZATION. VALENCIAN COMMUNITY (SPAIN). 2008-2014

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Background and aim

Improved knowledge of adverse events following vaccination, whether or not causal related to it, allows healthcare workers and parents to have correct information and expectations and thus helps avoid such potentialities as vaccine refusal. The human papillomavirus vaccine (HPV) was introduced into the immunization schedule of Valencian Community for girls aged 14 years in 2008. The aim of the study was to analyze adverse events following immunization (AEFI) related with the human HPV reported to the Vaccination Information System (SIV).

Methods

A retrospective descriptive analysis of the AEFI related with HPV vaccine reported by healthcare workers to the SIV of Valencian Community from 2008 to 2014 was done.

The SIV is the computerized nominal registry of immunizations of Valencian Community. Immunizations data were used to calculate the reporting rate (per 100,000 doses administered).

Study variables: age, vaccine, type of reaction and system organ class (according to MedDRA terminology).

Results

388,644 doses of HPV administered vaccines and 247 AEFI reports were registered in SIV during the study period (reporting rate 63.55 per 100,000; 95%CI: 55.63-71.48). By age group, 240 AEFI reports correspond to girls aged less than 16 years.

The most frequent reported reactions were dizziness (57; 14.67 per 100,000) and headache (58; 14.92 per 100,000).

Conclusions

Adverse events related with HPV vaccine and reported in SIV mostly coincide with the summary of product characteristics of vaccines. Reporting rates do not show an increase of the expected reactogenicity according to previous data.

ESPID-0709
Unallocated Posters

INCIDENCE OF COMMUNITY-ACQUIRED PNEUMONIA AMONG CHILDREN AGED LESS THAN 15 YEARS IN PRIMARY CARE. VALENCIAN COMMUNITY (SPAIN). 2008-2012

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Background and aim

Acute respiratory infections are an important cause of consultations in primary care and hospitals. Most published epidemiological studies have analyzed pneumonia in hospitals and very few include information on primary care, so the aim of this work will focus on the study of pneumonia episodes treated in primary care centers of Valencian Community.

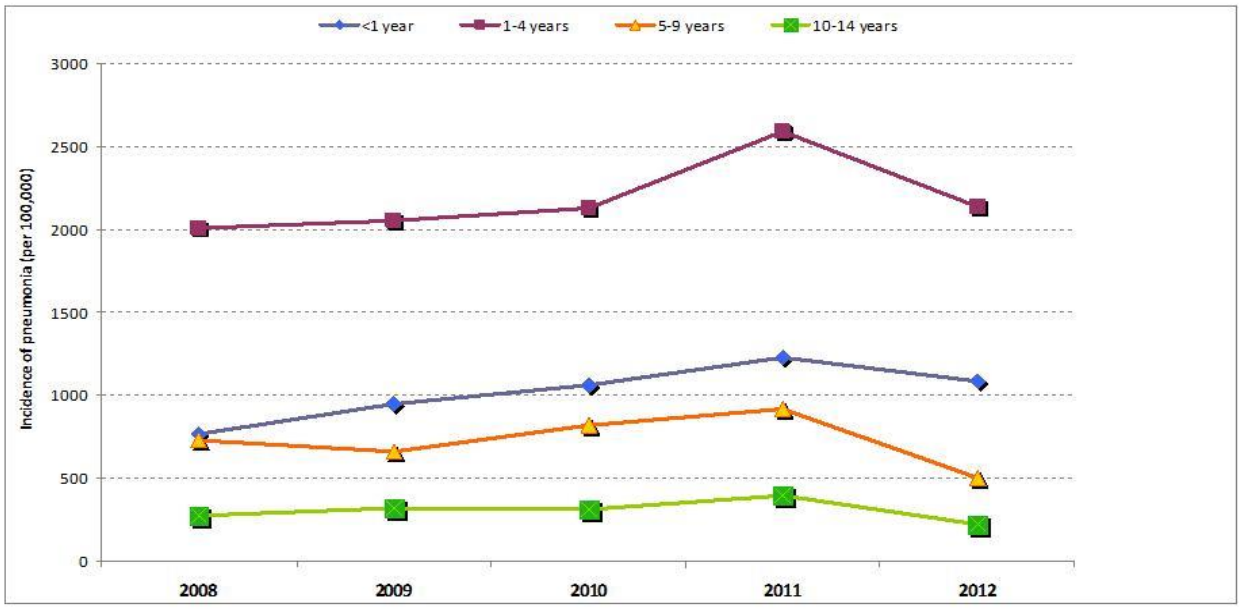
Methods

Data from Ambulatory System Information (SIA), Vaccine Information System (SIV) and Population Information System (SIP) were used to compare the incidence clinical diagnosis of pneumonia (codes ICD-9-CM 480-486) and vaccination status at pediatric consultations among children under 15 years from 2008 to 2012.

Results

The incidence of community-acquired pneumonia SIA recorded in pediatric patients experienced a steady increase from 2008-2011, reaching figures of 124 episodes/10^5children, decreasing significantly in the year 2012 to 896 episodes/10^5. 53% cases were male and the group aged 1-4 years had the highest incidence throughout the study period (Figure 1). Only 21.4 % of the patients under 1 year were vaccinated properly with the standard three-dose regimen [70.2% with heptavalent pneumococcal conjugate vaccine (PCV7) and 25.1% with PCV13]. Children from 1 to 2 years old were vaccinated correctly with 4 dose in 53.7% of cases (92.5% PCV7 and 5.5% PCV13).

Figure 1. Incidence of pneumonia episodes registered in SIA by age group (children <15 years)



Conclusions

The greatest incidence of pneumonia observed in 2011 and throughout the study period in children 1-4 years is probably related to a change in pneumococcal serotypes or a problem in coding of the disease and the higher prevalence of vaccination with PCV7 in that age group respectively.

ESPID-0226
Unallocated Posters

COMPARISON OF TUBERCULOSIS SKIN TEST AND QUANTIFERON®-TB GOLD IN-TUBE ASSAY FOR DIAGNOSTIC WORKUP OF CHILDHOOD PULMONARY TUBERCULOSIS.

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Background: The tuberculin skin test (TST) has been in use as a screening tool for TB for more than half a century. However, there is increasing evidence that indicate better specificity of interferon-gamma release assays (IGRA) compared to TST.

Objective: To compare performance of TST and QuantiFERON-TB gold in tube assay for the diagnosis of active TB in children.

Methods: A cross-sectional study was conducted in 281 TB suspected children at Tikur Anbesa Specialized Hospital. All study participants were investigated for TST, QuantiFERON®-TB Gold In-Tube Assay (QFT-GIT), HIV and bacteriological examination of gastric aspirate or sputum specimens.

Result: The overall TST and QFT-GIT positivity was 28.1% (79/281) and 24.6% (69/281). The sensitivity of TST and QFT-GIT against culture as gold standard was found 70 % and 60.3 % respectively. The specificity of TST and QFT-GIT was found 76.9% and 80% respectively. The concordance of the two tests was found 83.3%. Patient contact history with known TB cases, low weight for age, and culture or AFB positivity were found highly associated with both TST and QFT-GIT ($p < 0.01$).

Conclusion: There is no statistically significant difference between tuberculin skin test and QFT-GIT for detection of active pulmonary tuberculosis in children.

ESPID-0383
Unallocated Posters

TUBERCULOSIS IN ADOLESCENTS:CLINICAL AND EPIDEMIOLOGICAL FEATURES BETWEEN 2009 AND 2013 IN HOSPITAL II RAMON CASTILLA . LIMA-PERU

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Background and aims: Tuberculosis is a prevalent disease in Peru, the hospital II Ramon Castilla, is located in Lima-Cercado, Perú. the pediatrics service care for children and adolescents up to 17 years old., belong to a low social economical class. The aim is to discuss tuberculosis clinical presentation and epidemiological features in adolescents .
Methods: A retrospective, analytical and descriptive study of tuberculosis in adolesccents was perfomed in Hospital II ramon Castilla, betwen 2009 and 2013. All of the cases of tuberculosis diagnosed in adolescents
were included.
Results: Of the 60 adolescents reported betwen 10 and 17 years old , the highest number of cases was reported in 2009,. most of them boys (59.02%), the clinical presentations were : 80% of pulmonary TB and 20% extrapulmonare TB, most of them girls . Only 57% of the total cases were positibive TB the diagnois was established on clinical grounds, imaging diagnostics and BK results. 31 % of cases had some degree of malnutrtition in the initial diagnosis . The early symptomatology was respiratory. 11.5 % cases had hemoptysis.
Co-morbidities associated were Asthma Bronchial, Bronchopenumonia, Supurative Otitits Media.
Two patients abandoned the treatment in this period of time.
Conclusions: The pulmonary tuberculosis in adolsecent is prevailing
the diagnosis is base on clinical grounds and imagine diagnostics
the tubercolosis bacillus (BK) was positive in only 50% of the cases.

ESPID-0301
Unallocated Posters

ELEVATED TROPONIN I LEVELS IN INFANTS WITH ACUTE GASTROENTERITIS: IS IT ISCHEMIA OR ROTA ASSOCIATED CARDITIS

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background and aim.

Reports suggested that rotavirus could be found in extra-intestinal tissues including the heart following infection and fatal rotavirus myocarditis has been recently reported in 2 children.

We hypothesized that rotavirus may have a direct injurious effect on the myocardium of infants and this injury can be detected by the presence of cardiac troponin I(TnI).

Methods: Over 8 weeks period,50 of 150 infants(5-18 months) with acute gastroenteritis were found to have human rotavirus (HRV) gastroenteritis with rotavirus antigenemia. Sera of 150 infants were analyzed for TnI. If TnI value was above the screening limit (0.05 ng/ml), electrocardiogram (ECG) and cardiac ultrasound were performed.

Infants with primary conditions associated with elevated TnI were excluded.

Results: Thirty four infants (22.6%) had elevated TnI (0.06-2.5 ng/ml), 16 (47%) of them had HRV- GE (p=0.054). However, none of them had any sign of myocarditis or ischemia in their ECG or cardiac ultrasound scan and their TnI levels normalized within 24-72h after correction of dehydration.

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. Infants less than 1 year ,and those with dehydration, anemia or acidosis were more prone to have elevated cTnI(p=0.008,0.009,0.006,0.001 respectively).Multivariate logistic regression analysis, showed that severe dehydration and acidosis are still significantly associated with elevated TnI levels (adjusted OR, 95%CI= 22.9, 2.19-239 and 20.76, 6.15-70 respectively.

Conclusion: Our study is the first pediatric study to show that myocardial injury occurs in infants with gastroenteritis and this injury was precipitated by transient ischemia which may go unnoticed on the ECG. However, we could not document rotavirus myocarditis

ESPID-0062
Unallocated Posters

PROGNOSIS OF COMMUNITY ACQUIRED ACUTE BACTERIAL MENINGITIS IN CHILDREN

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Background:

Bacterial meningitis in children is still a life-threatening illness. It is an important cause of morbidity and mortality throughout the world.

Aim:

To identify prognostic factors in children with community-acquired acute bacterial meningitis.

Methods:

We conducted a retrospective study over a 10 year period [2002-2012]. All children aged between 1 month and 15 years with bacterial meningitis were included. Unfavorable outcome was defined by the occurrence of acute complications or sequelae. Prognostic factors were identified through logistic-regression analysis.

Results:

Mean age was 3.8 years. Sex ratio was 1.66. The clinical presentation was dominated by gastrointestinal symptoms in infants and neurological symptoms in children.

The CSF study identified the micro-organism in 15 cases. Culture was positive in 8 cases (11.1%). The pneumococcus was the most common micro-organism (9 cases).

The outcome was unfavorable in 24 cases (33.3%). Acute complications occurred in 17 cases (23.6%) dominated by seizures (11.1%) and brain empyema (6.9%). Subsequent sequelae were noted in 16 cases (22.2%). Mortality rate was 1.4%

Predictors of unfavorable outcome were: age < 42 months ($p = 0.033$), pneumococcus ($p = 0.05$), impaired general condition ($p = 0.05$) and presence of abnormalities at initial imaging ($p = 0.041$).

Conclusion:

Unfavorable outcome of bacterial meningitis remains high especially in children with pneumococcal meningitis. Therefore, the introduction of pneumococcal vaccination in the Tunisian immunization schedule must be a national priority.

ESPID-0068
Unallocated Posters

AN AUDIT OF DENGUE FEVER CASES IN THE YEAR 2012-2014 AT CIVIL HOSPITAL KARACHI-PAKISTAN

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Background: Dengue virus is endemic in Pakistan, and occurs throughout the year, but with often with peaks in certain seasons. Dengue virus remains a major cause of morbidity and mortality**.**
Methods: Patients suffering from high grade fever visiting Medical and Paediatrics outpatient departments as well as indoor patients of Civil Hospital, Karachi, Pakistan, in the year 2011-2013 (from Jan.to Dec.) were taken. Patients were initially screened for platelet count and test for Dengue fever. Blood was collected aseptically and CBC (Platelet count) was done on Sysmex Haematology autoanalyser and test for Dengue antibodies IgM and IgG was done by Rapid Immunochromatography and ELISA technique.
Results: Total 2321 patients were screened for Dengue fever, out of these 585 were reported positive for Dengue fever i-e 25.2%. 384 were males while 201 were females. Dengue Antibodies IgM and IgG (ICT) was done on 1118 samples, 585 were positive for IgM alone or both for IgM and IgG. i-e 26.39% Dengue Antibodies IgM and IgG (ELISA) was done on 260 samples 87 were positive for IgM (33%) and 28 were positive for IgG alone (10.77%). However, Dengue Antigen was done on 943 samples, 175 samples were reported positive for Dengue Antigen (18.5%).The result analysis indicated that the age group most affected was 20-40 years. Male /female ratio was found 2:1.Besides this,90% patients had low platelet count i-e less than 100,000/cumm, 10% had normal or near normal platelet count most of them showed decrease in platelet count later on.

ESPID-0069
Unallocated Posters

AN AUDIT OF MICROBIOLOGICAL ANALYSIS AND ANTIMICROBIAL RESISTANCE OF GHARO WATER SAMPLES (KARACHI-PAKISTAN) IN WINTER SEASON 2013

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Introduction: Gharo is a city in Thatta District, Sindh. The scarcity of water is a main issue of the inhabitants of this area as just rely upon limited water supply harboring predominantly with water borne diseases as well as gastro and diarrhoea.

Material and Methods: In this study, a team of SCRC visited and collected around 60 drinking water samples (1 Litre) from various spots of Gharo and immediately transported to IIDRL-KU. Microbiologically, all the samples were analyzed by Membrane Filtration Technique (MFT) on different selective and differential microbiological media. All these potential pathogens were identified by conventional and rapid (QTS 10) methods. Antibiotic susceptibility was determined by Kirby Bauer disc diffusion method and Minimum Inhibitory Concentration (MIC) was also determined by Micro dilution method.

Results: Almost all the samples tested were found positive for potential gram-negative particularly enteric microorganisms including *Escherichia. Coli (60%), Enterobacter aerogenes (40%), Proteus vulgaris (10%), Pseudomonas aeruginosa (28%), Shigella dysenteriae(25%), Salmonella typhi(20%), and Aeromonas hydrophila (2%)* and gram- positive include *Staph. aureus (35%), Staph.epidermidis (30%*). Moreover, a very high resistance pattern was observed against a panel of a dozen of antibiotics like Cephalexin (80%), Erythromycin and Tetracycline (48%), Ampicillin(66%), Novobiocin(70%) Doxycycline(99%), Amoxicillin(41%), Ceftrizoxime (95%), Chloramphenicol (40%) , Gentamicin (60%), Ofloxacin (30%) and Ciprofloxacin(20%).

Conclusion: Presence of *E.coli* in water as well as other serious pathogens is a strong indication of sewage or animal waste contamination, which may cause many a wide range of disease and entirely unfit for human consumption.

ESPID-0588
Unallocated Posters

BACTERIAL CONTAMINATION OF NEWBORN AND PREMATURE INFANTS IN NICU

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AIM: to determine species composition and antibiotics sensitivity of coagulase-negative staphylococci (CoNS) taken from newborn and preterm infants.

MATERIAL AND METHODS: within 2 years 450 CoNS strains taken from different biomaterials of infant in NICU were studied. Staphylococcus type determination was made with MALDI-TOF mass spectrometry at the Microflex analyser made by the Bruker Daltonics. Antibiotics sensitivity was determined with diffusion test in the Muller-Hinton broth using disks (BioRad) and the Vitek2 analyser. Methicillin-resistance of staphylococci (MRS) was made with the cefoxitin disk (BioRad).

RESULTS: 2 types of staphylococci – Staphylococcus haemolyticus, 48,3% and Staphylococcus epidermidis, 46,0% - were in the lead among 450 studied coagulase-negative staphylococci strains, Staphylococcus hominis and Staphylococcus warneri were found much rarer. Antibiotics sensitivity comparative results of 2 types of CoNS showed that MRS was found most of all among Staphylococci haemolyticus – 95,0%, for example, among Staphylococci epidermidis the number was only 70,3%. Frequency of gentamicin-sensitive strains was 44,4% in Staphylococci epidermidis and 0,0% in Staphylococci haemolyticus. All types of CoNS had high sensitivity level for netilmicin: 86,8% in Staphylococci haemolyticus, 93,1% in Staphylococci epidermidis, and for lincomycin – 94,7%, 93,3%, respectively. 97,1% of Staphylococci epidermidis strains and all strains of Staphylococci haemolyticus. Frequency of piperacillin/ tazobactam-sensitive strains was 12,4% in Staphylococci haemolyticus, 47,2% in Staphylococci epidermidis. All strains were sensitive to vancomycin and linezolid. To penicillin were sensitive 0,7%, 3,0% of strains respectively.

CONCLUSIONS: comparison study results of different types of CoNS sensitivity showed that the highest MRS frequency was noticed in Staphylococci haemolyticus.

ESPID-0042
Unallocated Posters

ASSESSMENT OF IMMUNO-VIROLOGICAL RESPONSE TO ART IN CHILDREN LESS THAN 15 YEARS OF AGE IN ADAMA REFERRAL HOSPITAL, ADAMA TOWN, OROMIA REGIONAL STATE, ETHIOPIA

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Background: WHO clinico-immunological approaches for initiation and monitoring of ART in Sub-Saharan Africa lacks viral load Determination and drug resistance monitoring, HIV infected children may be at risk for "unrecognized" virologic failure and the subsequent development of antiretroviral drug resistance.

Aims: To evaluate virological efficacy and immunological recovery of HIV/AIDS pediatric patients less than 15 years of Age on ART.

Methods: a cross- sectional study was conducted on Pediatrics patients taking ART at Adama hospital during February 2011and September 2013

Result: total of 100 children age <15 years of age who started ART during February2011 and October 2013 E.C were analyzed. Female were 50% with mean age at the start of ART 87.79± 41.35 months and median duration on ART was 21.24 months (SD=10.860).

The mean CD4+T cell countwas521.04cells/mm3 (SD=311.118), 698.84cells/mm3 (SD=400.545), 851.94 cells/mm3 (SD=576.808), 872.13cells/mm3 (SD=637.627) at 6 months, 12 months , 24 months and 36 months after initiation of ART respectively

Virological failure (HIV RNA >=1000 copies) was found in 24% of patients. Virological treatment failure (HIV RNA copies>= 1000 copies) was commonly found on 18 males

Significant association was observed between virological treatment failure and duration of months on antiretroviral treatment (p-value=0.028)

Conclusion: Having adherence level <95% & longer duration on ART was found to be the independent risk factors for virological treatment failure. Virological treatment failure was seen in clinically stable patients.

Based on above data inclusion of routine virological monitoring is the most important follow up parameter for patients on ART to detect early treatment failure.

ESPID-0508
Unallocated Posters

VISUAL FUNCTION STUDY IN A COHORT OF CHILDREN TREATED WITH ETHAMBUTOL FOR MYCOBACTERIAL INFECTION

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Background

Ethambutol (EMB) is a bacteriostatic agent usuallyprescribed of mycobacterial infections (tuberculosis and mycobacterial avium complex, MAC) The most serious side effect potentiallyrelated to EMB is retrobulbar optic neuritis (dose-dependent and reversibleafter treatment withdrawn). The aim of this study is to report the absence of visualimpairment in children exposed to EMB

Patients and Methods

Between June 2009 and September 2014, thirteen children(4 males) were admitted at our centre for a MAC infection of laterocervicallymph nodes (median age at diagnosis 5.75 years). All the children received EMB(dose 15 mg/kg/die) for 2 months (6 mos in one case) as a part of their first-linemultidrug therapy (including rifampin and claritromycin). All pts. weresubmitted to visual monitoring with twoscheduled assessment (before and short time after EMB treatment). Visual assessment encompassed ophtalmological clinical examination andvisual functional tests. 6 children weremonitored using red-green colour perception test (R/G CPt) and 7 with visualevoked potentials (VEPs).

Results

None of our patients had clinicalmanifestations of impaired visual function. Two of the 6 patients monitored with(R/G CPt) showedwere tritanopia at pretreatment assessment. Only 2 of the 7patients (28%) who had been monitored with VEPs testing showed minimal and notpathologic electrophysiological changes after EMB discontinuation (decreasedpeak time and higher latency).

Conclusions

Strict visual monitoring is mandatory inchildren treated with EMB, but our data prove the absence of side effect withcorrect ETB doses and low duration of treatment.

ESPID-0474
Unallocated Posters

THE FSBSI «SCIENTIFIC CENTRE OF CHILDREN HEALTH»: FIGHT AGAINST UNFOUNDED MEDICAL EXEMPTION FROM IMMUNIZATION

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Currently, vaccination is the field of medicine, which is being around a lot of discussion. If you ask a specialist (infectious disease doctor, epidemiologist), whether vaccination is needed, we will hear - this is the only thing safe and effective means by which to protect people from infections and is a major medical advance, to extend the life of a man for decades. Unfortunately, the analysis of the current situation, we have to admit that around this universal preventive technology, which is a vaccination, there are still many myths to debunk that should be progressive medical community. In the department of vaccinal children with disabilities in health of the Federal State Budgetary Scientific Institution "Scientific Centre of Children Health" for 2014 was consulted more than 7,000 children with different pathologies and conducted more than 10,000 vaccinations. The structure of somatic pathology was as follows: 36% of children with perinatal lesions of the central nervous system, 29% of children weighed down with allergic history (atopic dermatitis, food allergies, asthma, hay fever, and others.), 9% of disease in early childhood, as well as children with congenital malformations, diseases of upper respiratory tract, kidneys and others. Vaccination is usually held combined vaccines against infections included in the national immunization schedule. Based on the study of post-vaccination adverse reactions in children with the above deviations in health status, as well as estimates of the underlying and related diseases, it was found that vaccination tolerability comparable to that in healthy children.

ESPID-0657
Unallocated Posters

DIFFERENT SITE OF ACTION OF CLOSTRIDIUM DIFFICILE TOXIN B ON CHLORIDE SECRETION AND EPITHELIAL DAMAGE IN INTESTINAL EPITHELIAL CELLS.

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Background and aim: Clostridium difficile (CD) is the leading cause of severe diarrhea and exacerbations in subjects with IBD. Toxin A (CdtA) and B (CdtB) are the major virulence factors but the specific role in inducing diarrhea is unclear. CdtA is thought to be required for CdtB entry into the cell, but recently this association was challenged. The aim of this study is to evaluate CdtB effect on chloride secretion (enterotoxic mechanism) and epithelial damage (cytotoxic mechanism) in an *in-vitro* model of diarrhea.

Methods: To test the hypothesis that CdtB induced an enterotoxic effect, Caco-2 cell monolayers were exposed to the CdtB at different doses for 1 hour and the short circuit current (Isc) was measured in Ussing Chambers. The cytotoxic effect induced was evaluated by transepithelial resistence (TEER).

Results: CdtB induced a dose-dependent increase in Isc with a maximal effect at 10ng/ml (ΔIsc= +6,2±3,7 vs 1,1±1,3; $p<.05$) indicating a direct effect on chloride secretion. The Isc increase was observed upon apical but not basolateral side of Caco-2 monolayers. In addition, CdtB induced a significant decrease in TEER measurements at 48hrs (-78,3% vs control, $p<.05$) at basolateral but not apical side.

Conclusion: CdtB induces both an enterotoxic and cytotoxic effect in intestinal epithelial cells depending on the basolateral or apical side of the enterocyte. These findings suggest that the CdtB alone possesses a peculiar highly effective mechanism which may be responsible for the severity of diarrhea particularly in children with altered intestinal permeability such as those with IBD.

ESPID-0542
Unallocated Posters

MOLECULAR CHARACTERIZATION AND CLINICAL SIGNIFICANCE OF EXTRAINTESTINAL PATHOGENIC ESCHERICHIA COLI RECOVERED FROM A SOUTH INDIAN TERTIARY CARE HOSPITAL

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Background and aims: Infection with extraintestinal pathogenic *Escherichia coli* (ExPEC) is an important public health problem.Aims of our study were to molecular characterization of pathogenic *E. coli* causing extraintestinal infections and to correlate findings with clinical outcome of patients.

Methods: The descriptive study was conducted on 300 in-patients with ExPEC infection. Phylogenetic analysis (*chuA, yjaA* and *TSPE4.C2)* , virulence (*fimH, hlyA, papC, cnf1, iutA, neuC*) and drug resistance (ESBL: *TEM,SHV,CTXM,CTXM-15* ; plasmid mediated ampC ; MBL : *NDM-1*) genes were determined by multiplex PCR. Patient's follow up were done for up to 1 year.

Results: Of 300 patients with ExPEC infection, 10% expired,18% had relapses and 72% recovered. Phylogenetic analysis revealed 61 isolates belonged to phylogroup A, B1 (27), B2 (104) and D (108). Among virulence genes, percentage strains carrying *fimH* was 90%, followed by *iutA*(68%), *papC*(45%), *hlyA*(23%), *cnf* (23%) and *neuC*(5%) respectively. Among drug resistance genes, 70% possessed ESBL genes, 12% *CIT* -AmpC & 5% carried bla_{NDM1}.There was a significant negative association between *hlyA* and *cnf1* genes with ESBL negative isolates.pAmpC and NDM1 positive isolates were carrying less virulence genes when compared to negative isolates.

Conclusion: Results indicate there is an inverse relationship between resistance and virulence with reference to ExPEC causing extraintestinal infections.In correlation between outcome of infection with possession of virulence and drug resistance genes we found that *papC, cnf1, neuC* and *hlyA* play an important role in recurrent infections. We also observed virulence of infecting strain, as well as patient related factors are equally responsible for development and outcome of infections.

ESPID-0872
Unallocated Posters

PROFILE OF CHILDHOOD TUBERCULOSIS (TB) IN A PAEDIATRIC TERTIARY CARE CENTRE IN INDIA

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AIM:

India has the highest tuberculosis burden but has very few studies on TB in children. This study aims at description of childhood TB with respect to types, clinical presentation, investigations and culture positivity in an Indian paediatric setting.

METHODS:

Clinical and laboratory data of 46 children in the age group of 0 – 18 yrs diagnosed to have TB according to the WHO guidelines were prospectively included during the study period October 2012 to November 2013. Main diagnostic tools included tuberculin skin test, chest X-ray, sputum/gastric aspirate culture with sensitivity testing, and direct microscopy for acid-fast bacilli on available samples. Clinical characteristics and outcomes of the patients were examined.

RESULTS:

Out of 40 children, 16 (34.8%) were diagnosed with pulmonary TB and 30 (65.2%) with extrapulmonary TB. Neurological TB constituted 15/30 (50%) of the extrapulmonary TB. 26 children had a positive BCG vaccine scar (65.2%) and 22/46 (47.8%) had a positive tuberculin skin test. An adult TB contact was identified in 10 (21.7%) cases. On direct microscopy, acid-fast bacilli were found in 11 (23.9%) patients. Specimens – gastric juice (3), bronchoaleolar lavage fluid(6) ,lymph node(1),pus(1).Positive culture for *Mycobacterium tuberculosis* was found in 7 (15.2%).CXR was abnormal in 93.7%(15/16) children with pulmonary TB but only 13.3%(4/30) in extrapulmonary TB . One patient with disseminated TB with underlying immunodeficiency died during follow-up.

CONCLUSIONS:

Extrapulmonary TB was the commonest form at our centre with neurological TB constituting the majority. Bronchoalveolar lavage contributed to increasing the smear positivity rates in our study.

ESPID-0631
Unallocated Posters

EXTENDED SPECTRUM BETA LACTAMASE(ESBL)-PRODUCING BACTERIA CAUSING COMMUNITY-ACQUIRED URINARY TRACT INFECTIONS(CA-UTI) IN AN INDIAN SETTING

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Background & Aim: The incidence of ESBL UTI even from the community is on the rise. The aim of this study was to assess the frequency of and identify risk factors for CA-UTIs due to ESBL-producing microorganisms in an Indian setting.

Materials and Methods:

Retrospective case control study in a paediatric tertiary care centre from May 2013 to April 2014. 100 cases of CA-UTI (Age 1 month to 12 years) due to Gram negative organisms were included and predictive factors for ESBL were analysed (age < 1 year, uroprophylaxis, hospitalization within 3 months, recent antibiotic usage, clean intermittent catheterisation, structural renal anomalies and recurrent UTI). Antibiogram and clinical response to antibiotics including cephalosporins were studied.

Results:

Out of 100 gram-negative isolates, 80 were Escherichia Coli and 12 were Klebsiella pneumonia, 2 each of Pseudomonas aeroginosa, Klebsiella oxytoca, Proteus mirabilis & 1 each of Morganella morgani, and Citrobacter. 40 urinary isolates were ESBL producers; of which 46% were E.Coli and 25% were Klebsiella.

Though resistance to ceftriaxone & cefotaxime was seen in 68%, 13 (33%) in the ESBL group recovered with cephalosporins.

There was no statistically significant difference in risk factors for ESBL vs Non ESBL Groups.

Conclusion:

1.This study showed 40% of urinary isolates were ESBL producers with high in vitro resistance to ceftriaxone although one-third (33%) responded to it.

Therefore treatment with ceftriaxone for acute pyelonephritis (even if ESBL) in children is acceptable if there is good clinical response.

2.There was no risk factor that could predict ESBL producers

ESPID-0734
Unallocated Posters

A STUDY OF THE ANTIBIOGRAM OF SALMONELLA TYPHI IN AN INDIAN SETTING WITH THE EFFECTIVENESS OF AZITHROMYCIN IN ENTERIC FEVER

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Background: Typhoid fever has a high mortality rate of 30% which is reduced to 0.5% with treatment. Multidrug resistant (MDR) strains including nalidixic acid resistant strains (NARS) is on the rise in India, limiting treatment options.

AIM:

1. To determine current antimicrobial susceptibility pattern of Salmonella typhi in blood culture in Indian setting

2. To determine MIC values of azithromycin against Salmonella

3. To assess the clinical efficacy of azithromycin compared to cephalosporins

Materials & Methods:

Prospective analytical study from August 2013 to April 2014 in a pediatric tertiary care hospital in Chennai, India. Clinical details of 40 children one month to 18 years of age with confirmed enteric fever collected. Antibiotic susceptibility testing and azithromycin MIC of Salmonella typhi determined. Children treated with oral Azithromycin (20mg/kg/day) for 7 days or intravenous ceftriaxone (100 mg/kg/day), and followed up for relapse. Out of 40 children, 26 received azithromycin and 14 received ceftriaxone.

Results:

Ampicillin sensitivity 36/40(90%); ciprofloxacin sensitivity 21/40 (52.5%); ceftriaxone and azithromycin 100% sensitive. Nalidixic acid 100% resistant.

65% of the 40 isolates had azithromycin MIC <4µg/ml, 20% had MIC 6 µg/ml and 12.5% had MIC 8µg/ml. Only one (2.5%) had MIC of 12 µg/ml.

Clinical cure achieved in 96% in azithromycin group and 100% in ceftriaxone group; time to defervescence 84 hours and 96 hours respectively. There were no relapses.

Conclusion:

Azithromycin is very effective against uncomplicated typhoid fever in children with the advantage of once daily oral administration and short duration of therapy ensuring better compliance than parenteral ceftriaxone.

ESPID-0216
Unallocated Posters

COMBINATION MEASLES-MUMPS-RUBELLA-VARICELLA VACCINE IN HEALTHY CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF IMMUNOGENICITY AND SAFETY

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Background and aim A combined measles-mumps-rubella-varicella vaccine (MMRV) is expected to facilitate universal immunization against these four diseases by simplifying immunization delivery and thus enhancing compliance and coverage rates. The aim of this article is to provide current evidences studying immunogenicity and safety of MMRV in children.

Methods We searched PubMed, Embase, BIOSIS Previews, Web of Science and other databases through 9 September 2014. Study selection and data extraction were conducted in duplicate. Meta-analysis was conducted when appropriate.

Results Thirty-nine randomized clinical trials (RCTs) were included. Nineteen RCTs comparing single MMRV dose with measles-mumps-rubella combined vaccine with or without varicella vaccine (MMR/MMR+V) in healthy children aged 9-24 months. Results showed a similar immunogenicity with enhanced immune response to measles component, the geometric mean titer/concentration (GMT/GMC) ratios were 1.48 (95%CI 1.38-1.62) and 1.62 (1.51-1.70), respectively. Slight reduced immune response to rubella component, the GMT/GMC ratios were 0.81 (0.78-0.85) and 0.79 (0.76-0.83), respectively. Well-tolerated safety profiles were demonstrated except fever (relative risks ranged from 1.12 to 1.43) and measles/rubella like rash (relative risks were 1.44 and 1.45, respectively). Furthermore, MMRV was found to be immunogenic and well-tolerated when administered with several kinds of pediatric vaccines in children aged 8-24 months.

Conclusion MMRV was generally well tolerated and had comparable immunogenicity and overall safety profiles to MMR or MMR+V in healthy children based on the current evidences.

ESPID-0113
Unallocated Posters

APPROPRIATENESS OF ANTIBIOTIC PRESCRIPTIONS IN A PAEDIATRIC POPULATION AT AN EMERGENCY DEPARTMENT.

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Introduction: Antibiotics represent one of the most widely prescribed therapeutic agents in children. It has been estimated that 30-50% of antibiotic prescriptions for this population are inadequate. In this scenario, analysis of prescription data provides an invaluable source of information as a basis for implementing strategies for improvement in this field.

Objective: To assess the appropriateness of antibiotic prescriptions in a pediatric population at an Emergency Department(ED).

Methods: An observational, descriptive and cross-sectional study was conducted including patients under 14 years who attended the ED of “Hospital de la Merced” in Osuna (Sevilla) during 2013. A random sample of 630 patients was selected (confidence level 99%, accuracy 5%). To asses the adequacy of antibiotic prescriptions, the clinical practice was compared with an evidence-based guideline especially designed for this study.

Results: Antibiotics were prescribed in 104 (16,5%) patients. Antibiotic treatment was inappropriate in 54 (52,9%) patients. Unnecessary treatment was indicated in 22 cases, wrong antibiotics were chosen in 19 and the posology was incorrect in 13 of them. Most frequent diseases among the incorrectly prescribed were: acute otitis media, fever without a source, episodes of wheezing, acute pharyngotonsillitis and community-acquired pneumonia. We found a statistically significant association between the degree of appropriateness and the medical specialty, with pediatricians showing the highest adequacy levels.

Conclusion: antibiotic prescriptions seem to be inappropriate in up to half of the patients. Their use in pathologies in which there is not an indication, along with an incorrect choice of antimicrobial, are the main causes of inadequateness.

ESPID-0327
Unallocated Posters

TIGECYCLINE AND COLISTIN SALVAGE TREATMENT IN A PEDIATRIC PATIENT

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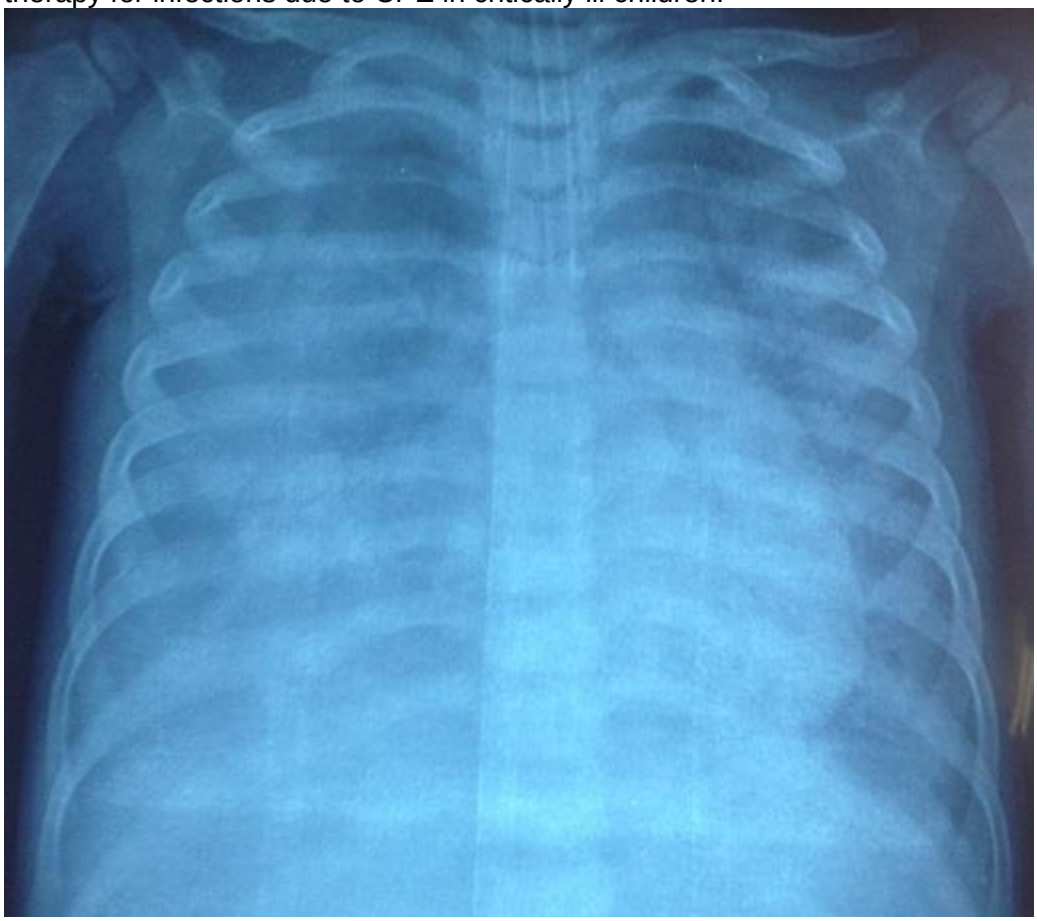
Introduction: Infections due to carbapenemase producing enterobacteriaceae (CPE) have increased in recent years. Tigecycline and colistin combination is an effective alternative treatment for CPE infections in adults. However, experience about this combination in pediatric patients is scarce.

Case report: A 3-year-old boy who had undergone bone marrow transplantation due to Thalassemia Major 10 days ago was consultated because of fever and cough. His body temperature was 38.5°C. Oropharyngeal hyperemia and central venous catheter (CVC) were present. Laboratory investigations revealed white blood cell, 1500/mm^3; absolute neutrophil count, 80/mm^3; C-reactive protein, 135 mg/dl. Chest X-ray was normal. Cefoperazone-sulbactam (80 mg/kg/d) was started. Because of persisting fever, vancomycin (40 mg/kg/d) was added on the second day. 2 days later, fever proceeded, thoracal computed tomography and serum galactomannan were normal. Antibiotic treatment was arranged as meropenem (60 g/kg/d), amikacin (15 mg/kg/d), vancomycin, and caspofungin (50 mg/m^2/dose). The folowing day, CVC was removed because of unresolved fever and carbapenemase-producing *E. coli* grew in peripheral and catheter blood cultures, sensitive to meropenem, amikacin, tigecycline, and colistin. On the tenth day, due to respiratory distress, he was intubated, tigecycline (2.4 mg/kg/d) and colistin (5 mg/kg/d) were started as salvage treatment (Figure 1). After then, fever started to subside, respiratory symptoms resolved, and control cultures were negative. Tigecycline, colistin, and concomitantly meropenem were given for 14 days with no obvious side effects, while other antibiotics were discontiuned.

Conclusions: Tigecycline and colistin combination can be used safely as salvage therapy for infections due to CPE in critically ill children.



ESPID-0697
Unallocated Posters

DETERMINANTS OF UNDER 5 YEARS CHILDHOOD DIARRHOEAL DISEASE SEVERITY IN BANGLADESH IN URBAN-RURAL DIFFERENTIALS: OBSERVATION FROM FOUR DIFFERENT DIARRHOEAL DISEASE HOSPITALS.

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Background and aim: Childhood diarrhea still contributing a lead morbidity with distinct severity. Thus, the study aimed to identify the major determinants of under-5 childhood diarrhoeal severity in urban and rural Bangladesh.

Method: Data were extracted from data archive of four diarrheal disease surveillance systems of icddr,b from 2010-2013. A total of 4,225 under-5 children in urban Dhaka, 2,068 in urban Mirpur Treatment Centre, 2,165 in rural Matlab and 3,570 in rural Mirzapur were enrolled irrespective of sex, and severity. Severity was classified as mild, moderate, and severe to very severe. Multinomial logistic regression analysis was done separately for all sites.

Results: Higher odds were found for rotavirus [adjusted OR-1.76 (95% CI-1.53-2.03); 1.57 (1.21-2.03)], *Vibrio cholerae* [1.92 (1.33-2.78); 6.59 (4.32-10.05)], wasting [1.31 (1.10- 1.55); 1.74 (1.33-2.27)], 24-59 months children [1.36 (1.08-1.72); 2.38 (1.69-3.33)], and distance traveled (≥5 miles) [1.29 (1.06-1.56); 1.46 (1.03-2.08)] in Dhaka for moderate severity and severe to very severe severity respectively. For Mirpur, it was rotavirus, *Vibrio cholerae*, and wasting. For Matlab, *Vibrio cholerae* was only associated for both moderate severity and severe to very severe severity, but, rotavirus, *Shigella* spp. and seeking care outside before coming to hospital [1.94 (1.39-2.71)] were associated for moderate severity and 24-59 months children with severe to very severe severity. For Mirzapur, all 3 pathogens are responsible for severe to very severe severity diarrhea including all other predictors.

Conclusion: Geographical diversity was observed for childhood diarrhoeal severity, though rotavirus, *Shigella* spp. and *Vibrio cholerae* are the major responsible pathogens.

ESPID-0887
Unallocated Posters

ACUTE INTERSTITIAL NEPHRITIS AS EXCLUSIVE MANIFESTATION OF HUMAN PARVOVIRUS B19 INFECTION

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Acute interstitial nephritis is a rare affection, can be the manifestation of autoimmune or infectious diseases and sometimes a side effect of medication.

We report on a 14 years old girl, who was admitted in our hospital with severe abdominal pain. She suffered since weeks from fatigue without temperature or exanthema and did take occasionally NSAIDs. At admission serum creatinine (220µmol/l) and CRP (59mg/l) were elevated, in the urine proteinuria, leukocyturia and hypoosmolarity were noticeable. We observed weight gain, oliguria and rising creatinine (max. 320µmol/l) during following two days. Increasing lumbal pain was caused by marked enlargement of both kidneys. Serum values of C3, C4, ANA, ANCA and ASL were unremarkable. Kidney biopsy revealed acute tubular damage with interstitial oedema, signs of inflammation and erythrocyte extravasates beside unaltered glomeruli.Serological tests excluded Hantavirus-Infection and Leptospirosis. Solely ParvovirusB19-DNA was identified in blood and also in renal tissue. Uveitis, exanthema or eosinophilia couldn´t be registered. Kidney function recovered without specific therapy and was unaltered after six weeks. During the past 30 months no relapse appeared.

Infections with ParvovirusB19 are reported as trigger for haematological, dermatological, cardiovascular, pulmonological, neurological, hepatobiliary and rheumatological diseases. Well known manifestation in children is erythema infectiosum. Acute glomerulonephritis due to ParvovirusB19 infection is rarely found, interstitial nephritis caused by HPVB19 infection is published only in case of immunodeficiency so fare. Here we report the association of ParvovirusB19 and interstitial nephritis in immunocompetent host for the first time.

ESPID-0177
Unallocated Posters

CHILDREN WITH CHRONIC HEALTH DISORDERS TRAVELING TO THE TROPICS: A PROSPECTIVE CASE-CONTROL STUDY IN A FRENCH INTERNATIONAL VACCINATIONS CENTER

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Background: The number of travels to the tropics for children with chronic health disorders is increasing.

Methods: All the children with chronic health disorders (CHD) who attented in the international vaccination center of Robert Debré's hospital, Paris, France, from 05/13 to 02/14 before traveling to the tropics were included in a prospective, case control study. They were paired for age with 2 healthy children and were followed for one month after their return.

Results: 56 children with CHD and 107 healthy children were included. The median age was 6 years old. 77.9% of them traveled to West Africa mainly to visit relatives. The median duration of stay was 42 days. Their age, destination and the duration were similar among the 2 groups. Sickle cell disease (41.1%), asthma (28.6%) were predominant in the group of children with CHD. The children with CHD experienced more clinical events than healthy patients ($p<0.05$). Nevertheless, there was no difference when decompensations of the chronic disease were excluded ($p=0.64$) or when only the stay abroad period was considered ($p=0.24$). One child with a recently diagnosed of hemolytic uremic syndrome atypical died of a decompensation. Compliance with pre-travel advice was insufficient, for both groups.

Conclusions: Health problems among children with CHD traveling abroad are mainly related to decompensations of the chronic disease, which mostly occur after the children return but not during the stay. Some specific diseases requiring a very specialized care in case of decompensation should lead to avoid a travel in tropical resources limited countries.

ESPID-0855
Unallocated Posters

THE IMPACT OF FALSE POSITIVE BLOOD CULTURES ON MANAGEMENT DECISION, IN TERTIARY HOSPITAL; OMAN.

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Introduction:

Blood culture is one of the major investigations done for almost all children presenting with febrile illness. Proper approach and treatment of a febrile child is considered a big challenge for a pediatrician. It's important to determine the exact organism and its sensitivity to establish the appropriate therapy.

Methods:

A retrospective analysis of all children (

Results:

344 positive blood cultures were identified in 225 patients with. 185 (54%) were classified as true-positive, and 159 (46%) as contaminant (false-positive). 49 isolates (26.5%) were *CONS* that were identified considered significant pathogens based on the patient's clinical picture, followed by *EC* 18 (9.7%). In contaminant cultures, *CONS* was 108 (67.9%) isolates, followed by Streptococcal-spp 11 (6.9%). The second group was younger in age (mean 1.4 years versus 2.6 years; *ppp* values *p* values

Conclusions:

False positive culture results generate unnecessary hospitalizations, antibiotic therapy and use of microbiologic tests. Careful disinfection, rapid microbiology diagnostic tests are needed to help differentiate true pathogens from contaminants.

ESPID-0483
Unallocated Posters

URINARY TRACT INFECTION IN OMANI CHILDREN: ETIOLOGY AND ANTIMICROBIAL RESISTANCE. A COMPARISON BETWEEN FIRST EPISODE AND RECURRENT INFECTION.

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Background & Aims:

Urinary tract infection (UTI) is common in infants and children, and *Escherichia coli (EC)* is the leading pathogen. The aims of this study were to compare first episode of UTI with recurrent infection, reveal organisms that cause UTI, uropathogen resistance, and presence of bacteria producing *extended-spectrum β-lactamase (ESBL).*

METHODS:

A retrospective study included Omani children with any documented UTI presented to SQUH between September 2008 and August 2012. Comparison was made between both groups using Chi-squared ($\chi 2$) test as appropriate.

Results:

The first-UTI group included 175 children. *EC* was the leading pathogen (69%), *Klebsiella pneumonia* (17%;*P<0.001*), and *ESBL* (3%). 230 isolated uropathogens from 74 patients with recurrent UTI. The most common isolated pathogen was *EC* 187 (81.3%; *P<0.001*), followed by *K.pneumonia* 12 (5.1%), and *ESBL* (7%; *P=0.042*). Overall resistance to IV antibiotics was less evident than oral antibiotics, with least resistance to *Meropenem* and *Imepenem* (1% each). Higher resistance was found in recurrent UTI to *Augmentin*, *Cefuroxime*, *Ceftriaxone*, *Cefotaxime*. Oral *Nitrofurantoin* showed least resistance in first and recurrent UTI, but increased in non-E.Coli uropathogens.

Conclusions:

E.coli and *ESBL* were more common in recurrent UTI, while *K.pneumonia* were found more in first-UTI. *Meropenem*, *Imepenem*, *Amikacin*, and *Piperacillin/Tazobactam* can be used as a first line, while *Cefotaxime* and *Ceftriaxone* cannot be used in both groups. Our report shows high resistance rates to *Ampicillin*, *Cefuroxime*, and *Amoxicillin/Clavulanate*. First-generation cephalosporin is not recommended for use as empiric therapy. We recommend the use of *Nitrofurantoin* as empiric treatment in both UTI groups.

ESPID-0580
Unallocated Posters

CONGENITAL CYTOMEGALOVIRUS INFECTION SCREENING IN PREMATURE AND SMALL FOR GESTATIONAL AGE NEWBORNS: 2010-2012 PROGRAM IN A SINGLE SPANISH TERTIARY HOSPITAL

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BACKGROUND – AIMS
Routine serological screening for cytomegalovirus (CMV) during pregnancy is not yet recommended. Up to 35% of congenital cytomegalovirus infected infants are born prematurely, 50% are small for gestational age (SFGA). We evaluated a urine screening in premature newborns to optimize future strategies.

METHODS
Prospective study of premature infants (< 37 weeks) born in a tertiary care children's hospital (December 2009 - December 2012). Screening was performed using a shell vial urine culture assay (Vircel®) in first week of life. Hearing screening was performed using evoked otoacoustic emissions. During the study period, CMV culture was also performed in SFGA full-term infants.

RESULTS
1200 premature newborns (52% male) tested. Median gestational age: 33.6 weeks (range 23.7–36.9). Median birth weight: 1840 g (SD 590). Gestational age: < 27 weeks (8%), 27-31 weeks (16%), 31-34 weeks (31%) and 34-37 weeks (45%). One hundred eighty (15%) infants were SFGA. Congenital CMV infection was diagnosed in 2 asymptomatic and 1 symptomatic premature infants, only one SFGA. Prevalence of congenital CMV infection among preterm infants was 0.25% (0.16% between asymptomatic preterm infants). 2/3 patients presented a normal hearing screening evaluation. During the study period, 148 SFGA full-term infants were also screened for CMV: 4 were positive (3 asymptomatic). Prevalence of congenital CMV infection among all SFGA infants was 1.52% (1.22% between asymptomatic SFGA newborns).

CONCLUSIONS
Prevalence of congenital CMV infection in premature infants born in our hospital is low. Screening might be desirable in SFGA newborns, regardless of gestational age.

ESPID-0235
Unallocated Posters

INVESTIGATION OF ROSMARINUS OFFICINALIS L EXTRACT ON THE BACTERIA CAUSES GENITAL INFECTION

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Background and aim:

Some microbial causes in creating vaginitis are *streptococcus group B* and Gardnerella *vaginalis* which result in irrecoverable harms and increasing fatality, and providing infection in pregnancy period and transfer to the baby. With attention to the antibacterial effects some plants like Rosemary (Rosmar Inus officinalis) on vaginitis we can identify these kinds of plants and then give them to the people in the form of plant drugs. This research is an investigation of Rosemary and its antibacterial effect on the bacteria and also comparing this effect with common antibacterial.

Material and method:

This study of 96 women who suffered from this disease, all samples confirms with phenotyping method. The Disk diffusion method was used for comparing the effect of antibacterial total extract with common antibiotics.

Result:

The MIC result for each strain showed respectively; streptococcus 1/64, *Listeria* 1/128, *Candida Albicans* 1/2, *staph aureus* 1/128, *Gardenerella vaginalis* 1/64. In the disk diffusion method, the results were in this form which *streptococcus group B, staph aureus* and *Gradenerella vaginalis* were more sensitive than antibiotic disk in comparing with extract, While *Listeria monocytogenes* was more sensitive than antibiotic disk to the extract.

Conclusion: It is suggested that anti-virulence drugs could be used in combination with established or novel antimicrobials in a synergistic manner to increase the clinical performance and extend the lifespan of these drugs.

ESPID-0587
Unallocated Posters

APPENDICITIS: A MICROBIOLOGICAL APPROACH IN CHILDREN AT SANDWELL AND WEST BIRMINGHAM HOSPITALS (SWBH) – AN AUDIT

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Background/aims: Appendicitis is the most common abdominal surgical emergency[1], with peak incidence at 10-20[2] and 40,000 admissions per year in UK[3]. Use of antibiotic prophylaxis, in both 'simple' and 'complex' appendicitis is strongly evidenced[4], but 'complex' includes complications that also require treatment regimens. SIGN recommend agent choice is made at the local level[5], and SWBH use co-amoxiclav; gentamicin was added for indications of 'complex' cases after a 2010 audit showed high complication rate (7/17, 41%).

This audit reviewed adherence with and microbiological evidence for current antibiotic guidelines. Criteria reviewed were:
1) Appropriate Clinical Pathway? 2) Appropriate antibiotics? 3) Microbiological Evidence?

Methods: Retrospective audit of clinical records and 'Telepath' system data of 47 patients: admitted 1st Jan-31st Dec 2013 to SWBH, under 16 and underwent appendectomy.

Results: 1) 94% reviewed within 4 hours of surgical referral (median 1:38)

2) 40/47 (85%) received prophylactic antibiotics: 88% co-amoxiclav ±gentamicin. 8/20 (40%) indicated cases received gentamicin. 6/47 (13%) post op complications; no correlation to 'appropriate' antibiotics. 36/47 (77%) had post-op antibiotics: mean 2.3 days IV and 4.3 days oral.

3) 13/47 with theatre sample sent. Operative 'pus' in 22/47 (47%), 55% sample sent; 9/47 (19%) 'perforation', 78% sample sent. Organisms isolated 14/17 (82%) co-amoxiclav sensitive, 10/11 (91%) gentamicin sensitive.

Conclusions: Improvement needed in guidance for and usage of antibiotics in this common surgical emergency. Suggestion of gentamicin use improving 'complex' outcomes but further evidence required. Coamoxiclav ±gentamicin remained appropriate 1st choice agents, but increasing microbiological monitoring is essential in light of growing antibiotic resistance.

ESPID-0380
Unallocated Posters

MORBIDITY RATES OF CHILDREN WITH IUGR IN THE FIRST YEAR OF LIFE

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Intrauterine growth restriction (IUGR) contributes significantly to infant and child mortality, morbidity, life expectancy.

Objective: to study features of the health of children with intrauterine growth restriction in the first year of life.

The study included 315 children with IUGR born at term 37-41 weeks of pregnancy. Control group consisted of 119 children born with normal anthropometric measurements.

According to the research found that in children with IUGR incidence of diseases of the respiratory system is significantly higher 54,9 ± 2,8%, than in the control group 14,3 ± 3,2% (p1 <0,001). Endocrine, nutritional disorders occur in children with IUGR in the first year of life in 53,0 ± 2,8% cases, whereas in the control group was significantly less - in 12,6 ± 3,0% cases (p1 <0,001). Among the infectious and parasitic diseases of children with IUGR was 37,1 ± 2,7%, which was significantly higher than the control group 16,0 ± 3,4% (p1 <0,001). The incidence of pathologies of blood and hemopoietic organs among children in the first year with IUGR was 27,0 ± 2,5%, in the control group, this indicator was significantly less than 4,2 ± 1,8% (p1 <0,001). At 12,4 ± 1,9% of children with IUGR common diseases of the digestive system.

The greatest importance in the structure of morbidity in children with intrauterine growth restriction the age of one year have the respiratory system. For all nosological groups of diseases in children with IUGR there was a significant difference from the control group.

ESPID-0139
Unallocated Posters

FOLIC ACID AS ADJUNCT IN TREATMENT OF ACUTE DIARRHEA AMONG CHILDREN 4 MONTHS TO 4 YEARS AT A TERTIARY HOSPITAL

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Aim: This study evaluates the **e**fficacy of Folic acid as adjunct in treatment of acute diarrhea.
Method: A randomized double-blind placebo controlled trial was conducted among 180 patients 4 months to 4 years having acute diarrhea with "Some Dehydration" based on WHO guidelines admitted at a tertiary hospital from January to May 2012. Patients were given either Folic acid or placebo. The outcome was measured in terms of stool frequency, volume, time to reach stool consistency to type 5 based on Bristol Stool Chart, and improvement of stool consistency on follow-up.
Results: Stool frequency and volume were statistically insignificant for both groups. The time to reach stool type 5 was statistically significant (p value<0.0001). The mean number of days for stool consistency to reach type 5 was 2.7 days for Folic acid while 3.9 days for placebo. After 3 days, 88.8% of patients given Folic acid had stool type 5 while only 33.3% from placebo. There was no recurrence of diarrhea among 97 patients who followed-up after 3 days, 56 patients for Folic acid and 41 for placebo. Patients given Folic acid all had stool type 4, while 4 patients or 9.8% given placebo still had stool type 5. This was statistically significant (p value 0.02).
Conclusion: Patients with acute diarrhea given Folic acid achieves stool type 5 at a shorter duration and had better improvement of stool consistency compared to placebo on out-patient follow-up.

ESPID-0078
Unallocated Posters

COST BURDEN ESTIMATION OF PEDIATRIC VARICELLA HOSPITALIZATION IN VALENCIAN COMMUNITY FROM 2004 TO 2013

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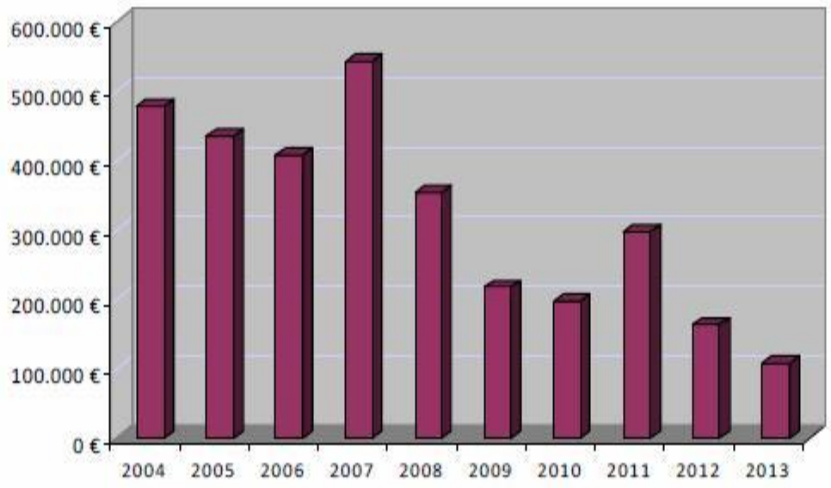
BACKGROUND AND AIMS: In 2006 varicella vaccine was introduced in official vaccination schedules for 12 years old non-immune children (vaccination coverage: 11,3%, 2013). Some children are previously vaccinated, after their first year of life, by pediatricians recommendation (vaccination coverage: 32,9%, 2013). The aim of this study is to evaluate the cost of hospitalizations for varicella in children under 15 years old to assess the burden of this disease and the impact of the vaccination.
METHODS: Data from Minimal Basic Data Set (CMBD) were used to estimate costs of hospitalizations because of varicella and varicella-related conditions (CIE-9-MC 052.0–052.9) among children 0-14 years old in all public hospitals (n=29) of this region from 2004 to 2013. Main Outcome Measures: hospitalizations, stays (days) and estimated costs on the basis of length of hospital stay.

RESULTS: There were 1,136 hospitalizations, accounting for 6,255 bed days. Median length of hospital stay was 4 days. According to year, highest cost value corresponds to 2007 (€543,816). Annual hospitalization cost decreased by 77.5%, from €478,209 in 2004 to €107,636 in 2013.

CONCLUSIONS: High incidence and associated costs of varicella hospitalizations keep supporting varicella vaccination. Time spent in intensive care unit, drug prescriptions, diagnostic tests and indirect costs were not taken into account so our figures heavily underestimate actual costs.

Varicella Hospitalization. Estimated cost by year.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Hospitalizations	190	157	159	139	131	92	78	64	72	54
Stays	933	850	798	1061	691	425	387	581	319	210

ESPID-0077
Unallocated Posters

TRENDS IN PEDIATRIC HOSPITALIZATIONS FOR CHICKENPOX IN VALENCIAN COMMUNITY FROM 2004 TO 2013

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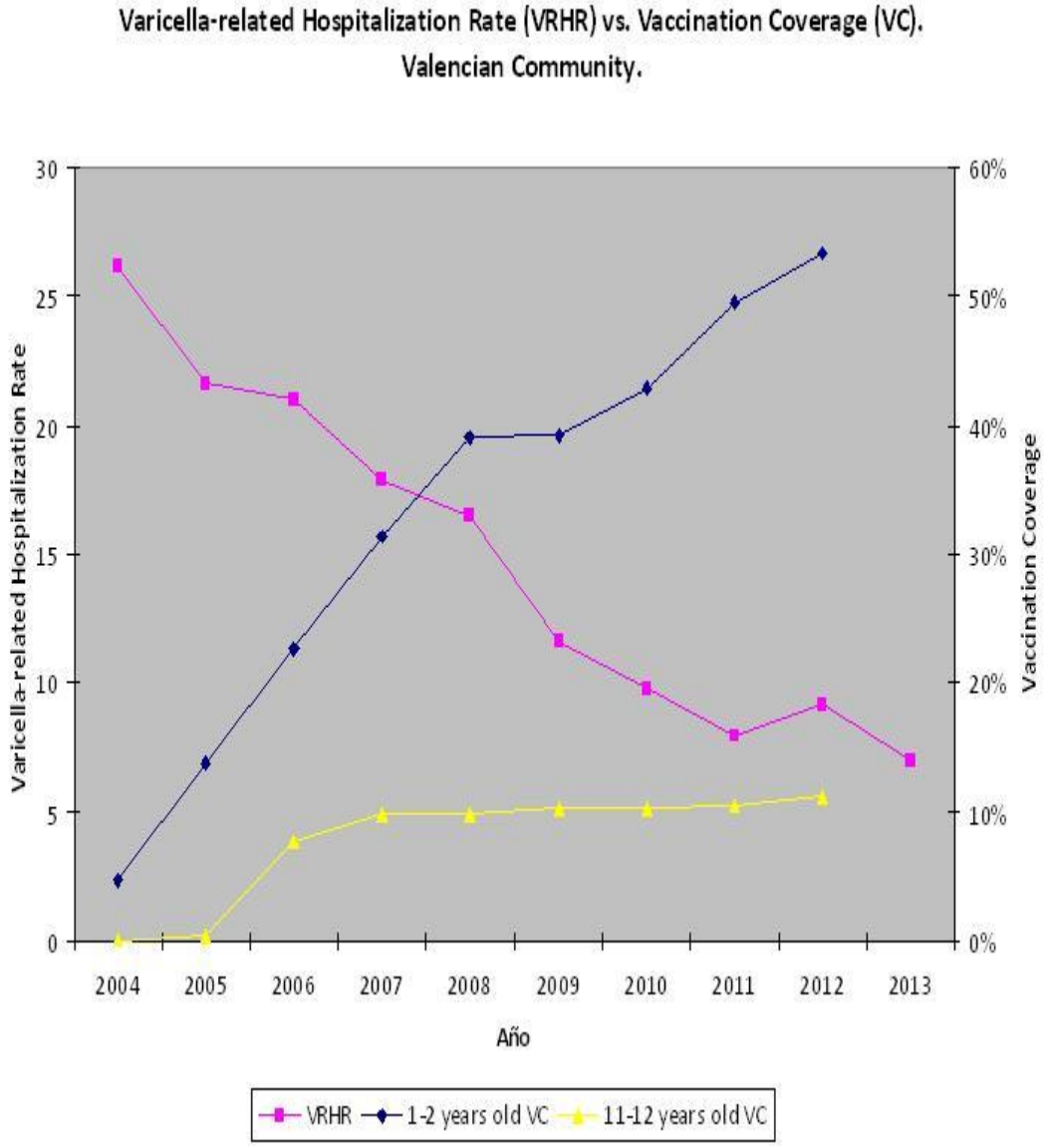
BACKGROUND AND AIMS: Chickenpox is normally a benign and self-limited childhood disease, but infection with varicella virus can cause severe morbidity and mortality, mainly due to complications. In 2006 varicella vaccine was introduced in Valencian Community vaccination schedule for 12 years old non-immune people although some children are vaccinated after their first year of life. This study is aimed to know trends in vaccinal coverage, varicella-related hospitalization, complication and fatality rates.

METHODS: Data from Minimal Basic Data Set (CMBD), Vaccine Information System (SIV) and Poblational Information System (SIP) were used to compare rates of hospitalization and complications among pediatric patients (aged 0-14) hospitalized with varicella from 2004 to 2013. Main Outcome Measures: sex, age, vaccinal coverage, number and rate of varicella hospitalization and complications.

RESULTS: There were 1,136 hospitalizations. The mean length of stay was 5.51 days (range: 0-234). Varicella hospitalization rate decreased from 26,19 to 6,94 per 100,000. 32.3% (n=367) presented varicella complications, the most common being viral pneumonitis (17.17%, n=63). Of 1,136 case patients 18 had been vaccinated (1, one dose; 17, two doses). Four cases resulted in death. The in-hospital case-fatality rate was 3.52 per 1,000.

CONCLUSIONS: There was a trend toward decreased hospitalizations in line with increased vaccinal coverage. Continued implementation of existing vaccine policies should lead to further reductions of varicella disease in this community although it remains to be seen the impact on public health of foreseeable decreasing vaccination

rate within 1-2 years old population henceforth.



ESPID-0711
Unallocated Posters

CHRONIC HEPATITIS B VIRUS INFECTION IN CHILDREN OF CHANGES IN BIO-ENERGY ON THE SEVERITY OF THE DISEASE.

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Chronic hepatitis B virus (HBV) infection in children presents a challenge for the practitioner infection disease. Decisions regarding selection of patients who may benefit from treatment, appropriate timing of treatment, and the choice of antiviral therapy are complex and are compounded by the limited number. Currently, biological oxidation is defined as a set of substrate oxidation reactions in living cells whose primary function – providing energy metabolism.

Aims: To define the mechanisms by which NADH/ NAD and of lactate/ pyruvate plays an antifibrogenic role in chronic HBV infection in children .

Methods: Examination of lactate and pyruvate levels was carried out by enzymatic method which is based on the oxidation of lactic acid to pyruvic by enzyme lactate dehydrogenase with the parallel reduction of NAD+ to NADH2.

Results: Metabolic disorders, which are characterized by the correlation NAD+/NADH2 and increase of NAD+ (0.322+0.02 mmole/l) concentration in comparation with NADH2 (0.0016+0.001 mmole/l) what makes the reaction slower in connecting with acceleration of lactate/pyruvate correlation and in result the speed of gluconeogenesis is decreased, are observed at the chronic hepatitis B virus infection in children.The most excessive metabolic disorders are observed at the patients with fibrosis, which can be undesired sign of antivirus therapy and can require of its correction.

ESPID-0492
Unallocated Posters

EVALUATION OF THE IMMUNOGENICITY OF MODERN INFLUENZA VACCINES IN CHILDREN WITH ALLERGIC PATHOLOGY.

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Actuality: Influenza is a highly contagious viral infection that can develop in severe inflammatory disease of the respiratory tract, leading to a fatal outcome. Influenza is especially dangerous for children with various chronic diseases, including allergic ones. The only reliable way of prevention of the disease is vaccination.

Objective: To study the immunogenicity of influenza vaccines "Influvac" (Abbott) and "Grippol plus" (Petrovax) in children with allergic pathology.

Materials and methods: The number of vaccinated children is 228, aged 3-17 years, with atopis dermatitis and bronchial asthma. The group of comparison consists of 107 healthy children. The antihemagglutinin antibodies assesed in the serum of all three serotypes of influenza virus, contained in the vaccines, in 1 and 6 months after immunization.

Results: There is no any significant differences in the immunogenicity of both influenza vaccines in patients with allergic diseases compared with healthy ones ($p \geq 0,05$). The fourfold increase in antibody titers 1 month after administration of the vaccine "Grippol plus" was in the range of 77-90%, of vaccine "Influvac" the seroconversion was observed in 73-93%. The proportion of patients with protective levels was quite high and in the range of 70-91% in patients with bronchial asthma, and 75-91% in patients with atopic dermatits. As it is shown, after the immunization of both vaccines antibody levels in serum were maintained for 6 months.

Conclusion: Thus, both vaccines have demonstrated high immunogenicity so in children with various forms of allergic pathology, as in healthy ones for a 6 months period after immunization.

ESPID-0999
Unallocated Posters

GUILLAIN-BARRE SYNDROME – INFECTION DUE TO MEDITERRANEAN SPOTTED FEVER

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Guillain-Barre syndrome (GBS) is an acute poyneuropathy with various causes. The disease is usually triggered by an infection. We present a child with GBS due to *Rickettsia conorii* infection.

CASE: A four-years-old boy was referred from another hospital with ataxic gait and blurred speech. He was living in Algeria and had came from there 6 days ago. His cerebrospinal fluid analysis was completely normal, common bacterial and viral work-up for herpesviruses 1 and 2, varicella-zostervirus, human herpesvirus 6, cytomegalovirus, Epstein-Barr virus and *Mycoplasma pneumoniae* were all negative. Cranio-spinal neuroimaging revealed contrast enhancement at lomber area. Electromyogram showed motor neuropathy compatible with GBS, and the patient received intravenous immunoglobulin for the diagnosis of GBS. The clinical status improved and the patient was discharged after two weeks with minimal disarticular speech. His blood test for rickettsial etiology could be achieved later and immunofluorescence test for *R. conorii* IgM was positive at 1/96 titer. The patient was diagnosed retrospectively as Mediterranean spotted fever(MSF). He was completely well at follow-up.

CONCLUSION: MSF is endemic in southern Europe and northern Africa. Travel history to endemic region is very important to consider the diagnosis of infections related to the causative agent *R. conorii*. The prognosis is reported extremely well in this infection. To our knowledge, this is the first pediatric case report with GBS due to MSF.

ESPID-1004
Unallocated Posters

WEST NILE VIRUS: AN EMERGING INFECTION IN TURKEY

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BACKGROUND: West Nile virus (WNV) is a mosquito-borne zoonotic arbovirus belonging to the genus Flavivirus. Cases from Turkey has been reported rarely, hence we present two patients admitted to our hospital during summer last year with encephalitis due to WNV.

CASE 1: A four-years-old boy presented to Emergency Department with fever and generalized tonic-clonic seizure. He had been on oral antibiotic therapy for three days for upper respiratory infection. His laboratory tests and neurological exam were normal. Cranial neuroimaging and electroencephalogram were also normal butthere were 200 lymphocytes/mm^3 in cerebrospinal fluid, with glucoseand protein levels in normal range. The patient received antibacterial and acyclovir therapy pending bacterial and viral work-up. The patient was intubated because of repeated convulsions. Polymerase chain reaction test for WNV was found to be positive and all other microbiological tests were negative. He was followed for 1 month at hospital and was discharged as his status became stable.

CASE 2: An 11-years-old girl admitted with fever, vomiting, agitation and confusion. He was diagnosed as gastroenteritis one week ago because of fever, abdominal pain and diarrhea. He had blurred consciousness, positive meningeal signs and recurrent myoclonic convulsions. His respiration was irregular and he was followed in intensive care unit for 9 days. Lumbar puncture could not be performed due to unstable general status and immunoglobulin M for WNV waspositive. The patient recovered after five weeks of supportive therapy.

CONCLUSION:WNV infection should be considered in any meningoencephalitis with unknown etiology.

ESPID-0217
Unallocated Posters

BLACK TONGUE DURING INFANCY

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BACKGROUND: Black tongue is the black color change over tongue due to filiform hyperkeratosis of upper part of it and is associated with food, cigarette or chromogen bacteria/yeast producing porphyrin. Generally it has been reported in smoking people over 40 years ofage who consume alcohol and those with poor mouth hygiene. Black tongue ininfants has been reported very rarely. Microbial overgrowth was accused as etiology and lesions were regressed with observation in cases reported in literature.

CASE:A 40-days-old male baby referred to our hospital with a recent black color change over his tongue. Neither his mother nor him had been received any medication. His past history was unremarkable. The physical examination was completely normal except a slightly raised painless and centrally located black plaque on his tongue. Lingual swab culture yielded gram-positive cocci with *Candida crusei*, which were considered as normal flora in this age group. He was followed up with no intervention. The lesion regressed spontaneously starting at each lateral borders after 2. week with complete resolution at the end of 4. week. No recurrence was observed during 9 months of follow-up.

CONCLUSION:Black tongue in infancy is a rare phenomenon and close follow-up is a useful approach before performing biopsy for histopathological examination. This case was presented because of rare occurrence.

ESPID-0315
Unallocated Posters

MENINGOCOCCAL BRAIN LESION: AN ABSCESS OR INFARCT?

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BACKGROUND: Meningococcemia, caused by *Neisseria meningitidis*, is an important cause of septic shock. Prognosis is closely related to urgent antibiotherapy as well as proper intensive care intervention. We present a patient with meningococcal septic shock who had a cerebral abscess or infarct.

CASE: A six-years-old girl presented to Emergency Department with fever, somnolance and diffuse maculopapular-petechial rash progressing into purpura/ecchymotic lesions. Meningococcemia with septic shock was the initial diagnosis; aggressive fluid therapy along with ceftriaxone were started pending culture results. Her Glascow coma scale was 8 and she was intubated for mechanical ventilation support. She had thrombocytopenia associated multiorgan failure, bleeding diathesis and hypotension unresponsive to medical treatment. Plasmapheresis and continuous veno-venous hemofiltration with cytokine clearing membrane was performed. Blood culture remained sterile, polymerase chain reaction of serum sample was positive for *N. meningitidis* serogroup W135. The patient was extubated on 7. day and plasma exchange therapy was stopped due to her stable cardiorespiratory and hematologic status. On 9. day, the patient suffered from confusion with no meningeal signs or neurological deficit. Cranial magnetic resonance imaging showed a hyperintense lesion (15x13 mm) near to capsula interna with mild contrast enhancement, suggesting early ischemia or an abscess. The antibiotherapy was extended to 6 weeks and the lesion evolved into subacute infarct on serial radioimagings.

CONCLUSION: Brain abscess is rare during meningococcemia, in which septic emboli leading to ischemia could play a role in pathogenesis. The cerebral lesion may be due to an event common with septic and ecchymotic skin involvement.

ESPID-0939
Unallocated Posters

NOROVIRUS GASTROENTERITIS IN CHILDREN BEFORE AND AFTER UNIVERSAL ROTAVIRUS VACCINATION IN FINLAND

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Noroviruses are the second cause, after rotaviruses, of acute gastroenteritis in children. In Finland, RotaTeq® was added into the National Immunization Program (NIP) in September 2009. While RVGE cases have decreased, the proportional role of NoVs is expected to increase. The aim was to examine the role of NoVGE during the universal RV vaccination.

We conducted prospective surveys of AGE in children seen in Tampere University Hospital in pre-NIP years 2006-2008, at the beginning of RV vaccination in 2009-2011 and in post-NIP years 2012-2014. Each survey was conducted in same settings, using the same methodology. The presence of norovirus was studied by RT-PCR followed by sequencing of capsid and polymerase regions for genotyping.

In pre-NIP years NoV accounted for 24% of 809 AGE children seen in hospital (196 cases). In 2009-2011 NoV GE cases showed a decreasing trend in absolute numbers, but the proportional role of NoV increased to 34% (111 of 354 cases) and NoV became the leading cause of acute GE in children. In 2012-2014, 27% (101 of 379 cases) were associated with NoVs.
The majority (97-99%) of NoVs belong to GII genogroup. In 2006-2008, GII.4 accounted for 89%, in 2009-2011 for 65% and in 2012-2014 for 54% of NoV cases. At the same time, new GII.4 variants have been detected.

RV vaccination has not affected the absolute number of NoV gastroenteritis cases. NoV has become the most common single cause of AGE in children. Development of a vaccine against NoVGE, particularly GII.4, in children is in priority.

ESPID-0016
Unallocated Posters

PREDICTORS OF CYTOMEGALOVIRUS INFECTION IN CHILDREN WITH RENAL TRANSPLANTATION, A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract

Introduction: Cytomegalovirus infection is one of the serious complications of renal transplantation in children. In this meta-analysis, we assessed the incidence and risk factors of cytomegalovirus infection in pediatric renal transplant recipients.

Data Sources: Massive search was done in searching systems such as PubMed, Ovid, MD-consult and ProQuest databases until February 2014. We also assessed reference lists of all articles which were included in this meta-analysis.

Study selection criteria: Any study that was about the cytomegalovirus infection and its risk factors in pediatric renal transplant recipients.

Results: Eight articles were included in this meta-analysis. Totally 876 pediatric recipients were assessed. In the different studies, cytomegalovirus infection ranged from 7.5% to 40% with a pooled incidence of 25.1%. Positive donor for CMV IgG regardless of serostatus of the recipient was the most important independent risk factor for CMV infection in this meta-analysis (relative risk:4.17, 95%CI: 2.62-6.64, Pv<0.0001). There was not any association between the use of anti-lymphocyte antibodies, recipient sex and age and source of transplant with the incidence of CMV infection.

Conclusion: In summary, D+ serostatus is an important risk factor for CMV infection/disease in pediatric renal transplantation. We think that recipients with CMV positive donors regardless of their serology are suitable candidates of prophylactic treatment.

ESPID-0073
Unallocated Posters

PREGNANT WOMEN'S ACCESS TO PMTCT AND ART SERVICES IN SOUTH AFRICA AND IMPLICATIONS FOR UNIVERSAL ANTIRETROVIRAL TREATMENT

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Objectives: We describe womens' access to PMTCT and ART services in KwaZulu-Natal, South Africa. We also compare birth outcomes including inutero transmission among women who received PMTCT prophylaxis, women eligible but did not commence ART and women eligible and commenced ART.

Design: A cross-sectional analytical postnatal audit.

Methods: This postnatal audit was conducted at a District Hospital. Women were interviewed and

maternity records examined to describe their access to VCT, CD4 Counts, AZT/NVP or triple ART and reasons for limited access to any of the listed services. Birth outcomes were compared among the 3 groups of women.

Results: The antenatal HIV prevalence was 39.0%; PMTCT prophylaxis was optimal (96.7%) but access to ART was neglected (29%). 97% had a CD4+ test performed; 35% did not receive their results; 40% had a CD4<200 and would have required ART and 29.1% initiated ART. With current WHO recommendations, 71% of the HIV positive pregnant women would have been eligible for ART

(CD4<350). There were significantly more preterm births among HIV+ve women (p=0.01). Women

who received ART were no more at risk of preterm deliveries (OR0.73;95%CI 0.39-1.36;p=0.2). Nine

infants were confirmed HIV infected at birth (2.4%;95%CI 1.1-4.5).

Conclusion: If >70% of HIV+ve pregnant women in an urban South African community are requiring ART under current guidelines, and access to CD4 count is limited, the country's HIV management policy for pregnant women needs to be revisited for change towards universal treatment.

ESPID-0323
Unallocated Posters

MONITORING MEASLES MORBIDITY IN REPUBLIC OF KAZAKHSTAN

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Background and aims: Since 2008 European region faced few measles outbreaks predominantly among non-vaccinated individuals. CIS countries, including Kazakhstan were also involved in epidemic process. The main aim of our investigation was to study the age structure and vaccination status of individuals affected by measles in 2014 as well as to determine measles virus genotypes in Kazakhstan.
Methods: The monthly statistical data from regional epidemiological surveillance departments and results of virus isolation and identification from laboratory tested specimens collected in all cases clinically suspected measles.
Results: In age structure of measles cases proportion of non-vaccinated children under 1 year was 35%, between 1 – 14 years 8%, older than 15 years 57%. In 2011 and 2012 measles virusD4 strain was detected, in 2013 – 2014 measles virus D8 was detected (Table 1).
Table 1. Results of virus detection in clinically suspected cases in 2011 – 2014 in Kazakhstan

Year	Number of investigated samples	Number of positive samples	Genotype
2011	26	10	D4
2012	3	1	D4
2013	8	1	D8
2014	32	5	D8

Conclusion: Age proportion of measles cases showed high prevalence among non-vaccinated children less than one year old. Also measles cases were detected among people older than 15 with vaccination history more than 10 year ago. Results of virus identification during 4 years demonstrated circulation of different genotypes in different years. In 2011 – 2012 D4 was identified. Since 2013 – genotype D8 was circulated.

ESPID-1065
Unallocated Posters

IMPACT OF ROTAVIRUS VACCINATION ON HOSPITALIZATION, DISEASES SEVERITY AND ROTAVIRUS GENOTYPE CIRCULATION IN BOLIVIA

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Background and Aims
Rotavirus is the most important etiological agent of severe diarrhea in Bolivia. Rotarix vaccine was introduced in Bolivia in 2008. This study was conducted to evaluate impact of rotavirus vaccination on hospital admissions, disease severity and rotavirus genotype circulation among children less than 5 years of age.

Methods
The study was conducted in Bolivia between 2005-2014 as part of National Rotavirus Surveillance System. Diarrheal stool specimens, clinical and epidemiological data were collected from hospitalized children. Stool samples were analyzed by ELISA followed by RT PCR to determine rotavirus G-P-genotypes. Disease severity was measured by Vesikary score. Linear regressions were used to compare trends of diarrhoea hospitalizations before and after vaccine introduction.

Results
Following vaccine introduction, significant decrease in the rotavirus prevalence among hospitalized children and reduction of disease severity was observed. The median hospitalization rates for pre-vaccine and post-vaccine years were 46% & 22 % respectively. Reduction in diarrheal hospitalizations was more pronounced in <1-year-old than in older children. Along this period cycling of diverse rotavirus strains and high prevalence of P[8] and G2P[4] strains, concurrently with the emergency of new (G3P[6]) was observed.

Conclusions:

The data demonstrate the effect of rotarix vaccine on reducing rotavirus disease burden and decreasing trend in all-cause diarrhoea-related hospitalizations in children <5 years of age in Bolivia. Despite cycling of diverse rotavirus strains, vaccination provided strong protection against rotavirus hospitalizations highlighting the value of the rotavirus vaccine against diarrhoeal diseases and supporting its introduction into other developing countries.

ESPID-0148
Unallocated Posters

DIFFERENT EXPRESSIONS OF THE TOLL-LIKE RECEPTORS (TLRS) AND RELATED FACTORS IN PERIPHERAL BLOOD OF PRETERM INFANTS

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Objective: TLR insufficiency increases newborn's susceptibility to infectious disease. The aim of this study was to analyze TLR changes and its signaling pathway associat ed factor expressions in non-infected premature newborns.

Methods: The peripheral blood of ten premature births has been collected weekly fro m the 28th gestational week (GW) until maturity at 36th GW. Microarray assays were used to derive dynamic follow-up data of TLR1-
10 and other TLR signaling pathway associated factor changes.

Results: The follow-
up results showed that the transcription level of TLR1 increased at the 36th , TLR 3 d ecreased at the 33rd and TLR7 increased at the 34th GW significantly, whereas NFk B and its activator TBK1 were highest transcribed in the 28th and 32nd GW. Low TLR 4 transcription in addition to late MD-
2 maturation (33rd GW) indicated a lack of defense mechanisms against bacterial inf ections in preterm births particular in the first weeks after birth. Late transcriptional en hancements of TLR1 and MYD88 (35th week) as well as β 2 microglobulin (35th GW) also indicated a weak immune system in the early maturation stages.

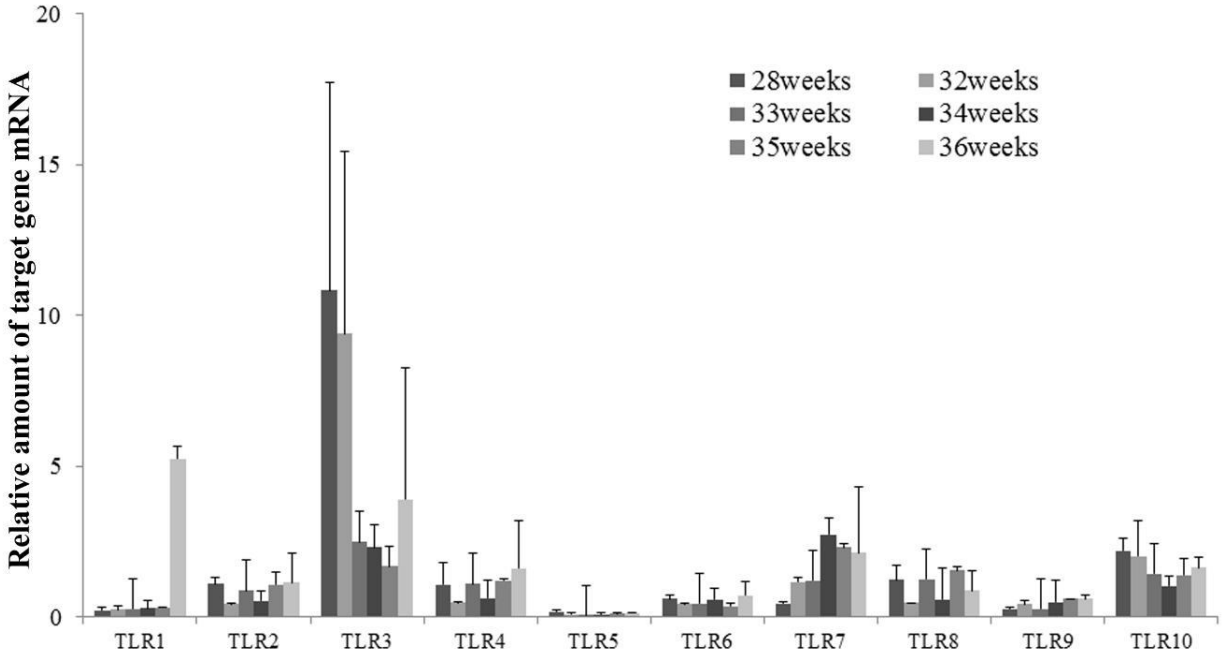

Figure 1: The expression of TLR1-10 from the 28th to 36th gestational weeks

Conclusion: The transcription levels of TLR1, 3, 7 and the signaling pathway associated cofactors were different transcribed during the 28th and 36th GWs of the premature newborns. In the early stage after preterm birth, beside peak transcriptions of NFkB and TBK1, the immune system is not fully developed and maturation takes place mainly between the 33th and 35th GW.

ESPID-0150
Unallocated Posters

THE BASE LINE STUDY "SCREENING OF SEN VIRUS IN THALASSEMIC PATIENTS-A SELECTED GROUP OF KHYBER PAKHTOON KHWA PAKISTAN"

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Abstract

The SEN virus is a blood-borne rounded single stranded DNA. (ssDNA) virus, possessing nine genotypes from A to I. SENV-D and SENV-H genotypes have strong link with patients with unknown (non A to E) hepatitis infections. Blood-borne viral infection is second important cause of death in thalassemia patients. The purpose of this study was to screen out SEN virus in thalassemia patients. For this a general PCR was used. The genotype SENV-D and SENV-H genotypes viraemia was detected by performing nested-PCR in thalassemia patients 250 blood plasma samples and 200 healthy blood donors from different origin of Khyberpakhtoonkhwa Pakistani. The Prevalence of SENV-D viraemia was significantly higher than SENV-H among thalassemia patients as compared to healthy individuals. This Prevalence of SENV infection among thalassemia patients suggests that blood transfusion was the main route of transmission of infection. High frequency of SENV infection in transfusion patients indicate that blood transfusion is also an important for the spreading of virological infection. Prevalence of 12% of SENV infection among thalassemia patients and 4% among healthy individual of which 4% were SENV-D and 3% were SENV-H and rest referring to other genotype (A, B, C, E, F, G and I) was detected. In conclusion, SENV isolated from different origin of Khyberpakhtoonkhwa Pakistani population might have a pathogenic effect on thalassemia patients.

ESPID-0721
Unallocated Posters

STAPHYLOCOCCAL SUPERANTIGEN AND RHEUMATOID ARTHRITIS DISEASE

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Backgroundand objectives: We hypothesize that staphylococcalsuperantigen as biomarker may have been present in the body fluid of patientswith rheumatoid arthritis as in some cases, while thereare signsand symptoms of rheumatoidarthritis, the diagnostic laboratory factors are reported as normal condition.Thus, we suppose that the classicsuper-antigens may have a role in causing the disease. The aim of thisinvestigation was to identify Staphylococcal superantigen (enterotoxin D and or*ent*D gene) in the blood of rheumatoid arthritis patients.

Materialsand Methods: Inthis study, samples of blood 103 patients with rheumatoid arthritis wereinvestigated. Based on reference Gene (M28521.1) a specific primer pair wasdesigned and was evaluated bioinformatically and the PCR protocol was performed.All blood samples were then subjected to DNA extraction and were assayed. Thefinding data was descriptively analyzed.

Results: The results of thePCR assay indicated that 42 (40/77 %) of patients with rheumatoid arthritis hadpresence of the Staphylococcal superantigen D (entrotoxin D) in their blood.The sequencing of the PCR products confirmed the accuracy of results.

Conclusion: This finding may indicatethat in addition of food poisoning, anotherrole of the staphylococcal superantigen is in inflammatory disease such as rheumatoid arthritis.Therefore, diagnostic method and treatment protocols may be need to reconsider.

ESPID-0728
Unallocated Posters

CHARACTERISTICS OF BORDETELLA PERTUSSIS INFECTION AMONG INFANTS AND CHILDREN ADMITTED TO INTENSIVE CARE UNITS (ICU) IN GREECE

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BACKGROUND AND AIM: Pertussis is globally the fifth leading cause of vaccine-preventable deaths. Its incidence and the associated mortality are increasing, especially among infants. We attempted to describe the clinical features of severe pertussis infection and to identify factors associated with poor outcome.

METHODS: A retrospective analysis of all pertussis cases admitted nationally to (six) ICUs in Greece from 2003 to 2013. The diagnosis of pertussis was based on clinical case definition and laboratory criteria, according to the Council of State and Territorial Epidemiologists (CSTE) Position Statement (CDC).

RESULTS: Thirty one children were included and 90.3% were younger than 12 months. Cough was the most prominent symptom, being present in 87% of patients. An increasing trend was observed from 2006 to 2013. Mechanical ventilation was applied to 42% of patients. Six patients (19%) died because of respiratory (2) or multiorgan system failure (4). The characteristics of survivors versus non survivors are presented on the table. Three patients were diagnosed with pulmonary hypertension and only one of them survived. Two patients received exchange blood transfusion.

CONCLUSION: Young infants are at risk of severe pertussis, resulting in serious complications or death. Elevated WBC and low serum sodium are associated with higher mortality. Maternal immunization, "cocooning" strategies and timely immunization of infants and children should be the goal of prevention.

ESPID-0020
Unallocated Posters

MUCORMYCOSIS IN CHILDREN WITH ONCOHEMATOLOGICAL DISEASES IN SAINT PETERSBURG, RUSSIA

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Background and Objectives. We analyzed - aetiology, clinical signs and symptoms, results of treatment of mucormycosis in children with oncohematological diseases in St. Petersburg, Russia. **Methods.**The prospective study during 2004-2013 yy. The diagnosis of mucormycosis was made according to EORTC/MSG criteria (2008). **Results.** We observed 16 children with oncohematological diseases and mucormycosis. The median age of patients-11 years (range 5-17), male and female ratio 1:2.Main underlying diseases in children with mucormycosis and hematological/oncological were: AML (5), ALL (5), AL (1), neuroblastoma (1), MDS (1), aplastic anemia (1), Fanconi's anemia (1), myeloid sarcoma (1). Main clinical forms of mucormycosis were: pulmonary (63%), sinusitis (31%), osteomyelitis (25%), CNS (25%), gastrointestinal (13%), and subcutaneous (13%). Two and more organs were involved in 50% patients. Diagnosis was established by histology and/or microscopy in all patients. In 69% cases the diagnosis was confirmed by culture. Aetiologic agents included: *Lichtheimia corymbifera* (5), *Rhizopus oryzae* (1), *Rhizopus* sp. (3), and *Rhizomucor* sp. (2). Antifungal therapy was performed in 13 patients (3 cases were diagnosed post-mortem). Amphotericin B lipid complex was used in 77% patients, posaconazole -62%, caspofungin –46%, amphotericin B deoxycholate -15%. Combination therapy (amphotericin B deoxycholate + caspofungin, amphotericin B lipid complex + caspofungin, amphotericin B deoxycholate+ posaconazole) was used in 69% patients. Twelve weeks overall survival was 38% (6/16). **Conclusions:** in all patients with oncohematological mucormycosis was a nosocomial infection; pneumonia was most common clinical manifestation (63%); two and more organs were involved in 50% of patients; twelve weeks overall survival was 38%.

ESPID-0304
Unallocated Posters

PERTUSSIS IN CHILDREN IN THE SOUTH-EASTERN REGION OF UKRAINE FROM 2008 TO 2012

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Background and aims: Many countries recently reported an increase of pertussis cases especially in infants despite of high vaccination coverage against pertussis. In Ukraine the pertussis immunization program includes 4 doses of the whole cell diphtheria-tetanus-pertussis vaccine (wDTP) at 3, 4 ,5 and 18 months. The objective is to describe the epidemiology of pertussis in the South-Eastern region of Ukraine to discuss future vaccination strategies.

Methods: Data from routine Pertussis surveillance systems for children from 0 to 17 years and regional vaccination coverage for 3 and 4 doses of the wDTP vaccine were used from January 2008 to December 2012. Data were analysed to describe incidence rates by age group, deaths among notified cases and vaccination coverage.

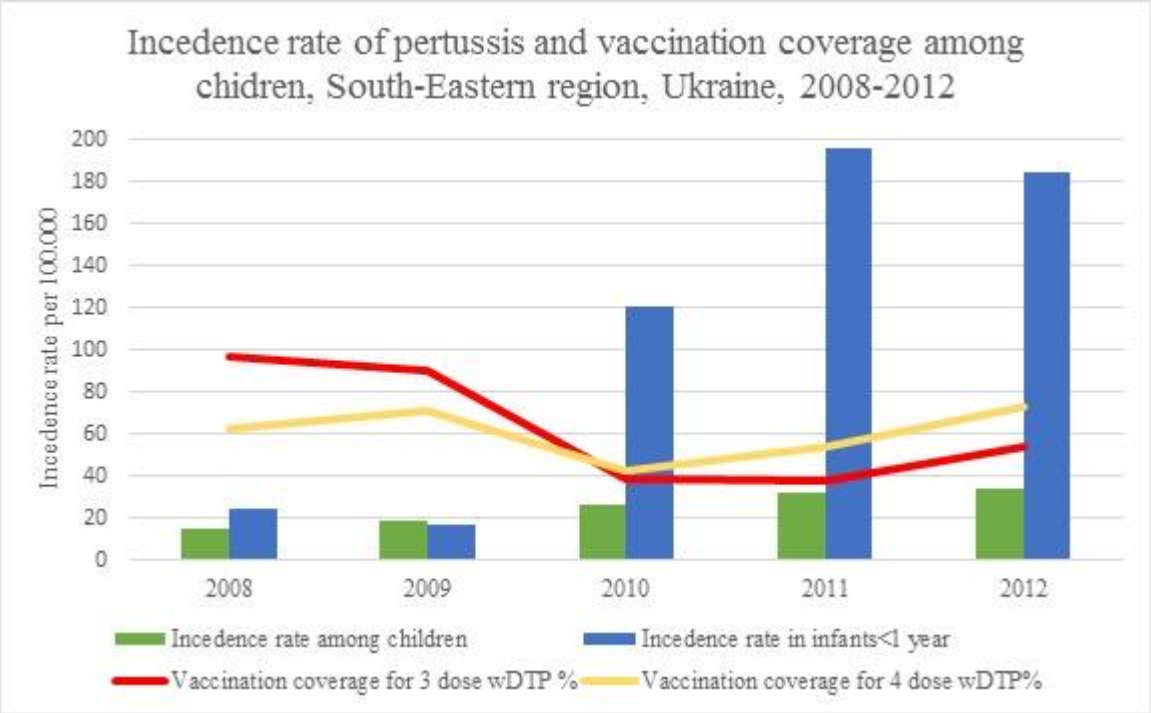
Result: The coverage for 3 dose of the wDTP vaccine decreased from 97% in 2008 to 54,3% in 2012 due the complicated economic and political situation in Ukraine.

Children younger than 1 year had the highest incidence during the entire period that increased from 24 per 100,000 in 2008 to 184,8 in 2012.

Two deaths occurred among the confirmed cases and patient's age was two and six months.

Conclusion: High vaccination coverage for wDTP vaccine should be a public health priority in Ukraine to reduce the number of cases and to reduce the impact of the

disease in children younger than one year.



ESPID-0037
Unallocated Posters

CHARACTERISTICS OF RESPIRATORY SYNCYTIAL VIRUS INFECTION IN CHILDREN UNDER THE AGE OF TWO

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Aims: To estimate the prevalence of RSV infection and to describe the characteristics of clinical presentation of RSV infection in children during the first 2 years of life (15.02.2011-15.04.2011).

Methods: A retrospective analysis of 91 case histories of children under two years of life.

Results: During the observation period 319 children were hospitalized with acute respiratory disease. Of these 319 children 29% (n = 91) were two years of age or younger. 22% of these 91 children (n = 20) tested positive for RSV by the rapid immunochromatography test. Gender did not seem to be an effect modifier. Children between the ages of one and two accounted for 60% (p>0.05) of all the RSV infections observed. The course of RSV infection was significantly more severe than other types of respiratory infection (OR = 4,18; 95% CI 0,95-18,48). Disease severity was significantly increased in the presence of bronchial obstructive syndrome (BOS) (OR = 10,4: 95% CI 3,38 – 32,11) and respiratory failure (OR = 2,9; 95% CI 0,96-8,98). 25% of patients with RSV infection required therapy in an intensive care unit. Of which 60% of the RSV positive children exhibited the clinical symptoms of a mixed infection.

Conclusions: RSV infection was diagnosed in every fifth child admitted with respiratory disease and with RSV infection the chance to have a severe course of the disease is 4 times higher. RSV infection is associated with a threefold higher risk of respiratory failure and a tenfold higher risk of respiratory failure when accompanied by BOS.

ESPID-1073
Unallocated Posters

VIRAL ETIOLOGY OF INFLUENZA-LIKE ILLNESSES AMONG CHILDREN IN RUSSIA (2013-2015)

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Background and aims

Respiratory viruses are predominant causes of influenza-like illnesses (ILI), but infection etiology is complex and difficult for etiological determination.

Methods

Detection of 14 respiratory viruses by real-time PCR Detection of 14 respiratory viruses, including IFVA, IFVB, PIV 1-3, RSV, HMPV, HCoV-OC43, HCoV-229E, HCoVNL63, HCoV-HKU1, ADV, HRV and HBoV, was performed using a Amplisens ORVI-scrin-FL RT-PCR Kit (Russia) according to the protocols.

Results

We studied the viral etiology of ILI in 2013-2014, 2014-2015 seasons. Among all patients tests, 300 (69,4%) were found positive for at least one virus with respiratory viruses detected at the highest positive rate in children less than 7 years old. Single infections accounted for 56,5% (244/432), while co-infections accounted for 12,9% (56/432). Respiratory syncytial virus was the most frequently identified in winter 2014 accounted for 46,2% (128/277) of all samples collected in 2013-2014 season. Rhinovirus was detected in 10,8% (30/277) of cases of ILI in that period. Influenza viruses were identified in 5% (14/277) and other viruses were found less than 5% of the samples. In 2014-2015 season 36,8% (57/155) of the samples were positive for rhinovirus; bocavirus was detected in 18,1% (28/155) of the cases; other viruses were identified less than 10% of the samples.

Conclusions

Thus viral etiology of ILI was confirmed in 69,4% of the cases with co-infection rate for 12,9% of all cases. The most frequent detected viruses were respiratory syncytial virus and rhinovirus. Report presents the detailed etiological structure of ILI, including Human Influenza.

ESPID-1082
Unallocated Posters

Tuberculous otomastoiditis in children: a rare event to suspect

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Background. Tuberculosis is still one of the most challenging infectious disease. Extrapulmonary infections represent 12-15% of all registered tuberculosis cases and middle ear localizations are observed only in

Aim of the study. To analyze the incidence of tuberculous otomastoiditis in hospitalized children and describe the clinical characteristics and the treatment outcome.

Material and methods. Retrospective review of children (0-18 years) admitted to Bambino Gesù Children's Hospital for chronic otomastoiditis and underwent middle ear surgery between January 1995 and December 2011.

Results. Among 4077 identified children, only three children were found to have mycobacterial otomastoiditis. One patient was excluded because of the isolation of Mycobacterium Avium. As for the others, 4 year old boy and 5 year old girl, a Mycobacterium tuberculosis (MT) was found in cultures. They were referred to our Hospital because of a history of recurrent otorrhea refractory to a broad antibiotic treatment. Perforation of tympanic membrane and simil-cholesteatomatous material were described in association with a conductive hearing loss. Nevertheless, in the first case tubercolin skin test and Quantiferon were positive but no other localization of infection was found suggesting the diagnosis of primary tuberculous otomastoiditis, treated with a three-drug therapy. The second patient had a history of treated pulmonary and mediastinal TB at 7 months of age. MT was also cultured in a bronchoalveolar lavage leading to diagnosis of a recurrence of disease with a secondary localization. Isoniazid and rifampin resistant MT grew on culture so a treatment with linezolid, moxifloxacina, pyrazinamide, etambutolo, PAS was prescribed.

Conclusions Tuberculous otomastoiditis in children is a rare event which should be suspected in the case of recurrent otorrhea unresponsive to therapy, particularly in patients with positive anamnesis for tuberculosis infection.

ESPID-0770
Unallocated Posters

ASSOCIATION OF ENTEROVIRUS 71 3C PROTEASE PROTEIN ACTIVITY WITH CLINICAL FEATURE

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Objectives:

EV71 is the most important enterovirus related to the fatal and morbid cases. Todelineatepathogenesis of EV71 infection, we had studied EV71 viralgenetics and correlated the results with theirclinical outcome.

Methods:

We studied EV71 viral genetics and tried to find the associationwith clinical outcome. EV71 3Cis a important part for viral replication and possesses proteolysis and RNA binding activities. We used site-directed mutagenesisto create mutant 3C at 79th amino acid (T79A, T79I, and T79V). Then we over-expressed wild EV713C and mutant EV71 3C in SF268 cells and analyzed the proteaseactivity by Western blot with antibodies of 3C substrates. We produced EV71 infectious clonewith wild 3C and mutant3C, which were transfected into RD cell. We accessed theviral replication rate by plaque assay. Finally, we analyzed host-virus proteininteraction by immunoprecipitation of cell lysates.

Results:

We found that the polymorphisms of EV713C 79th amino acid affect the clinical outcome.There were no difference of protease activityamong the different variant EV71 3C. However, we found that EV71 with mutant 3C T79V had highest virus replication rate,followed by wild-type 3C. We identified some important interactingproteins including modulation and degradation of mRNA,vesicle trafficking protein, and ATP synthase.

Conclusion:

We found up-regulation of COX-2 by wild 3C but not mutant 3C. We also identified viral interaction with important host proteins, which might have important roles on EV71 infection and mayhave further clinical application.

ESPID-0910
Unallocated Posters

PEDIATRIC HEPATITIS C VIRUS CHRONIC INFECTION IS A CURABLE DISEASE. EFFICACY AND SAFETY OF TREATMENT WITH PEGYLATED INTERFERON ALFA-2B IN COMBINATION WITH RIBAVIRIN

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Background

Hepatitis C virus (HCV) affects about 3% of the worldpopulation and is classified by WHO among the six major oncogenic viruses. In Europeand US pediatric population, mother-to-child transmission of HCV is theprevalent way of infection. Its impacton morbidity includes a 26-fold increase risk of liver-related death (chronic hepatitisCHC, liver cirrhosis, hepatocellular carcinoma) when acquired during childhood.

Current standard of care of CHC includes pegylatedinterferon (PEG-IFN) in combination with ribavirin (RBV).

Patients andmethods

Out of 35 children HCV perinatally infected diagnosed at ourcenters, 10 (6 males, median age 12 years, range 8-16 yr) were eligible for antiviraltherapy. Genotype (G) distribution was as follows: G1b 3 pts; G 2 1 pt; G 2a/c 3 pts; G3a 3 pts). PEG-IFN alfa 2-b (60 mg/m^{2}one-weekly) plus RBV (15 mg/kg/die in two doses) were given for 24 (G2 and G3)or 48 weeks.

Results

Sustained virological response(SVR, undetectable plasma HCV-RNA at 24 weeks after treatment) was attained by8/10 (80 %; G1: 33%, G2 and G3: 100%). Two pts (both G2) discontinued treatmentbecause of failure (HCV detectable at +24wk). Treatment was well tolerated withoutmajor side effects. During follow-up (median 20, range 9-26 mos) no relapseswere observed.

Conclusions

Our data confirm the safetyand high efficacy of standard treatment of children with PEG-IFN and RBV. The benefits of early therapy in childhood oradolescence include lifetime negative serum HCV-RNA, decreased risk of cirrhosisand hepatocellular carcinoma and burden of infection.

ESPID-0159
Unallocated Posters

INTESTINAL PARASITIC INFECTIONS INCLUDING CRYPTOSPORIDIOSIS AND IMMUNOLOGICAL ASPECTS AMONG MALNOURISHED CHILDREN.

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This is a case-control study, which involved 194 malnourished children below 5 years of age who were attending Basrah Maternity and Children Hospital. About 84% have marasmus, 8.2% marasmus-kwashiorkor, 6.2% kwashiorkor and 1.6% under weight. Parasitic infections were more frequent among malnourished children (59.8%) than well-nourished children (33%), with increased frequency among malnourished children with diarrhea (32.5%). Cryptosporidiosis was found in 6.9% of children with increased frequency among malnourished children with diarrhea 14.9% compared to 11% in malnourished children without diarrhea. Only 2% were noticed among well-nourished children with diarrhea while no case has been recorded in well-nourished children without diarrhea. Depressed cellular immunity characterized by decrease in total lymphocytes was found among malnourished children either with or without diarrhea. While humoral immunity (IgG, IgM, IgA) was significantly elevated among malnourished children with or without diarrhea in comparison to well-nourished children. C3 and C4 were increased in malnourished children without diarrhea with significant difference in C4 only. While there were decreased in malnourished children with diarrhea, with significant difference in C3. In addition, phagocytic activity showed a significant decrease in malnourished children with or without diarrhea compared to well-nourished children.

ESPID-0966
Unallocated Posters

CLINICAL FEATURES OF GASTROENTERITIS (RGE) CAUSED BY ROTAVIRUS G3P8 AND G4P8 SEROTYPES IN MINSK, BELARUS

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InMinsk we marked annual changing of the season peak (February-April) dominantrotavirus serotype: 2005-G4P8 (69%), G1P8 (11.3%); 2008-G4P8 (53.3%), G2P4(22.9%); 2009-G2P4 (46.7%), G4P8 (31.2%); 2010-G4P8 (60.0%), G2P4 (29.1%); 2011–G3P8 (53.6%), G4P8 (24.8%); 2012–G4P8 (45.6%), G3P8 (27.6%); 2013–G4P8(58.3%), G1P8 (12.5%). Vaccination against rotavirus doesn't a routine inBelarus. The aim was to study clinical features and differences between RGEcaused by G3P8 and G4P8 serotypes in children who were treated in thePaediatric Infectious diseases Minsk City Clinic (PIDCC).

Materialsand methods: The research was performed at the PIDCC at 2005-2013. The “RGE”diagnose was confirmed by detection of a rotavirus antigen in stools (EIA andserotypes by PCR).

Results:We observed 33 children with RGE G4P8 atthe age of 2 - 60 months Me (P25-P75) 18 (12-34) and 21 - with RGE G3P8 at the age of 3 - 48 months 18 (12.5-29). G3P8 RGE clinicalfeature developed slower and their patients were admitted at the Clinic later 1-10 days 1.5 (1.0-4.0)than G4P8 1-4 (1.0 (1.0-2.0)). RGEseverity (Vesicary's scale) was 12.5 score (10.0-14.0; n=31) G4P8 vs. 11 (9-12.5; n=21) G3P8. 7children (n=21) G3P8 and 5 (n=31) G4P8 were admitted at the Clinic with “acuterespiratory diseases” diagnose and the gut dysfunction developed on the secondday. Catarrhal syndrome we marked 26(n=33) patients (78.9%) with G4P8 RGE and 17 (n=21) (81.0%) c G3P8.

Conclusion: RGEcaused by G4P8 serotypes has more severe clinic than G3P8. G1P8 is rare last 10years. Serotypes control is important for epidemiology.

ESPID-0015
Unallocated Posters

ETIOLOGICAL AND DEMOGRAPHIC CHARACTERISTICS OF NEONATAL MORTALITY AND MORBIDITY FROM PAKISTAN

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Background

To determine the etiology, management, bacteriological spectrum and outcome of neonatal patients admitted in Civil Hospital Karachi (CHK) and to examine the factors associated with it.

Methods

This hospital based descriptive study of 1463 patients from both sexes who were admitted to Paediatric department, CHK from 1st January 2008 till 31st December 2010 with an established cause according to modified Wigglesworth classification and fulfilling other inclusion criteria were included in the study. Data regarding their demographic profile and potential risk factors was collected on a well structured proforma. Cases were followed until discharge or expiry. Data was analyzed using descriptive statistics.

Results

The male to female ratio in our study was 1.12:1. Seven hundred and thirty-four patients were delivered at home (50.2%) and 1010 were less than 7 days old (69%). Out of the total cohort of expired subjects, 89 participants (74.8%) were < 7 days of life. Mortality was more in neonates born at home in rural areas to illiterate mother; 74 patients (62.2%). Most of the deaths; 57 were in neonates suffering from specific infections (47.9%) followed by 38 deaths in immaturity group (31.9%) and 19 related to asphyxial conditions (15.9%). The most common isolates were Staphylococcus aureus (28.7%), Klebsiella (24.8%) and Pseudomonas aeruginosa (16.6). One hundred and nineteen (8.13%) of the neonates died in our study group.

Conclusions

These results suggest that neonates with illiterate mothers with high parity and below average socioeconomic level were more susceptible to mortality in the early neonatal period.

ESPID-0079
Unallocated Posters

INCIDENCE OF HOSPITALIZATIONS FOR PNEUMONIA AMONG CHILDREN YOUNGER THAN 15 YEARS IN VALENCIAN COMMUNITY(SPAIN)2008-2013

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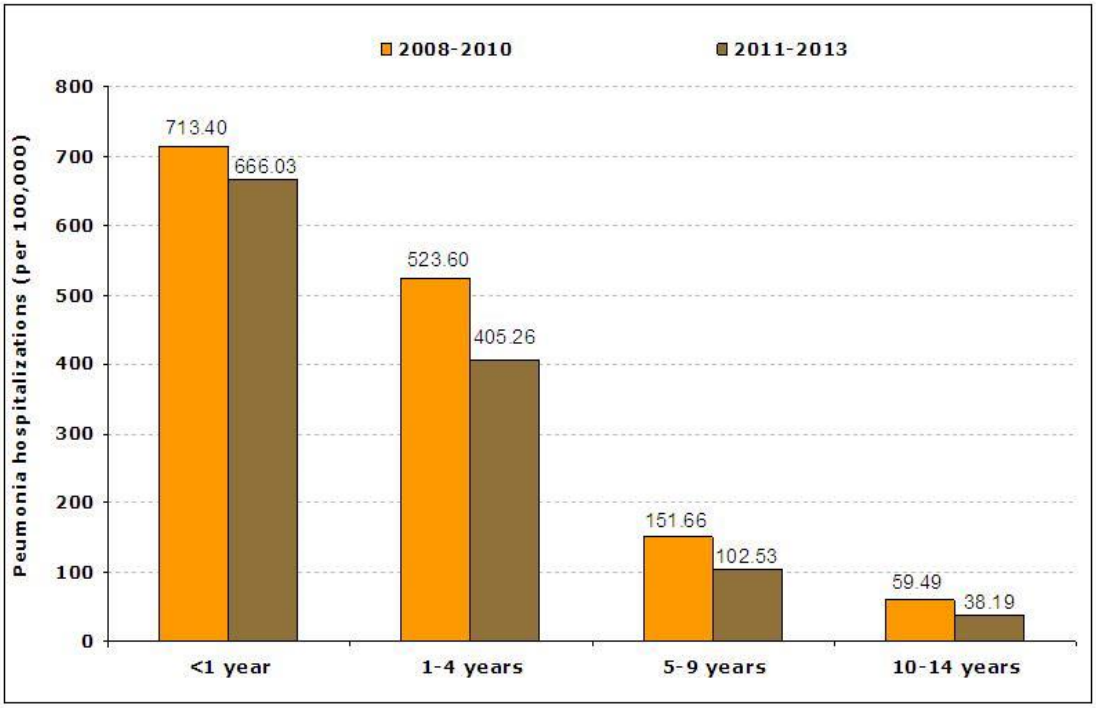
Background and aim: Childhood pneumonia is an important cause of morbidity in the developed world. Approximately one-half of children younger than five years of age with community-acquired pneumonia require hospitalization. The aim of the study is to analyze the evolution of the incidence of pneumonia hospitalizations (PnH) in Valencian Community from 2008 to 2013 and assess its likely relationship with introduction to the market of 13-valent pneumococcal conjugate vaccine (PCV13) at the end of 2010.

Methods: Minimal Basic Data Set (CMBD) from 2008 through 2013 was used to estimate the annual number of PnH (codes ICD-9-CM 480-486) among children aged <15 year. Annual total, sex and age-specific hospitalization rates were obtained according demographic data from Population Information System (SIP).We estimated the age-specific average annual rates of pneumonia for two periods: 2008-2010 (pre-PCV13) and 2011-2013 (post-PCV13).We also calculated the hospital length of stay.

Results: There were 11,179 PnH (53.4% boys) and 56.6% of admissions were from children aged 1 to 4 years. The annual rate of PnH has been reduced 39.1% throughout the study period, mostly from 2012, with statistically significant differences and was highest at children <1 year. The average stay was 5.96 days (S.D.8.33), with the longest stays corresponding to younger than 1 age group. Pneumonia was the first listed diagnosis for 83.5% of these hospitalizations.



Average annual rates of hospitalizations for pneumonia among Valencian Community children in 2008-2010 and 2011-2013

Conclusions: Reduction observed in hospitalizations for childhood pneumonia was especially relevant from 2011, probably due to the introduction of PCV13 vaccination program in infants. There was no decline in length of stay.

ESPID-0554
Unallocated Posters

PAPULAR-PURPURIC "GLOVES AND SOCKS" SYNDROME ASSOCIATED WITH B19V INFECTION IN A 10-YEAR-OLD KUWAITI CHILD: A CASE REPORT AND LITERATURE REVIEW.

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Papular-purpuric "gloves and socks" syndrome (PPGSS) is a rare, self limited acute dermatosis characterized by a papular-purpuric edematous rash in a distinct "gloves and socks" distribution often accompanied by oral lesions and fever. It is mainly caused by parvovirus B19 (B19V) but other viruses and drugs such as trimethoprim/sulfametaxol or chemotherapics may be involved. It occurs mainly in young adults; nevertheless it has been also reported in children. We are reporting a case of PPGSS and PVB19. We also reviewed the literature for PPGSS in children. This will highlight the clinical manifestation and the natural history of this syndrome in children empowering paediatrician to diagnose it and avoid unnecessary investigations and treatment which creates further parental anxiety.

Case:

A healthy 10yr old Kuwaiti girl admitted with fever, and headache. She was found to have itchy erythematous fine maculopapular rash over hands & feet. There was edema above the upper lip & chin. She was sick, lethargic and had petechia on the lower limb. She developed bilateral nonpurulent conjunctivitis. Investigations excluded bacterial infection, and collagen disease. Virology screan was positive for Parvo B19 IgM & IgG. Within few days her fever subsided and the rashes became faint and she was discharged in a good condition.

Conclusion:

Papular purpuric gloves & socks syndrome is a self limited dermatosis that in recent years is found to be increasingly prevalent in children worldwide. The distinctive clinical characteristics of PPGSS in children should be recognized by all pediatricians in order to avoid unnecessary investigations.

ESPID-0535
Unallocated Posters

VARICELLA GANGRENOSA WITH TOXIC SHOCK-LIKE SYNDROME DUE TO GROUP A STREPTOCOCCUS INFECTION IN A 3 YEAR OLD GIRL : A CASE REPORT FROM KUWAIT

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Background and objective:

Chickenpox (Varicella) is a common childhood infection which is usually regarded as a trivial condition. Varicella gangrenosa is one of the rare most serious life threatening complications of chickenpox. Varicella gangrenosa is a term used to describe the gangrenous ulceration of the skin and/or deeper tissues that may follow chicken pox infection. We report a case of an immunocompetent child with varicella gangrenosum caused by group A streptococcal superinfection of the skin lesions due to chickenpox. With the prompt recognition and plastic surgery management beside intensive medical treatment, this patient survived with the least possible body disfigurements. Awareness and early aggressive intervention might reduce the high morbidity and mortality associated with this condition.

Case Summary:

A three year old girl presented after mild chicken pox with toxic shock like syndrome. She had a huge hemorrhagic cutaneous necrosis involving bilateral hips along with clinical and laboratory features of disseminated intravascular coagulation. Group A streptococcus was isolated from the skin lesion. She improved with antibiotics, acyclovir and immunoglobulin infusion. After the gangrenous area was demarcated she under went surgical debridement followed by split thickness skin grafting. Finally, she was discharged home after 35 days of hospitalization in well condition.

Conclusion:

Chickenpox is not always benign infection. It can present with unusual serious complications. Awareness of Varicella gangrenosa as a potentially life threatening complication of chickenpox will enable prompt diagnosis, more aggressive management and better prognosis. Multidisciplinary team approach of plastic surgery beside medical management will yield excellent clinical outcomes.

ESPID-0234
Unallocated Posters

PHARMACOKINETICS OF FORMED COLISTIN FOLLOWING A SINGLE DOSE INTRAVENOUS COLISTIMETHATE SODIUM IN CRITICALLY ILL NEONATES

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Background and aims: Infections caused by multi-drug resistant Gram-negative bacilli are serious complications in critically ill neonates worldwide. Intravenous colistin is sometimes the only effective available antibiotic for these infections. The aims of this study were to study the pharmacokinetics and safety of colistin following intravenous administration of colistimethate sodium (CMS) in critically ill neonates with Gram-negative bacterial infections.

Methods: A prospective pharmacokinetic study was conducted in 7 neonates following a single dose of CMS (5 mg colistin base activity (CBA) per kilogram corresponding approximately to 150,000 IUs/Kg). Blood samples to evaluate colistin plasma concentration were collected before and 15 minute, 2, 4, 6 and 24 hours after CMS administration.

Results: The median gestational age and birth weight were 38 weeks (range 34-40) and 2,920 g (range 1,540-4,015), respectively. The age at enrollment was 13 days (range 5-15). Mean (±SD) plasma colistin maximum concentration (C_{max}), area under the concentration-time curve ($AUC_{0\text{-}24h}$), and time to reach the maximum concentration (T_{max}) were 3.03±0.67 µg/mL, 21.10±8.11 µg·h/mL, and 1.25±0.94 h, respectively. The clearance of formed colistin (CL/fm) was 0.61±0.34 L/h/Kg.

After 6 hours in all neonates plasma levels of formed colistin were below the minimum inhibitory concentration (2 µg/mL) set for *A. baumannii, P. aeruginosa and K. pneumoniae* by the CLSI. No adverse reactions were observed after CMS administration and all neonates survived.

Conclusion: The administration of a single daily dose of 5 mg CBA/kg body weight via intravenous route to critically ill neonates was associated with suboptimal plasma concentrations of colistin.

ESPID-1043
Unallocated Posters

ANTI-RESPIRATORY SYNCYTIAL VIRUS ACTIVITY OF PHYTOCHEMICAL FRACTIONS SOURCED FROM ALCHONEA CORDIFOLIA

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Background: Respiratory syncytial virus (RSV), a single-stranded negative sense RNA virus which belongs to the *Pneumovirus* genus of the Paramyxoviridae family, is on a global scale the most important cause of viral lower respiratory tract illness (LRTI) in infants and children Unfortunately, there are only limited options for management of the disease, hence the need to continue to search for novel therapeutic options against the RSV. Antiviral activity of extract and fractions from the lichen *Alchonea cordifolia* were evaluated as a preliminary way of identifying lead compounds with potency against RSV.

Methods: Anti-Respiratory syncytial virus activity was evaluated by cell culture infectivity inhibition and cell viability profiling.

Results: Initial investigation of extract of *Alchonea cordifolia* lead to identification of an ethyl-acetate fraction showing anti-RSV activity with IC_{50} = 11.33µg/ml. Corresponding assay for the cytotoxic effect against utilized cell line gave TC_{50} = 63.86µg/ml. Further fractionation of the ethyl-acetate fraction of *Alchonea cordifolia* lead to differentiation into fourteen sub-fractions (1-14) having differing expressions of anti-RSV activity and cell viability profiles.

Conclusions: Fractions of *Alchonea cordifolia* may be a source of useful anti-RSV chemotherapeutic compounds.

ESPID-1064
Unallocated Posters

PHARMACOKINETICS AND PHARMACOVIGILANCE OF VORICONAZOLE IN CHILDREN WITH CANCER

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Background : Voriconazole is First line therapy for invasive aspergillosis. Pharmacokinetics of voriconazole in children with cancer can be affected by:High individual variability ,age, pharmacogenetics,Drug interactions, and Administration route.
Aim: To determine the pharmacokinetics, dose adjustment and the safety profile of voriconazole in children with the recommended dose (14mg/kg/day)
Patient and Methods:

Results: 68 voriconazole plasma level were obtained from 14 children. Mean age 10.1 years (range 3-14) ,57% (8/14) males . The diagnosis of cancer was 3 Acute Lymphoblastic Leukemia , 6 TPH , 3 Solid Tumors and 2 Medullary Aplasia . There were no statistical differences in the diagnosis of IFI: possible (5) probable (4) and proven (5).

Conclusion : Therapeutic Drug monitoring is highly recommended in children: At least 50% of children required dose adjustment at recommended dose of voriconazole (14mg/k/day). According to our results:a daily dose ≥400 mg/day (not mg/k/day) is necessary to achieve voriconazole target level

ESPID-0639
Unallocated Posters

LUNG SEGMENTATION IN DIGITAL CHEST X-RAY IMAGES USING GRAPH CUT OPTIMIZATION METHOD

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Background: Chest X-Ray is performed to diagnose or monitor treatment for conditions of pneumonia, emphysema, lung cancer, line and tube placement and tuberculosis by Physicians. This work is used to extract the Lung Boundary and to trace severity of Pneumonia Infection.

Method: The work is divided into three segments,

- Content-based image retrieval approach for identifying training images (with masks) most similar to the patient CXR
- Creating the initial patient-specific anatomical model of lung shape using SIFT-flow for deformable registration
- Extracting refined lung boundaries using a graph cuts optimization approach with a customized energy function.

Results: This Research work is carried out for the detection of Pneumonia infection in chest X-Ray images. In order to compare segmentation quality with the segmentation performances in the literature, three commonly used metrics The Jaccard Similarity Coefficient, Dice's Coefficient, Average Contour Distance are compared.

Conclusion: In earlier approach the accuracy rate was 95.4%. By combining the Integral values this work tries to increase the accuracy level to 96.5% by optimizing the graph cut values. This research work will help the Doctors to identify the severity of the infection with the chest X-Ray image itself, instead of going for other expensive diagnosis tests. This Lung Segmentation will help the physict to find any type of infection in the patients.

ESPID-1012
Unallocated Posters

COAGULASE-NEGATIVE STAPHYLOCOCCUS (CONS) BACTEREMIA IN NEONATES IN A NATIONAL REFERRAL HOSPITAL 2013-2014

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Coagulase-negative Staphylococcus (CoNS)bacteremia are the most common cause of sepsis in Neonatal Intensive Care Units (NICU), where the initial empiric treatment with vancomycin.
Retrospective descriptive study of episodes of CoNS bacteremia.Demographics, management and adjustment of vancomycin, serum creatinine and trough vancomycin level were included. Identification of isolates and sensitivity was performed.
56 episodes of bacteremia were analyzed for CoNS belonging to 49 patients which was newborn preterm (<37 weeks) 79.6% and weight mean 2.67kg .Diagnosis was late sepsis in 66.1% and catheter related bloodstream infection (CRBSI), 33.9%. From the typing of isolates obtained (n : 46, 82.1%) were S. epidermidis 67.4% .Resistance to methicillin (M) was 92.9%. VAN MIC was determined 94.6%, all isolates had less than 4 mg/dl.
Regarding the dosage of vancomycin trought in 80.3% was conducted in the first dosing schedule, with ≤2 mg/ml in 6.7% , 2-9,9mg/ml in 46.7% , 10-14,99mg/ml in 20% and ≥15mg/ml 26.7%.
Therapeutic failure in those who died within 10 days after the last isolation (n:3) was considered, patients with a diagnosis of CRBSI and without suppurative thrombophlebitis positive persisted despite removed the catheter n:1 and those with persistent catheter-related infection for more than seven days n:1. Vancomycin trought concentration was perfomed in 4 of the 5 patients, of which 3 had dosages 15mg/ml and only one had 1 ml ≤10mg/ml.
The importance of clinical follow-up of CoNS with dosage of vancomycin trought to obtain a pharmacokinetic- pharmacodynamic parameter whit a good surrogate between therapeutic efficacy and appropriate range of vancomycin trought in this age group.

ESPID-0105
Unallocated Posters

CLINICAL SPECTRUM OF DENGUE FEVER IN PEDIATRIC AGE GROUP IN A TERTIARY CARE HOSPITAL IN LAHORE.PAKISTAN

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BACKGROUND. Dengue fever (DF) is an acute infectious disease of antiquity. It is probably the most important arthropod-borne viral disease in terms of human morbidity and mortality, with 100 million infections occurring annually for which no effective therapy exists. Up till now study done locally, that shows the clinical spectrum of dengue fever in infants and children, is scarce. Dengue fever presents differently in different countries and during last epidemic Lahore was the main city to be affected.

AIMS: To assess frequency of various clinical presentations of dengue fever in pediatric age group in a tertiary care hospital

METHODS: Study completed in Nine month from Dec 2012 to Sep 2013 in pediatrics department Jinnah hospital Lahore. Cross sectional survey.

RESULTS: Out of 150 patients enrolled mean age of 8.4 years and standard deviation (SD) of ± 2.8 years. Age ranges from 1 year to 14 years. Amongst all 150 subjects 86 (57.3%) were males and 64 (42.7%) females. Male to female was 1.3: 1Fever was present in all 150 patients (100%).Diarrhea present in 21(14 %) patients. Petechia was present in 25 (16.3%).Epistaxis was present in 20 (13.3%).Hematemesis present in 8 (5.3%) Hepatomegaly was observed in 33(22%) patients .Splenomegaly was noted in 15 (10%) subjects.

CONCLUSION: Most of dengue fever cases were from 5 to 10 years of age group. Fever was the most common clinical manifestation of dengue fever followed by hepatomegaly, petechiae and diarrhea, epistaxis, splenomegaly and then hematemesis. . Dengue fever was more common in males as compared to females.

ESPID-0162
Unallocated Posters

IMMUNOGENICITY OF POLIOVIRUS VACCINES IN CHRONICALLY MALNOURISHED INFANTS: A RANDOMIZED CONTROLLED TRIAL IN PAKISTAN.

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Background

Efficacy of oral poliovirus vaccine (OPV) varies particularly children with malnutrition. We compared whether inactivated polio vaccine (IPV) can be used to rapidly close the immunity gap among chronically malnourished (stunted) infants in Pakistan.

Methods

A phase 3, multicenter 4-arm randomized controlled trial conducted at five Primary Health Care (PHC) centers in Karachi, Pakistan. Infants (9-12 months) were stratified by length for age Z score into groups of chronically malnourished (stunted) and normally nourished and were randomized to one dose of either bOPV alone or bOPV+IPV. Baseline seroprevalence of poliovirus antibodies and serum immune response to study vaccine dose were assessed by neutralization assay. Vaccine poliovirus shedding in stool was evaluated 7 days after a bOPV challenge dose.

Findings

Sera and stool were analyzed from 852/928 (92%) enrolled children. At baseline, the seroprevalence was 85·6% (n=386), 73·6% (n=332), and 70·7% (n=319) in malnourished children against poliovirus types 1, 2 and 3 respectively; and 94·1% (n=448), 87·0% (n=441) and 83·6% (n=397) in the normally nourished group (p<0·05). One dose of IPV given to malnourished children increased their serological protection (PV1, n=201, 97.6%; PV2, n=198, 96.1% and PV3, n=189, 91.7%) to parity with normally nourished children who had not received IPV (p=<0.001). Shedding of polioviruses in stool did not differ between study groups and ranged from 2·4% (n=5) to 7·1% (n=15).

Interpretation

Chronically malnourished infants were more likely to be unprotected against polioviruses than normal infants. IPV helped close the immunity gap better than bOPV alone.

ESPID-0459
Unallocated Posters

BACKGROUND INTUSSUSCEPTION TRENDS AMONG CHILDREN IN ENGLAND: RETROSPECTIVE ANALYSIS USING HOSPITAL EPISODE STATISTICS AND DATA LINKAGE TO COMPARE HES WITH THE BRITISH PAEDIATRIC SURVEILLANCE UNIT

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Aims To estimate background trends in intussusception admissions prior to rotavirus vaccine introduction in the UK. To compare Hospital Episode Statistics (HES) with intussusception data from the British Paediatric Surveillance Unit (BPSU).

Methods Retrospective analysis of the NHS inpatient HES was carried out to estimate background intussusception trends among children in England, 1995-2009. Data linkage was performed between HES and previously obtained BPSU data on intussusception among infants, 2008-2009.

Probabilistic data linkage was performed to match HES records with BPSU cases followed by manual confirmation of matched/possibly matched pairs (2008-2009). Capture-recapture methods allowed assessing HES accuracy and completeness of both data sources for intussusception.

Results Of 11,259 intussusception records identified in HES and after excluding 2538 (22.5%) duplicates, 8721 (77.5%) cases were retained for trends analysis. Significant decline in background trends was observed among infants from 86.0/100,000 in 1997 to 34.0/100,000 in 2009 (60% reduction, p=0.001).

Data linkage between 254 cases in HES and 190 cases in BPSU (2008-2009) resulted in 163 matched pairs. Reporting completeness was 85.8% for HES (163/190 BPSU cases) compared to 81.5% for BPSU (163/200 HES cases). Positive predictive value of HES was 78.7% (200/254 confirmed cases). The Lincoln-Petersen estimate yielded 233 cases (95% CI: 227.4 to 238.8). Estimated annual intussusception incidence among infants in England increased from 24.2/100,000 (unvalidated) to 28.9/100,000 (validated, 2008-2009).

Conclusions Background intussusception trends have declined among infants in England. The high quality of HES for intussusception highlights the usefulness of routinely-collected data in monitoring rotavirus vaccine safety in England.

ESPID-0638
Unallocated Posters

CLINICAL FEATURES AND LONG TERM PROGNOSIS OF CHILDHOOD BRUCELLOSIS IN NORTHEAST IRAN

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Background and Objectives: Brucellosis is a prevalent disorder in children of developing countries. The aim of this study is to describe the epidemiology and long term prognosis of Brucellosis in Khorasan.
Method: This is a descriptive cross-sectional study from November, 2003 to February, 2006. In this study the diagnosis of Brucellosis is based on clinical signs and symptoms and serology. Response to treatment was accessed by following patients via telephone calls and if necessary by clinic visits in November 2008.

Results: During a 38 month s we had 82 children with Brucellosis. The mean age was 8.02 years, and 40% of them were girls (male to female ratio =1.21). Summer with 45.9% of the cases was the peak season. History of having unpasteurized dairy products, direct contact with farm animals, living in village, and Brucellosis in the close family members was found in 91.6%, 76%, 70.2% and 41.1% of the study group respectively. The chief complaint was joint pain in 79.7 % of the cases. Fever, arthritis, splenomegaly and lymphadenopathy was found in 72.9%, 60.9%, 16.9% and 7.5% of the patients respectively. The therapeutic regimen of 48.7% of the patients was Co-trimoxazole and rifampin. We followed 74.3% of the patients for at least 3 years which showed a relapse rate of 6.5 %.
Conclusion: With at least six weeks treatment with two antibiotics and with close follow up, we can decrease the relapse rate in Ped B to zero, even without repeating the serology during or after treatment.

ESPID-0650
Unallocated Posters

PEDIATRIC HIV/AIDS ACQUISITION THROUGH BLOOD TRANSFUSION IN TURKMENISTAN

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Pediatric HIV/AIDS acquisition through blood transfusion in Turkmenistan

Background: In the past decade almost all cases of pediatric HIV/AIDS in the world have been perinatally transmitted. Transfusion acquired HIV is a rare event these years.

Report of cases: The author (a pediatric infectious diseases specialist and expert in Pediatric HIV/AIDS) works in Mashhad which is the second city of Iran with 3000,000 populations. Mashhad is 250 km far from Ashgabat , the capital of Turkmenistan and therefore is the main city of Iran for Turkmen health tourism.

During the last year (2014) the author has personally diagnosed 4 Turkmen children (2 infants and 2 children) with AIDS, which have been reported to the governmental health center of Mashhad. All the 4 kids had HIV negative mothers and all of them had history of blood transfusion in Turkmenistan.

Key words: HIV, AIDS, Pediatric, Turkmenistan

ESPID-0795
Unallocated Posters

DELAY OF TREATMENT OF FEBRILE URINARY TRACT INFECTIONS AND ITS ASSOCIATION WITH THE DEVELOPMENT OF SEVERE RENAL LESIONS

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Background: The association of delay of treatment initiation for febrile urinary tract infections (UTI) in children younger than 2 years with the development of renal lesions is controversial.

Aim: To evaluate the relationship of the duration of fever before the initiation of treatment of febrile urinary tract infections (FBT) with acute renal lesions or with renal scarring based on dimercaptosuccinic acid scintigraphy (DMSA) findings.

Methods: The inpatient records of 148 children [median age: 2.4 months (11 days-24 months)] with a first episode of febrile UTI during a three-year period, were analyzed. DMSA findings, clinical and laboratory parameters were evaluated.

Results: Seventy five children (51%) had acute renal lesions; 19 (25.3%) mild and 56 (74.66%) moderate/severe renal lesions. Renal scarring was found in 40% of patients with mild, 72% of those with moderate and in all patients with severe acute lesions.

The likelihood of acute renal lesions increased when FBT was ≥72h, without reaching statistical significance (P=0.068). The development of renal scars was significantly more frequent when FBT was ≥72h (P=0.014). No relationship was found between FBT 24 or 48 hours and the likelihood or the severity of acute renal lesions or renal scarring.

Conclusions: Delay in treatment initiation ≥72 hours is a risk factor for the development of renal scars. Duration of fever of ≥72h tends to influence the probability of acute renal lesions, although further studies are needed for verification. Delaying treatment for <72h in children with febrile UTI is not related with the development of renal lesions.

ESPID-0324
Unallocated Posters

THE NASOPHARYNGEAL CARRIAGE RATE, SEROTYPE DISTRIBUTION AND ANTIMICROBIAL RESISTANCE OF HAEMOPHILUS INFLUENZAE INFLUENZAE AMONG CHILDREN WITH UPPER RESPIRATORY INFECTION IN BEIJING

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Background and aims Haemophilus influenzae is an important human pathogen that causes severe infections including meningitis, sepsis, and bacteraemic pneumonia, mostly affecting young children. To investigate the nasopharyngeal carriage rate, serotype distribution and antimicrobial resistance of *Haemophilus influenzae* among children visiting an outpatient department in Beijing Children's Hospital with upper respiratory infection from March 2013 to February 2014. **Methods** The serotypes were determined by the latex-agglutination and the antibiotic susceptibility was tested by E-test method. **Results** The nasopharyngeal carriage rate for *Haemophilus influenzae* was 9.2% (271/2930), major in April to June. The number of boys was larger than that of girls', and mostly aged 4~6years old. All of the isolates were non-typable. The susceptibility to tetracycline, chloramphenicol, amoxycillin/clavulanate, and cefuroxime were 97.0%, 96.0%, 91.0% and 82.0%, respectively. The non-susceptibility to penicillin was 35.0%. The carriage rate of beta-lactamase was 23.0%. **Conclusions** About 9.2% of children with upper respiratory infection were nasopharyngeal colonized by *Haemophilus influenzae*. The infection is closely related with age, gender and season in Beijing. The non-susceptibility to penicillin was high, and the beta-lactamase positive rate of *Haemophilus influenzae* was high and increased rapidly.

ESPID-0401
Unallocated Posters

THE SEROTYPE DISTRIBUTION AND ANTIBIOTIC RESISTANCE OF STREPTOCOCCUS PNEUMONIAE SHOWED DISTINCT DISCREPANCY BETWEEN THE INPATIENTS' AND OUTPATIENTS' ISOLATES IN BEIJING CHILDREN'S HOSPITAL, CHINA

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Backgroud: We aim to compare the serotype distribution and antibiotic resistance of *S.pneumoniae* isolated from inpatients and outpatients.

Methods: Research subjects are the patients under 5-year-old from the Beijing Children's Hospital among March 2013 to February 2014. The serotype was determined using Quellung reaction with antisera, the antibiotic resistance against 13 antimicrobials were tested using the E-test method or disc diffusion.

Results: 140 non-invasive pneumococcal isolates were collected from inpatients. The prevailing serotypes were 19F(32.9%), 19A(20.7%), 23F(10.7%), 6A(10.0%), 14(8.6%) and 15B(6.4%). The coverage rates of 7-valent pneumococcal conjugate vaccine (PCV7), PCV10 and PCV13 were 55.7% (78/140), 56.4% (79/140) and 87.9% (123/140), respectively. 140 *S.pneumoniae* isolates were selected randomly from outpatients. The frequent serotypes were 19F(13.6%), 23F(12.9%), 6A(10.0%), 6B(10.0%), 19A(7.9%) and 34(5.0%). The coverage rates of PCV7, PCV10 and PCV13 were 40.7% (57/140), 41.4% (58/140) and 61.4% (86/140), respectively. The rates of serotype 19F and 19A in inpatients' group were significant higher than the ones in outpatients' group ($P<0.01$). The coverage rates of the vaccines in inpatients' group also exhibited significantly higher level ($P<0.01$). The non-susceptibility rates against penicillin, amoxicillin-clavulanic acid, imipenem, cefuroxime, cefaclor and trimethoprim-sulfamethoazole in inpatients' group (7.1%, 7.1%, 65.7%, 92.8%, 93.6%, and 85.0%) were higher than those of the outpatients' group (0.7%, 0.7%, 38.6%, 50.0%, 53.5%, and 65.7%).

Conclusions: The serotypes 19F and 19A were more frequent in *S.pneumoniae* isolates collected from pediatric inpatients than those from outpatients. The PCVs

could cover more inpatient isolates, which were determined more resistance against antimicrobials, especially the β-lactams.

ESPID-0510
Unallocated Posters

EMPOWERING YOUNG WOMEN AGAINST HIV/AIDS IN AFRICA - A GHANAIAN PERSPECTIVE

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Background: Since the emergence of HIV/AIDS in Ghana, the pandemic is on the ascendency even the current global effort to help prevent the further spread. In Ghana, young women are the highest victims of the pandemic.
Aim: This work is to empower young women to prevent the further spread of HIV/AIDS pandemic in Ghana and Africa continent.
Method: Fifty schools and thirty community groups from the ten regions in Ghana were selected for the study. Ten scientific study on HIV/AIDS and social work were also drawn from ten African countries representing Central, North, East, West and South Africa. Questionnaires, oral and written interviews and personal contact were used for the study. Methods were structured to access the awareness and knowledge level of HIV/AIDS among young women.
Result: Knowledge level of HIV/AIDS was very low. Seventy percent of young women could not identify one scientific mode of HIV/AIDS transmission as they attributed the spread to ancestral curse as a result of one's evil character. It was revealed, eighty percent of young women were not allowed by their parents to issues related to HIV/AIDS as parents considers such as taboo. Ninety percent of young women isolate themselves from Persons Living With HIV/AIDS (PLWHA). No effective community, private or public structure into HIV/AIDS and STI's
Conclusions: Public and private institutions should educate young women and parents on HIV/AIDS to increase their knowledge and awareness level to help them make informed decisions and healthier choices. Africa governments should allocate funds for comprehensive HIV/AIDS programme.

ESPID-0123
Unallocated Posters

MOLECULAR PREVALENCE OF TRANSFUSION TRANSMETTED VIRUS IN BETA THALASSEMIA CHILDREN

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Background: Recently a novel DNA virus transfusion transmitted (TT virus) has been identified in Japan and shown to be associated with elevated aminotransferase s levels after transfusion. However the exact role of TTV in pathogenesis of liver disease is yet to be established. The aim of this study was to determine the prevalence of TTV in thalassemia patients and its relationship with elevated alanine-aminotransfrase (ALT) and aspartate-aminotransfrase (AST). **Methods:** This cross-sectional analysis study was conducted on 452 thalassemia patients. Sera were collected from all of the patients, first ALT and AST levels were determined. Then, after DNA extraction, TTV DNA was amplified and detected using semi-nested PCR. **Results:** 160 of 452(35.40%) samples had TTV DNA detected by PCR. From 160 TTV DNA positive, 98(61.20%) were female and 62 (38.80%) of them were male(P=0.549).The mean ALT and AST values in TTV positive group were higher than in TTV negative group, and the difference was statistically significant ($p<0.0001$). **Conclusions:** The result showed that the prevalence of TTV in thalassemia patients in Jahrom is less than other studies in Iran and the mean ALT and AST values in TTV positive individuals were about 2 times more than in TTV negative individuals.

ESPID-0022
Unallocated Posters

OPEN GARBAGE DUMPS, A RISK FACTOR IN CANINE RABIES TRANSMISSION: CASE OF BIYEM-ASSI HEALTH DISTRICT IN CAMEROON

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Background

Rabies is a neglected enzootic disease caused by negative-stranded RNA viruses from the *Lyssavirus* genus. Free-roaming dog and stray dogs remain the main reservoir of the virus and the main vectors of the disease. In Cameroon, rabies disproportionately affects poor communities and particularly children. Human deaths caused by rabies are thwarted by the lack of community awareness. Therefore, a community KAP (knowledge- attitude-practice) study on risk factors of rabies was survey in Biyem-Assi health District.

Methods

Through a structured questionnaire, 420 heads permanent head household were interviewed. Overall 134 open garbage dumps were identified through a systematic check and observational method was used to characterize household wastes they contained. The approximate distance of each open garbage dumps to the nearest house was evaluated.

Results

About 35% of respondents knew the role of open garbage dumps in the increase of stray dog population. Most participants knew the role of dogs in rabies transmission as well as prophylaxis in case of bite. Overall solid household waste where stray dogs scavenging for food consisted of waste food. Stray dogs' nutrition places were wild garbage dumps (68.1%), markets (18.3%), and houses (13.6%). The feeding behaviour of stray dogs correlated significantly with the human rabies transmission ($Chi_2 = 154.12$, $df = 4$, $p < 0.05$).

Conclusions

Increased knowledge of respondents on rabies showed open garbage dumps and stray dogs as significant risk factors for canine rabies in Biyem-Assi Health District.

ESPID-0053
Unallocated Posters

ANTIBIOTIC SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE ISOLATED FROM PATIENTS WITH PNEUMOCOCCAL MENINGITIS

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Background and aims: Information about the serotypes' distribution and antibiotic susceptibility of pneumococci strains isolated from patients with pneumococcal meningitis in Uzbekistan.

Methods: The strains *of S. pneumoniae* were isolated from a cerebrospinal fluid of the patients aged from 3 month to 14 years and set up at the Tashkent City Hospital of Infectious diseases. The hospital has more than 40 pediatric admissions per week. Skilled personnel of the hospital performs lumbar punctures and collects in the laboratory collection point.

Results: 98 isolated strains *of S.pneumoniae* were successful for defining serotypes 1, 6A, 6B, 14, 17F, 19F**.** The sensitivity (> 90%) of *S.pneumoniae* strains remains to penicillin, cefotaxime and ceftriaxone (the minimal inhibitory concentration, MIC<2 mg/l). The culture of a pneumococcus with increased penicillin resistance in the range 0.5 <MIC<1 mg/l belonging to the serotype 6A, didn't show resistance to cefotaxime and ceftriaxone, but was resistant to co-trimaxozolum, ampicillin, oxacillin and to macrolides. All (100%) isolated strains of a pneumococcus were highly sensitive to vancomicin (MIC>1 mg/l).

Conclusions: Although present data suggests increased resistance of pneumococci to penicillin, however, according to our data, high sensitivity to penicillin still remains. The revealed serotypes of pneumococcus strains are part of pneumococcal vaccines and that proves the need of introducing children's vaccination against pneumococcal infections in a vaccination schedule of the Republic of Uzbekistan. The use of pneumococcal vaccines could prevent a substantial number of disease and deaths as well as decrease spread of multiresistant strains of pneumococci in Uzbekistan.

ESPID-0870
Unallocated Posters

SCIENTIFIC CENTER FOR CHILDREN'S HEALTH (MOSCOW): OUR EXPERIENCE OF VACCINATION OF CHILDREN AGAINST HEPATITIS B AT VARIOUS VIOLATIONS IN THE STANDARD VACCINATION SCHEME.

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In 2013, the Russian Federation was found in 1908 cases of acute hepatitis B, which was 1.3 cases per 100 thousand. Compared to 2004, the incidence rate decreased by 8 times, made possible by the mass immunization against viral hepatitis.
This is perhaps the most common of vaccinations. Unfortunately most often violated vaccination schedule is also hepatitis B. According to our data, 79% of vaccinated children had violations in the schedule, and only 21% had no deviations from standard (three doses) scheme. The main causes of disturbances in the scheme of vaccination against hepatitis B in children are: the refusal of parents to vaccinate, medical contraindications, non-compliance with the vaccination schedule parents and medical staff.
Were examined 124 children aged 1 to 6 years, first vaccinated against hepatitis B at birth and had significant deviations from the standard vaccination schedule. At the completion of vaccination to 3 years the level of antibodies to HBsAg was positive and significantly exceeds the value of 10 mIU/ml (in 56% of cases exceeded 1000 mIU/ml). At the completion of vaccination from 3 to 6 years in 34% of cases was not achieved protective level of seroconversion. The booster immunization was carried out only seronegative children. Blood tests revealed the high level (more than 1000 mIU/ml) of antibodies to HBsAg a month after the fourth dose.
In case of violation of the vaccination schedule more than 3 years is necessary to monitor the level of anti-HBs to address the booster dose.

ESPID-0026
Unallocated Posters

TRACHEAL COLONIZATION IN PRETERM INFANTS SUPPORTED WITH NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE

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Background: The aim of this study was to examine endotracheal bacteriological status in premature infants who are supported by nasal continuous positive airway pressure (CPAP) without any history of tracheal intubation.
Methods: In this prospective study,we enrolled 60 premature infants with respiratory distress; of these, 30 were supported by CPAP without tracheal intubation, and 30 were intubated and mechanically ventilated. Infants were enrolled at a postnatal age of <24 h. Endotracheal (ET) cultures were taken at 24 h and at the 5th day of life. In the CPAPgroup, a suction catheter was sterilely inserted into the trachea while directly visualizing the vocal cords using a laryngoscope.
Results: ET cultures taken on the 1st day of life showed colonization in 7/30 (23%) in the CPAP group versus 19/30 (63%) in the mechanically ventilated group (P = 0.002). Tracheal cultures on day 5 were positive in 5/30 (17%) and 11/30 (37%), respectively (P = 0.093). Klebsiella ssp. represented the most frequently isolated organism in both groups. A positive tracheal culture at 5 days was associated with a longer duration of respiratory support in the CPAP group (P = 0.05) but not in the ventilation group. Endotracheal culture at 5 days was associated with mortality in the ventilation group (8/11 vs 5/19, P = 0.02), but not in the CPAP group (1/5 vs 2/25, P = 0.45). Early endotracheal cultures did not relate with mortality in either of the groups.
Conclusion: The trachea of premature infants supported with CPAP is at risk for bacterial colonization. Predisposing factors, mechanisms and clinical implications of these novel findings need to be studied.

ESPID-0262
Unallocated Posters

HIGH PREVALENCE AND ANTIMICROBIAL RESISTANCE OF URINARY TRACT INFECTION ISOLATES IN FEBRILE YOUNG CHILDREN WITHOUT LOCALIZING SIGNS IN TAIWAN

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Backgrounds: Antimicrobial susceptibility data of current urinary tract infection (UTI) was very useful for physicians in selecting effective antibiotics in time and then improving outcomes of patients. This study was performed to determine the prevalence rate, bacteria distribution and antimicrobial susceptibility of urinary tract infection (UTI) in febrile young children at a teaching hospital in northern Taiwan.

Methods: From January 2011 to December 2011, all urinary isolates from suspected cases of UTI in febrile young children from 1 day to 36 months old visiting the Pediatric Emergency Room of Chang Gung Children's Hospital in Taiwan were identified by conventional methods. Antibiotic susceptibility was determined according to Clinical and Laboratory Standards Institute.

Results: A total of 5470 (78%) from 7009 eligible children were enrolled in this study, and 619 (11.3%) had a diagnosis of UTI. The most prevalent bacterium was *Escherichia coli* (68%) followed by *Klebsiella pneumonie* (8.1%) and *Proteus Mirabilis* (6.8%). Ampicillin, piperacillin and TMP-SMX showed higher resistance rate in the three predominant bacteriea. All tested bacteria showed higher resistance to ampicillin (79.3%) and trimethoprim-sulfamethoxazole (TMP-SMX) (44.1%), and lower resistance to cefazolin (17.7%) and gentamicin (13.0%). Fourteen percent of the isolates produced extended spectrum b-lactamase (ESBL), among which 93.33% were *E. coli* isolates.

Conclusion: The overall prevalence of UTI in this study was higher than previously reported in febrile children. Higher antimicrobial resistance was found in ampicillin and TMP-SMX. Among commonly used antibiotics, cefazolin and gentamicin are recommended to treat UTI in febrile children younger than three ages without localizing signs.

ESPID-0149
Unallocated Posters

IN SILICO PREDICTION OF HUMAN PROMISCUOUS MHC CLASS II RESTRICTED CD4+ T CELL EPITOPES IN THE PPE PROTEIN FAMILY OF MYCOBACTERIUM TUBERCULOSIS

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Background and aims. Tuberculosis (TB) is caused by infection with Mycobacterium tuberculosis (MTB), and is a major cause of morbidity and mortality worldwide. Despite the widespread use of the Mycobacterium bovis bacille Calmette-Guérin (BCG) vaccine, its true effectiveness has been debated for decades. In addition, sensitivity of the tuberculin skin test and the IFN-γ-release assay is suboptimal, and none of these tests distinguish between latent infection and active disease. Therefore, there is a pressing need to detect new TB antigens to develop effective vaccines and set up sensitive immunological assays. **Methods.** Through database access to protein sequences of the PPE protein family, some bioinformatics programs including SignalP4.1 server, SecretomeP 2.0 server, DAS server, and NetMHCII2.2 server were used to predict human promiscuous MHC class II restricted CD4+ T cell epitopes. **Results.** Ten promiscuous epitope peptides were identified, six from PPE8 and others from PPE12, PPE21 and PPE62. All ten bind to more than three human leukocyte antigen (HLA) molecules. **Conclusions.** Prediction analysis showed that these promiscuous epitope peptides may be important targets in subunit vaccines or diagnostic antigens against MTB. In addition, they could be used in immunological assays to evaluate the level of protection, the effect on pathology reduction, and the profile of cytokines and antibodies induced by them.

Table 1. Prediction of secretory proteins targeted to the non-classical secretory pathway

Gene name (H37Rv gene no.)	SecP score*	Predictive result
PPE8 (Rv0355c)	0.907728	Non-classically secreted protein
PPE12 (Rv0755c)	0.898589	Non-classically secreted protein
PPE21 (Rv1548c)	0.903741	Non-classically secreted protein
PPE39 (Rv2353c)	0.944247	Non-classically secreted protein
PPE62 (Rv3533c)	0.877718	Non-classically secreted protein

* Non-classically secreted proteins: SecP score >0.85

Table 2. Distribution of promiscuous CD4$^+$T cell epitopes

Peptide	Proteins on which the epitope polypeptides are located	Amino acid sequences of epitope polypeptides	Sites of epitope polypeptides (Length)	Alleles of Class HLA-II to which epitope polypeptides bind
p1	PPE8 (Rv0355c)	PQIPLLNFSLNIPVNIPIH	P2224-2242 (19aa)	HLA-DRB1*0901, HLA-DRB1*1501, HLA-DRB1*0701, HLA-DRB1*0405
p2	PPE8 (Rv0355c)	SGLFNMSLVAITTPALISG	P497-515 (19aa)	HLA-DRB1*0901, HLA-DRB1*1501, HLA-DRB1*0701, HLA-DRB1*0405
p3	PPE8 (Rv0355c)	HPAIISANRALFVSL	P106-120 (15aa)	HLA-DRB1*0701, HLA-DRB1*1101, HLA-DRB1*0301
p4	PPE8 (Rv0355c)	NSGLYNFATSSMGNSG	P2948-2963 (16aa)	HLA-DRB1*0901, HLA-DRB1*0701, HLA-DRB1*0405
p5	PPE8 (Rv0355c)	SPGFFNSTSAPSSGFF	P431-446 (16aa)	HLA-DRB1*0901, HLA-DRB1*0701, HLA-DRB1*0405
p6	PPE8 (Rv0355c)	VSGFYNTSAADFATP	P2384-2398 (15aa)	HLA-DRB1*0901, HLA-DRB1*0701, HLA-DRB1*0405
p7	PPE12 (Rv0755c)	TNSLRMYLGAGSRPLLAA	P11-28 (18aa)	HLA-DRB1*0901, HLA-DRB1*1501, HLA-DRB1*0701
p8	PPE21 (Rv1548c)	AASFSAVTSQLATGS	P42-56 (15aa)	HLA-DRB1*0901, HLA-DRB1*0701, HLA-DRB1*0405
p9	PPE21 (Rv1548c)	RGRLRSLVASNLLGQ	P114-128 (15aa)	HLA-DRB1*0901, HLA-DRB1*0701, HLA-DRB1*0405
p10	PPE62 (Rv3533c)	LVPFQQALQQLPNLGIGNI	P165-183 (19aa)	HLA-DRB1*0701, HLA-DRB1*0405, HLA-DPA1*0201-DPB1*0101

ESPID-0393
Unallocated Posters

HIV INFECTION,PREGNANCY AND RISK OF MOTHER-TO-CHILD TRANSMISSION: WHICH PROBLEMS ARE STILL TO FACE?

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Background: Over the past 20 years there has been an impressive progress in the reduction of mother-to-child transmission of HIV infection, mainly related to an increase in the use of antivirals during pregnancy and in the newborns and in delivery by elective cesarean section
Methods: We collect data from 123 HIV infected pregnant women followed in our Department from January 2005 to December 2014
Results: 98/123 pregnancies were followed till the delivery: 45/98 women were treated with HAART started before the conception or into the first 12 weeks of pregnancy and not always well tolerated. 96/98 delivered by cesarean (not elective in 19 of them) and 2 by vaginal delivery that was accidental in one of them and planned on the basis of high level of lymphocytes CD4+ and undetectable HIV-RNA in the other one. HIV vertical transmission rate was about 2%
Conclusions: In all countries where antiretroviral drugs are available and HIV infected pregnant women and their newborns are adequately managed, the mother-to-child HIV transmission rate can be kept almost entirely under control. Nevertheless, other problems remain to face: monotherapy regimens are needed for pregnant women with the aim to reduce the incidence of side effects of drugs and to obtain higher levels of adherence. Planned vaginal delivery should be offered to pregnant women taking HAART who are followed and have an undetectable HIV-RNA level, also considering the contraindications of cesarean section and the increased risks of morbidity associated with operative delivery in HIV infected mothers and infants

ESPID-0468
Unallocated Posters

INTERNATIONALLY ADOPTED CHILDREN: CLINICAL AND SEROIMMUNOLOGICAL SCREENING INTO AN INFECTIOUS DISEASES DEPARTMENT IN NORTHERN ITALY

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BACKGROUND AND AIMS Children adopted from developing countries are often inadequately immunized against vaccine-preventable diseases; poor or absent infant care due to low socioeconomic resources or growing in institutional settings contribute to increase potential risk for medical conditions. In the Department of Infectious Diseases-University of Pavia an outpatient Service is operative with the aim of evaluating noninfectious health problems and of screening for infectious diseases and immunity status of foreign born adoptees
METHODS From June 2007 to December 2014 94 adopted children and adolescents (aged from 6 months to 17 years) have been evaluated
RESULTS Most subjects were coming from Latin America (31.9%), Asia 26.6% and Africa (24.4%) . Two cases of HIV infection in African children and 1 of chronic HCV hepatitis in a Russian child were diagnosed. Just 40% of the screened patients resulted immunized against HBV infection but two Asiatic children had evidence of chronic HBV infection with HBsAg positive and impaired hepatic function. Although most children received adequate vaccine protection from tetanus and diphtheria, 15 cases not fully immunized against poliomyelitis and less than 50% of cases protected against measles, mumps and rubella were found. Moreover, multiple intestinal parasites were identified in about 56% of screened subjects
CONCLUSIONS Screening of infections for which internationally adopted children are at higher risk and assessment of adequacy of their vaccination record at the time of arrival are mandatory with the aim to cure them early, if needed, and to make their life safer in their new family.

ESPID-0018
Unallocated Posters

CO-INFECTIONS OF MALARIA AND GEOHELMINTHIASIS IN TWO RURAL COMMUNITIES OF NKASSOMO AND VIAN IN THE MFOU HEALTH DISTRICT, CAMEROON

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Human co-infection with malaria and helmimths is ubiquitous throughout Africa. Nevertheless, its public health significance on malaria severity remains poorly understood. A cross-sectional study was carried out to assess the prevalence of concomitant intestinal geohelminthiasis and malaria, and to evaluate its association with malaria and anaemia in Mfou. Finger-prick blood specimens from 263 participants aged 1-95 years were collected for malaria microscopy, assessment of haemoglobin levels, and molecular identification of Plasmodium species by PCR. Fresh stool specimens were also collected for the identification and quantification of geohelminths by the Kato-Katz method. The prevalence of malaria, geohelminths, and co-infections were 77.2%, 28.6%, and 22.1%, respectively. Plasmodium falciparum was the only malaria parasite species identified with mean parasite density of 111 (40; 18,800) parasites/µl of blood. The geohelminths found were Ascaris lumbricoides (21.6%) and Trichuris trichiura (10.8%), with mean parasite densities of 243 (24; 3,552) and 36 (24; 96) eggs/gram of faeces, respectively. Co-infections of A.lumbricoides and P.falciparum were the most frequent and correlated positively. There was a significant difference in the density of A.lumbricoides infection between the two localities ($P<0.05$). The overall prevalence of anaemia was 42%, with individuals co-infected with T.trichiura and P.falciparum (60%) being the most at risk. While the prevalence of malaria and anaemia were inversely related to age, schoolchildren aged 5-14 years were more susceptible to geohelminthiasis and their co-infections with malaria. Co-existence of geohelminths and malaria parasites in Nkassomo and Vian therefore enhances the occurrence of co-infections, and consequently, increases the risk for anaemia.

ESPID-0622
Unallocated Posters

INFLUENZA RELATED COMPLICATIONS AND DEATHS IN AUSTRALIAN CHILDREN: 7 YEARS OF SEASONAL SURVEILLANCE

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Background and Aims: Severe complications and deaths due to influenza in children were reported during the 2009 influenza A-H1N1 pandemic, however, there are few reports of serious complications and deaths in children during non-pandemic years. We describe severe influenza complications and deaths in children during 2008-2014.

Methods: National surveillance through the Australian Paediatric Surveillance Unit (APSU) 2008 to 2014, July to September each year, for children aged <15 years and admitted to hospital with severe complications of laboratory proven influenza. Information about presenting symptoms, pre-existing chronic conditions, vaccination, complications, treatment and outcome were reported by ~1350 paediatricians participating in APSU surveillance.

Results: A total of 371 cases were reported, including 18 deaths. The median age was 3 years (range: 0-14.8); 58.7% were boys. Most (280, 75.5%) had influenza A. Complications included pneumonia(65.9%), encephalitis(13.6%), myocarditis/pericarditis(4.2%), shock(3.2%), rhabdomyolysis(3.2%). Co-infection was reported in 15%. Of 371 children, 20(5.4%) were vaccinated for influenza. 139(37.4%) had pre-existing chronic conditions and 11(7.9%) of these were vaccinated. Eighteen children died (median age:6.8years). The highest number of deaths (n=6) was reported in 2012, 3 in 2009, 2 in 2010 and 2013, 1 in 2008 and 2014. Among the 18 deaths 10(56%) had pre-existing conditions including cerebral palsy and a variety of genetic syndromes; 8(44%) were previously healthy.

Conclusions: Although rare, serious influenza-related complications and deaths were reported every year 2008-2014, including among previously healthy children. Early diagnosis and treatment of influenza, and influenza vaccination especially among children with pre-existing chronic conditions, may prevent severe complications and deaths.