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Abstracts

# Selected Abstracts of the 2nd Congress of joint European Neonatal Societies (jENS 2017) • Session "Neonatal Infectious Diseases/Immunology"

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## ABS 1

## UPTAKE OF PERTUSSIS AND INFLUENZA VACCINES IN PREGNANCY

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### INTRODUCTION

Maternal immunisation may be a key strategy in reducing neonatal morbidity and mortality worldwide. In the UK, it is recommended that pregnant women receive one dose of pertussis-containing vaccine from 16-weeks gestation in addition to the annual influenza immunisation. Vaccine uptake remains poor, however, with considerable variation across the country. Our audit aimed to evaluate vaccine uptake at Barnet General Hospital, a district general hospital in London and explore factors influencing pregnant women's decisions to accept or decline immunisation.

### METHODS

A cross-sectional survey was conducted on 100 ethnically-diverse women over 18-years old on the postnatal ward in May 2016. A short, anonymised questionnaire was designed to collect data on patient demographics, vaccine status, awareness of recommended vaccinations, sources of information, and reasons for accepting or declining immunisation. Answers were cross-checked with patient notes (if recorded) to account for inaccuracy in self-reported vaccine status. Quantitative data was tabulated into Microsoft® Excel® and descriptive statistics calculated. Qualitative data from free text was manually analysed and divided into key common themes.

### RESULTS

Of the 100 participants, 32% had been vaccinated against pertussis and 36% against influenza during pregnancy. Of the women who had not been immunised with either vaccine, 63% (38/60) were aware of either programme but had still refused. The primary sources of information were GPs and/or midwives. The greatest barriers to uptake were paucity of information, particularly regarding the proposed benefits, uncertainty about potential risks to the fetus and lack of encouragement from professionals involved in their antenatal care.

### CONCLUSIONS

Uptake of both vaccines in this cohort was suboptimal. A significant proportion of women were either unaware, insufficiently informed or felt unsupported in taking these vaccinations. Therefore, we have implemented a series of changes focusing on improving education of relevant healthcare professionals, in order to ultimately boost patient knowledge and acceptance. New staff teaching sessions have been introduced and written information has been distributed specifically targeting those involved in antenatal care.

## ABS 2

## THE FREQUENCY OF MANNAN-BINDING LECTIN (MBL) DEFICIENCY IN PREMATURE BABIES AND THE EFFECT ON LONG TERM MORBIDITIES

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### INTRODUCTION

Mannan-binding lectin (MBL) is a plasma protein that has an important role in natural immune response and circulating MBL concentration is related to genetic variations in structural and promoter sites of MBL. The aim of this study is to detect the frequency of MBL deficiency and MBL gene polymorphism in premature babies aged less than 37 gestational weeks and to assess the MBL levels in terms of gestational age with consecutive measurements.

### METHODS

164 patients with gestational age 24-37 weeks, treated by hospitalization in neonatal intensive care unit between December 2012 and December 2014, were included in this prospective study. Weekly MBL levels of all babies were studied serially starting from the hospitalization date. An MBL level under 0.7 μg/ml was considered as deficient. MBL gene polymorphism was studied in all patients.

RESULTS

Serum MBL level was detected as low in 73 patients (44.5%) and genotype A/B or B/B was detected in 48% of these cases. MBL level was detected as low in all babies with a gestational age of 25 weeks. The rate of MBL deficiency was found to be 31% in babies aged above 37 weeks and it was observed that serum MBL levels were increasing in correlation with the gestational week. Neonatal sepsis rate was found as 31.5% in the babies with low MBL levels while it was found as 19.8% in patients with normal MBL levels however the difference was not statistically significant. Mean MBL levels were found as decreased in the cases with mortality compared to the cases without mortality. The rate of infection was detected significantly increased in cases with mortality. There was no significant relationship between the prematurity-related morbidities and serum MBL levels.

CONCLUSIONS

In this study, it was shown that MBL deficiency was seen in approximately half of the premature babies and MBL levels were increased in correlation with the gestational week and postnatal age. Lower serum MBL levels are related with higher infection and infection-related mortality rates and it was also shown that the MBL deficiency is observed physiologically in premature babies.

## ABS 3

## SEVERE COMBINED IMMUNE DEFICIENCY AND CONTINUED BREASTFEEDING: REPORT OF 5 OWN MOTHER'S MILK DONATION (OMM) AT THE REGIONAL ILE DE FRANCE MILK BANK

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INTRODUCTION

CMV seropositive mothers have to stop breastfeeding when severe combined immune deficiency is diagnosed. During an allogeneic stem cell transplant and gene therapy, breastfeeding is an additional mean of protection against secondary infections. It also helps maximizing the nutritional status.

METHODS

Between May 2013 and August 2014, the regional Ile-de-France (IDF) milk bank has pasteurized 5 milk samples of CMV seropositive mothers, whose child were placed in a sterile room. The Holder pasteurization (30 min at 62.5°C) and the bacteriologic milk analysis were conducted, following the 2008 good practices guide of the milk bank. A virological CMV analysis was also made on these milk samples.

RESULTS

The milk delivered was sterile and CMV negative whereas freeze milk contained CMV in 20% of cases. All 5 infants received their own mother's milk during their isolated period. Breastfeeding was continued even after coming back home.

CONCLUSIONS

All CMV seropositive mothers (50% of women in France) excrete CMV in their milk. Unlike freezing, pasteurization is the best way to stamp out CMV in human milk samples. We now initiate pasteurization for each mother's of SCID baby and have all ready pasteurized the milk of twelve mothers who could initiate and pursue breastfeeding. The contribution of milk banks should be more and more requested for promoting breastfeeding and thus favors the mother-child bond in case of sever combined immune deficiency.

## ABS 4

## MATERNAL CONTRIBUTION TO NEONATAL MICROBIOTA

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INTRODUCTION

It has been shown that first meconium is not sterile. Bacteria can reach the fetal gut through *in utero* swallowing of amniotic fluid. Bacteria of maternal digestive tract can reach amniotic fluid through the blood stream. It has been shown also that vaginal microbiota of mothers that delivered term and preterm infants are different, and that the use of intrapartum antibiotic modifies vaginal microbiota. The aim is to determine the bacterial source of first meconium of term and preterm infants.

METHODS

We included healthy term vaginal newborns and premature infants born at ≤ 32 weeks postmenstrual age. We collected vaginal swab prior to delivery, maternal stool and first meconium. All specimens were mixed with glycerol 1:1 and immediately frozen at -80°C until microbial DNA extraction. Microbial DNA extraction, 16S rRNA amplification and sequencing. We detected microorganisms present in meconium and those present in mothers. Microorganisms that are detected in meconium and mothers have a high probability to have maternal origin. The program calculates the chances of this origin be true. Source track is the name of the program [1].

RESULTS

We included 71 mothers and their respective newborns (vaginal swab, maternal stool and first meconium): 30 term/vaginal/no intrapartum antibiotic, 3 term/vaginal/intrapartum antibiotic, 11 preterm/vaginal/intrapartum antibiotic, 15 preterm/C-section/no antibiotic, 12 preterm/C-section/intrapartum antibiotic. Most (> 80%) of the meconium microbiota is derived from intestinal and vaginal maternal source in term and preterm infants regardless of type of delivery, gestational age or use of intrapartum antibiotic. Maternal intrapartum antibiotic decreases the frequency of *Lactobacillus* in the first meconium in term and preterm newborns. Diversity of meconium is different in term and preterm newborns.

CONCLUSIONS

Maternal vaginal and intestinal sources have similar importance for neonatal microbiota. Type of delivery and use of intrapartum antibiotic influence neonatal microbiota. The clinical significance of the neonatal microbiota for future health must be investigated.

DECLARATION OF INTEREST

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## ABS 5

## ANTIMICROBIAL ACTIVITY OF COPPER IN REDUCING ENVIRONMENTAL BURDEN IN A NEONATAL INTENSIVE CARE UNIT (NICU)

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INTRODUCTION

Neonatal infections are the most important cause of morbidity and mortality. Despite aggressive hand hygiene campaigns and routine cleaning, neonatal health-care associated infection (HCAIs) rates remain unacceptably high. It is proven that implementation of copper alloys on touch surfaces and objects in the Neonatal Intensive Care Units (NICUs) reduce the environmental bioburden. Objectives: To investigate the effectiveness of the application of antimicrobial copper alloys in a NICU in relation to the reduction of microbial flora.

METHODS

At a Level III Neonatal Intensive Care Unit of a pediatric hospital, with the capacity of twenty-six (26) incubators, antimicrobial copper was implemented on touch surfaces and objects. The copper alloy contains Cu 63% – Zn 37% (Lead Low). Microbiological cultures were taken in three different time periods, before and after the application of Cu+.

RESULTS

The reduction of microbial flora after the implementation of the antimicrobial copper on the selected surfaces and objects was statistically significant ($n = 15$, $p < 0.05$) and was recorded at 90%. The pathogens isolated at high rates (CFU/ml) prior to copper implementation were as follows: *Klebsiella spp.*, *St. epidermidis*, *St. aureus*, *Enterococcus spp.*

CONCLUSIONS

This study highlights the positive impact of antimicrobial copper and demonstrates that copper implemented surfaces and objects are effective in neutralizing bacteria, which are responsible for HCAIs in the nosocomial environment. The innovative implementation of antimicrobial copper in the NICU and the significant reduction of microbial flora, heralds the reduction of hospital-acquired infections, use of antimicrobial drugs and hospitalization time of premature babies.

## ABS 6

## ANTIBIOTIC EXPOSURE IN NEONATES AND IMPACT ON GUT MICROBIOTA AND ANTIBIOTIC RESISTANCE DEVELOPMENT: A SYSTEMATIC REVIEW

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INTRODUCTION

The gut microbiota is vital in the development of the immune system, digestive functions, protection against infections, and colonization resistance against antibiotic resistant bacteria. Antibiotics are the most commonly prescribed medications in neonatal units, but they can cause disruptions in the gut microbiota that are associated with necrotizing enterocolitis and several diseases later in life. Antibiotics also cause a selection pressure that favors antibiotic resistant bacteria. The aim of this study was to systematically review the impact of neonatal antibiotic treatment on changes in gut microbiota and/or antibiotic resistance development.

METHODS

We systematically searched PubMed, Embase, Medline, and the *Cochrane* Database using MeSH terms and text words. We supplemented this with manual searches of reference lists. Randomised controlled trials and observational studies were included if they provided data on different categories of intravenous antibiotic exposure (yes versus no, long versus short duration, and/or broad versus narrow spectrum) and changes in the gut microbiota composition and/or antibiotic resistance development in the neonatal period. Animal studies, case reports, and case series were excluded. Two reviewers assessed each potential study according to our criteria, extracted data, and evaluated risk of bias using the *Cochrane* Handbook, adapted to include observational studies.

RESULTS

From 3,380 unique citations, we identified three randomized controlled trials and 46 observational studies. Most studies were small and of poor to moderate quality. There was a significant association between prolonged antibiotic exposure and reduced microbial diversity in three observational studies. Five out of eight studies reported increased abundance of *Proteobacteria* among neonates with prior antibiotic treatment. Antibiotic exposure was associated with decreased prevalence and/or abundance of *Bifidobacteria* and/or *Lactobacilli* in three out of four studies. There were independent associations between extended-spectrum beta lactamase producing gram-negative bacterial colonization/infection and antibiotic treatment in two out of three studies, prolonged antibiotic treatment in three out of three studies, and broad-spectrum antibiotic treatment in three out of three studies.

CONCLUSIONS

Neonatal antibiotic treatment was associated with decreased proportions of beneficial bacteria in the gut microbiota, and prolonged treatment was associated with reduced microbial diversity. Neonatal antibiotic treatment, and especially prolonged treatment and broad-spectrum treatment, was associated with colonisation and/or infection with extended-spectrum beta lactamase producing gram-negative bacteria.

## ABS 7

## EFFECT OF CATHETER DWELL TIME ON RISK OF CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTION IN NEONATES IN A DEVELOPING HEALTHCARE SYSTEM

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INTRODUCTION

Despite the advances in neonatal care, late onset sepsis (LOS) and central line associated blood stream infections (CLABSI) remain common challenges contributing to significant mortality and morbidity, especially in very low birth weight infants (VLBW). The literature on the relationship between catheter dwell time and risk of infection in neonates is conflicting. No studies on this topic have been published from the Middle East where the care model and infection risks are likely to be different. The objective of this study is to assess the effect of catheter dwell time and the risk of CLABSI/LOS in the largest neonatal service in the UAE.

METHODS

A retrospective cohort study on infants admitted to NICU and stayed ≥ 72 hours during 2015 was conducted. The standard CDC definition for LOS with pathogenic organisms was used. A modified

**Table 1 (ABS 7).** Risk of central line associated blood stream infections (CLABSI) in relation to catheter dwell time from time of insertion.

| Time since insertion in weeks | Number of lines present | Number of CLABSI | Odds ratio compared to first week (95% CI) | p | Odds ratio compared to previous week (95% CI) | p |
|---|---|---|---|---|---|---|
| 1 | 445 | 3 | | | | |
| 2 | 325 | 19 | 9.15 (2.68-31.18) | < 0.001 | 9.15 (2.68-31.18) | < 0.001 |
| 3 | 129 | 9 | 11.05 (2.94- 41.45) | < 0.001 | 1.21 (0.53-2.74) | NS |
| 4 | 66 | 8 | 20.32 (5.24-78.77) | < 0.001 | 1.84 (0.67 -5.01) | NS |
| 5 | 36 | 4 | 18.42 (3.95-85.85) | < 0.001 | 0.91 (0.25-3.24) | NS |
| > 5 | 24 | 8 | 73.67 (17.85-304.03) | < 0.001 | 3.37 (0.44-4.06) | NS |

CLABSI : central line associated blood stream infections.

CDC definition for LOS and CLABSI was used to include sepsis with skin commensals, as it is not routine to do two cultures for each episode on our unit. Infection with a skin commensal was considered a CLABSI if there was no other site-specific infection and there were clinical and lab indicators for sepsis. Data was analysed using IBM® SPSS® version 23 utilizing appropriate univariate and multivariate analysis.

RESULTS

445 central venous lines were inserted in 281 (33%) of 852 eligible infants during the study period. 71% of infants who had a central line inserted were VLBW. 24% of the lines remained *in situ* beyond 14 days. Infants who had central lines inserted were of significantly lower gestational age and birth weight, had longer hospital stay, with lower survival and developed more LOS. Coagulase Negative Staphylococci were the most common organisms isolated in LOS (51.1%) and CLABSI (62.7%). The risk of CLABSI increased in the second week after catheter insertion and remained elevated for the rest of the line duration compared to the first week (**Tab. 1**). The mean time to line infection was 14.4 days (95% CI 9.6-19.2). On multivariate analysis with gestation and birth weight included the occurrence of a CLABSI significantly increased hospital stay by an average of 42 days ($p < 0.001$) but had no effect on survival.

CONCLUSIONS

The risk of CLABSI increased during the 2nd week after catheter insertion and then remained elevated until removal. The occurrence of a CLABSI significantly increased the length of hospital stay independent or birth weight or gestation. The increase in length of stay attributable to CLABSI in our study population is much higher than internationally reported figures and may be related to the unique characteristics of our patient population and the care model in the region.

## ABS 8

## 20 YEARS OF EARLY NEONATAL SEPSIS DUE TO *E. COLI*: SHOULD WE CHANGE EMPIRICAL ANTIBIOTIC THERAPY?

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INTRODUCTION

*E. coli* early-onset sepsis (EOS) is a major cause of mortality and morbidity in neonates, particularly in preterm newborns and those having a very low birth weight (VLBW). Over recent years, several studies have demonstrated an increase in neonatal *E. coli* EOS, especially in VLWB newborns, and an increase in antibiotic resistant *E. coli* strains.

METHODS

Epidemiological, clinical, and microbiological data from neonates with proven *E. coli* EOS from January 1994 to December 2014 were retrospectively collected in a single tertiary care hospital in Barcelona (Spain).

RESULTS

Seventy-eight *E. coli* EOS cases were analyzed. An increase in the incidence of *E. coli* EOS was observed during the study period, due to a rise in the term newborn group. Incidence in VLBW newborns remained stable, although it was the group with higher incidence and mortality. There was an increase in resistant *E. coli* strains causing EOS, with especially high resistance to ampicillin and gentamicin. Nonetheless, resistant strains were not associated with poorer clinical outcomes. There was no relationship between antibiotic resistance and mortality, gestational infection or intrapartum antibiotic use. Substantial diversity in the virulent traits and genetic lineages was found in *E. coli* causing EOS.

CONCLUSIONS

An overall increase in the incidence of *E. coli* EOS and antibiotic resistant *E. coli* strains was seen in our setting. Resistance to antibiotics commonly used as first-line therapy was particularly high and a cause for concern. There is an urgent need to reconsider the empirical therapy used in neonatal EOS, particularly in VLBW newborns.

## ABS 9

## COMPARISON OF THE INCIDENCE, CLINICAL FEATURES AND OUTCOMES OF INVASIVE CANDIDIASIS IN CHILDREN AND NEONATES

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INTRODUCTION

Invasive candidiasis differs greatly between children and neonates. Rare studies have compared invasive candidiasis in neonates with those in children. We aimed to investigate the different therapeutic approaches and their effects on treatment outcomes of these two groups.

METHODS

Episodes of neonatal invasive candidiasis were compared with non-neonatal pediatric episodes during a 12-year cohort study. Clinical isolates were documented by matrix-assisted laser desorption/ionization-time of flight mass spectrometry and DNA sequencing, and antifungal susceptibility testing was performed.

RESULTS

A total of 342 episodes of invasive candidiasis (113 neonatal and 229 non-neonatal pediatric episodes) in 281 pediatric patients (96 neonates and 185 children) were identified. *C. albicans* was the most common pathogen causing invasive candidiasis in neonates and children (47.8% vs. 44.1%). The antifungal susceptibility profiles were not significantly different between neonates and children. More neonates received amphotericin B as therapy, whereas more children received fluconazole or caspofungin. Compared with children, neonates had a significantly longer duration of fungemia, higher rates of septic shock (34.5% vs. 21.8%; p = 0.013), sepsis-attributable mortality (28.3% vs. 17.5%; p = 0.024) and in-hospital mortality (42.7% vs. 25.4%; p = 0.004) than children. Independent risk factors for treatment failure of invasive candidiasis were septic shock (odds ration [OR] 16.01; 95% confidence interval [CI] 7.64-33.56; p < 0.001), delayed removal of intravenous catheter (OR 6.78; 95% CI 2.80-17.41; p < 0.001), renal failure (OR 5.38; 95% CI 1.99-14.57; p = 0.001), and breakthrough invasive candidiasis (OR 2.99; 95% CI 1.04-8.67; p = 0.043).

CONCLUSIONS

Neonatal invasive candidiasis has worse outcomes than non-neonatal pediatric candidiasis. Neonatologists and pediatricians must consider age-specific differences when developing treatment and prevention guidelines, or when interpreting studies of other age groups.

## ABS 10

## HAND HYGIENE COMPLIANCE IN NICU; AN OBSERVATIONAL STUDY

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INTRODUCTION

The hands of health care workers (HCWs) are the most common source of transmission of pathogenic microorganisms between patients. Most hand hygiene opportunities occur during nurse-patient

**Table 1 (ABS 10).** Demographics characteristics and comparison of the duration of contact with the patient and hand washing between healthcare workers.

| | n (%) | The duration of contact with the patient | The duration of hand washing |
|---|---|---|---|
| | | mean ± SD | mean ± SD |
| **NICU workers** | | | |
| **Yes** | 49 (73.1) | 291.42 ± 207.98 | 10.57 ± 9.16 |
| **No** | 18 (26.9) | 184.16 ± 147.67 | 6.88 ± 5.77 |
| **Test and p** | | **t = 2.006; p = 0.049** | t = 1.588; p = 0.117 |
| **Health workers** | | | |
| **Nurse** | 35 (52.2) | 340.71 ± 216.23 | 12.82 ± 9.60 |
| **Doctor** | 29 (43.3) | 176.89 ± 138.89 | 6.65 ± 5.19 |
| **Technicians/Technicians** | 3 (4.5) | 180.00 ± 103.92 | 0.00 |
| **Test and p** | | **F = 6.649; p = 0.002** | **F = 7.345; p = 0.001** |
| **Gender of health workers** | | | |
| **Female** | 38 (56.7) | 293.28 ± 203.88 | 11.44 ± 10.00 |
| **Male** | 29 (43.3) | 222.41 ± 186.88 | 7.13 ± 5.25 |
| **Test and p** | | t = 1.461; p = 0.149 | **t = 2.106; p = 0.039** |

The independent t test was used to compare data. All statistical tests are based on a significance level of $p < 0.05$.

interactions. Observational studies have examined hand hygiene rates of health care workers in hospitals, and found that compliance scores vary between 40 and 78%. The aim of this study is to investigate the compliance of hand hygiene among the health care workers in neonatal intensive care units (NICUs) in a tertiary university hospital.

METHODS

The design of this study was open, non-participating observations, utilizing the standardized hand hygiene observational tool, developed and validated by WHO to investigate the hand hygiene compliance in health care providers. The observer was placed inside the NICU. Hand hygiene compliance of HCWs for "My Five Moments for Hand Hygiene" (MMH) of the WHO (which defines the key moments when health care workers should perform hand hygiene indications), was determined by observer. MMH identified in this strategy include (1) prior to patient contact, (2) prior to a clean or aseptic procedure, (3) after contact with body fluid, (4) after patient contact, and (5) after contact with the patient environment. All HCWs were observed once for 20 ± 10 minutes, according to acknowledged standards.

RESULTS

The duration of contact with HCWs in NICU was 291.42 ± 207.98 seconds and the mean duration of their hand washing was 10.57 ± 9.16 seconds, the duration of contact with HCWs who non-service hospital employees was 184.16 ± 147.67 seconds and the mean duration of their hand washing was 6.88 ± 5.77 seconds. It was found that the service workers had higher contact with the patient than the non-service health workers and the difference between them was statistically significant ($p < 0.05$). It was determined that the mean duration of nurses' hand washing had 12.82 ± 9.60 seconds, doctors had 6.65 ± 5.19 seconds and technicians had 0.00 seconds, and the difference between the groups was statistically significant ($p < 0.05$) (**Tab. 1**).

CONCLUSIONS

Effective hand hygiene for this survey was based on recommendations of WHO; when washing hands, wetting hands with water and applying enough soap to cover all surfaces, then rinsing hands with water (40 to 60 seconds). Although mean hand washing times of nurses are significantly higher, there is too lower of standards values of WHO. We have seen poor compliance with the hand washing times in the study. So we included educations instead of risking babies.

## ABS 11

## NEONATAL SEPTIC ARTHRITIS IN NICU

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INTRODUCTION

Septic arthritis in neonates is a relatively rare condition, but very serious and can have serious

consequences. Also, there are diagnostic challenges and delays as the presenting signs and symptoms differ from those found in older children.

METHODS

Out of 799 hospitalized neonates in our NICU during the year 2015, we are presenting five cases diagnosed with neonatal septic arthritis.

RESULTS

Amongst 5 patients included, 4 were born on term, and 1 preterm. The mean age at hospitalization was 16.4 days. The most common signs at presentation were joint edema, limited movements and local erythema. All patients had their white blood cells within normal range, while erythrocyte sedimentation rate and C-reactive protein were elevated, 70 (20-110) mm/h and 67.5 (23-96) mg/dL, respectively. Hemoculture resulted positive for *St. aureus* in one patient, while in the remaining four it was sterile. A single joint was affected in four patients, while one patient had two joins affected. Humeroscapular and hip joints were affected in two cases each, while knee and radiocarpal joint were affected in one patient. None of the patients was diagnosed with any other disease. Median time of hospitalization was 21.8 (17-25) days. All patients have been followed-up for more than 12 months and no sequelae are reported to date.

CONCLUSIONS

Even though a rare condition, neonatal septic arthritis requires carefulness while diagnosing and treating as a way in preventing lifelong disability.

## ABS 12

## CURRENT PRACTICE AND NEONATAL STAFF'S KNOWLEDGE ON ANTIBIOTIC USE AND ANTIBIOTIC STEWARDSHIP PROGRAMMES ACROSS TWO NEONATAL NETWORKS

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INTRODUCTION

High risk neonates with non-specific sepsis signs often need empirical antibiotic therapy. Whilst the benefits of antibiotics are unquestioned, inappropriate/excessive use of antibiotics is associated with adverse outcomes and emergence of multi-resistant organisms. Antimicrobial stewardship (AS) is a programme dedicated to improve, monitor and promote judicious use of antimicrobials involving coordinated interventions and multidisciplinary team approach (NICE 2015). Understanding the principles of AS is the key to reducing antibiotic exposure, microbial resistance and improve outcomes. We assessed awareness and knowledge of AS programmes amongst neonatal staff across two neonatal networks.

METHODS

A 10 point questionnaire based on the Start Smart-Then Focus AS Toolkit (Start Smart-Then Focus Antimicrobial Stewardship Toolkit for English Hospitals 2015, Public Health England) was designed to assess existing knowledge, awareness and understanding of the principles of AS including antibiotic prescribing practices. All medical, nursing and midwifery staffs involved in antibiotic prescribing and/or administration on neonatal units within the Central Newborn Network and Trent Perinatal Network were invited to complete the questionnaire.

A Survey Monkey link was emailed to all clinical leads to forward to their staff. The questionnaire was live for a 6 week period between 27th April and 5th May 2017.

RESULTS

10 out of 14 hospitals across the two networks responded. Of 201 responses, 73% were from level 3 neonatal units, 57% from qualified neonatal nurses, 15% from doctors and 28% from non-neonatal qualified nurses or midwifes. Even though 98% felt limiting antibiotic exposure is important, 60% of the respondents were unaware of AS programmes or guidelines on a local, regional, national or international scale. 54% felt antibiotics were prescribed frequently. Local antibiotic prescription practices including guidelines, route and communication were judged to be always or mostly appropriate. 25% felt the indication and review date documentation could be improved. Finally, 94% respondents believe the prescriber is the key person responsible for AS followed by the neonatal consultant (70%), the nurse or midwife administering the antibiotics (64%) and the microbiologist (61%).

CONCLUSIONS

The survey demonstrated a lack of awareness and understanding of AS programme by the front line staff involved in the prescription and administration of antibiotics. A targeted AS education programme will help raise awareness of key concepts, in an attempt to embed responsible antibiotic prescribing and administration into clinical practice.

## ABS 13

## S100-ALARMIN-INDUCED INNATE IMMUNE PROGRAMMING PROTECTS NEWBORN INFANTS FROM SEPSIS

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### INTRODUCTION

Neonatal sepsis is a major risk factor for childhood mortality. The high susceptibility of neonates to septic diseases has been linked to immaturity of innate immunity. This concept is based primarily on experimental studies that found impaired inflammatory responses of neonatal innate immune cells to microbial challenges. However, one hallmark of sepsis in newborns is an extremely rapid course with a hyperinflammatory immune response. This inconsistency between experimental and clinical findings is currently unresolved, which indicates that the molecular mechanisms of immaturity and postnatal maturation in the immune system are still unclear.

### METHODS

The response of human adult and neonatal monocytes to lipopolysaccharide (LPS) from gram-negative bacteria was analyzed using transcriptomic, epigenetic and immunological approaches. Birth-associated transcriptional programming by S100-alarmins was elucidated in cell culture models and verified in mice models of LPS and *St. aureus*-induced neonatal sepsis comparing wild-type (WT) and S100a9 knock-out (-/-) mice. S100A8/A9 serum levels were analyzed in a cohort of term and premature born infants and correlated with the incidence of sepsis.

### RESULTS

Human adult and neonatal monocytes were inversely regulated with respect to steady-state and LPS-induced transcription patterns. High amounts of the perinatal alarmins S100A8 and S100A9 specifically altered MyD88-dependent gene programs preventing hyper inflammatory responses without impairing pathogen defense. TRIF-adaptor-dependent regulatory genes were epigenetically silent and remained unaffected by perinatal S100 programming. They increased gradually during the first year of life, shifting immune regulation toward the adult phenotype. Disruption of this critical sequence of transient alarmins programming and subsequent re-programming of regulatory pathways increased the risk of hyper inflammation. S100 application at birth rescued S100a9-/- newborns from septic death. In human newborns, low S100A8/A9-level at birth was associated with an increased sepsis risk.

### CONCLUSIONS

Collectively, our findings suggest that the immune response of newborns is not impaired but differentially regulated. Alarmin-mediated programming at birth might be a transient protective mechanism in newborns that prevents harmful hyper inflammation without impairing antimicrobial protection. Treating neonates at high risk for sepsis with S100 alarmins might be a valuable preventive option.

## ABS 14

## HUMAN BREAST MILK SUPPLIES NEWBORN INFANTS WITH HIGH AMOUNTS OF S100-ALARMINS PROTECTING FROM SEPSIS

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INTRODUCTION

Breast milk (BM) has beneficial effects on the incidence of infectious diseases and immunological development. Underlying mechanisms are only partly understood. We previously showed that massive release of S100A8 and S100A9 at birth plays a key role in regulating neonatal innate immune responses. They prevent excessive inflammation and fatal sepsis. Direct antimicrobial effects have also been reported, but only for the heterodimer S100A8/A9 at high concentrations.

This study was to assess whether BM contains S100A8/A9 that – *via* the enteral route – has regulatory and/or antimicrobial activity relevant for the pathogenesis of neonatal sepsis.

METHODS

Ninety-seven BM samples stratified for gestational age, mode of delivery and days after birth were analyzed for S100A8/A9. Antimicrobial activity was assessed in growth inhibition tests with pathogens relevant for neonatal sepsis. Development of gut microbiota was compared between wild type (WT) and S100a9 knockout (-/-) mice. Effects of enteral application of S100-alarmins were tested in a neonatal sepsis model.

RESULTS

S100A8/A9 were massively elevated in BM after birth. Levels were significantly higher after term birth compared to preterm birth and after vaginal delivery compared to caesarean section. BM inhibited the growth of *St. aureus*, *E. coli* and *Group B Streptococci* by the presence of S100A8/A9. In fecal samples of S100a9-/- mice, aerobic bacteria were already detectable from day 1 of life whereas in WT mice they could not be found before day 10 of life. Enterally applied S100a8/a9 and S100a8 protected S100a9-/- mice from hyperinflammation and fatal septical courses.

CONCLUSIONS

BM supplies neonates with significant amounts of S100A8/A9 contributing to the protective properties of BM by reducing risk of neonatal sepsis and influencing intestinal colonization via antibacterial and immune-regulatory effects. Our data provide first evidence for supplementation of formula with S100-alarmins as a new option to decrease infectious morbidity and mortality in neonates and to influence developing gut colonization.

## ABS 15

## PREDICTORS OF MORTALITY IN NEONATAL SEPSIS

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INTRODUCTION

Neonatal sepsis remains one of the leading causes of mortality both among term and preterm infants. Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection affected multi system organ. It is confirmed on positive culture of blood from sterile site. There are different outcomes between clinically diagnosed and proven sepsis. The aim of study is to define the case fatality rate of neonatal sepsis and to analyze the predictors of mortality outcome among neonates with sepsis in a level 2 Neonatal Unit.

METHODS

Medical records of neonates with sepsis, admitted to Kariadi Hospital between January and December 2015, were retrospectively reviewed. The diagnosis of neonatal sepsis was based on clinical condition and the result of laboratory examination. All subjects

**Table 1 (ABS 15).** Predictors of mortality in neonatal sepsis.

| Condition | Deceased n = 19 (%) | Surviving n = 67 (%) | OR (95% CI) | p |
|---|---|---|---|---|
| **Assisted labour** | 12 (14.0) | 42 (48.8) | 1.02 (0.35-2.93) | 0.970 |
| **Apgar score < 7** | 19 (22.1) | 44 (51.2) | 0.69 (0.59-0.82) | 0.003 |
| **Low birth weight** | 18 (20.9) | 37 (43.0) | 14.59 (1.84-115.70) | 0.002[a] |
| **Preterm delivery** | 18 (20.9) | 40 (46.5) | 12.15 (1.53-96.47) | 0.004[a] |
| **Bleeding disorder** | 9 (11.5) | 2 (2.6) | 15.51 (3.55-67.68) | 0.000[a] |
| **Leukocytosis or leukopenia** | 5 (5.8) | 1 (1.2) | 23.57 (2.55-217.71) | 0.000[a] |
| **Thrombocytopenia** | 10 (11.6) | 4 (4.7) | 17.5 (4.52-67.75) | 0.000[a] |
| **Elevated CRP** | 14 (16.3) | 39 (45.3) | 2.01 (0.64-6.22) | 0.221 |
| **Positive blood culture** | 11 (12.8) | 21 (24.4) | 3.01 (1.05-8.58) | 0.035[a] |

Chi-square, [a]significant.

underwent a blood culture. Proven sepsis is defined as a positive blood culture in the presence of clinical signs and symptoms of infection. Normally of data was analyzed by Kolmogorov-Smirnov. Statistic analysis was performed using Chi-square test.

RESULTS

There were 86 subjects, consisted of 41 male and 45 female babies. The frequency of positive blood culture was 37.2% in neonatal sepsis. The mortality of 12.8% was seen in proven sepsis and significant statistically, OR 3.012 (95% CI 1.057-8.580; p = 0.035). Low birth weight, preterm delivery, bleeding disorder, leukopenia, thrombocytopenia and positive blood culture were higher risk factors of mortality in neonates with sepsis ($p < 0.05$) (**Tab. 1**).

CONCLUSIONS

Case fatality rate of neonatal sepsis is 22.1%. Low birth weight, preterm delivery, bleeding disorder, leucopenia, thrombocytopenia and positive blood culture are associated with mortality in neonates with sepsis.

## ABS 16

## DIAGNOSTIC VALUE LYMPHOCYTE TO NEUTROPHIL RATIO IN PRETERM INFANTS WITH LATE ONSET SEPSIS

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INTRODUCTION

Sepsis is a complicated and still a big problem to both developed and developing countries. Nosocomial late-onset sepsis (LOS) mortality and morbidity in premature infants are even higher in the best neonatal intensive care units (NICU). The diagnosis of sepsis in the infants is difficult because most of the signs of sepsis are associated with uncertain and other noninfectious conditions. The lymphocyte to neutrophil ratio (LNR) is an easily accessible marker that has been reported to represent disease severity in adult trials. We aimed to investigate the potential association between lymphocyte to neutrophil ratio (LNR) on diagnosis of culture proven nosocomial sepsis and clinical prognosis.

METHODS

This prospective trial was conducted in the level III NICU at Tepecik Training and Research Hospital, between January 2014 and January 2015. Preterm infants with birth weights ≤ 1,500 g and/or ≤ 32 gestational weeks were eligible for the study. Exclusion criteria included major congenital anomalies, congenital infections, infants born to mothers with clinical chorioamnionitis or who had early onset neonatal sepsis, perinatal asphyxia, and patients in a terminal state. The postnatal age of all included infants were over 3 days with clinical and laboratory signs of sepsis. According to the results of blood cultures, the studied infants were classified into 2 groups: the culture-proven septic and suspected septic one. Demographic characteristics, laboratory data, as well as mortality were noted.

RESULTS

A total of 127 infants were involved in the study; 57 culture proven sepsis, 75 suspected sepsis. There were no significant differences between groups regarding gestational age, gender, birth weight, delivery mode and postnatal age. LNR was significantly decreased in culture-proven septic preterm infants when compared separately to suspected septic infants ($p < 0.001$). There were no significantly differences between laboratory findings.

CONCLUSIONS

Our study highlights the role of LNR in LOS. This is the only study investigating the association between LNR and LOS in preterm infants. We concluded that it is a reliable and sensitive marker in detecting sepsis in preterm infants. It is easy to assess and can also provide an early warning of culture positive sepsis in preterm babies.

## ABS 17

## C-REACTIVE PROTEIN: AN ADJUNCT OR DILEMMA FOR DIAGNOSIS OF NEONATAL MENINGITIS

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INTRODUCTION

The estimated incidence of early onset neonatal bacterial meningitis is 0.3 per 1,000 live births. Despite frequent lumbar puncture in neonatal units, the yield is very low [1]. CRP is one of markers

**Table 1 (ABS 17).** Indicators for lumbar puncture.

| | Always | Sometimes | Never | Others | No comment |
|---|---|---|---|---|---|
| **Clinical assessment of baby alone** | 25 | 18 | 2 | 1 | 3 |
| **Clinical condition and elevated CRP** | 22 | 25 | 2 | 1 | 5 |
| **Clinical Condition, elevated CRP and leukocytosis/ leukopenia** | 19 | 24 | 3 | 0 | 5 |
| **Clinical Condition, elevated CRP, leukocytosis/leukopenia and thrombocytopenia** | 22 | 19 | 4 | 0 | 4 |
| **Elevated CRP alone** | 1 | 24 | 19 | 0 | 5 |
| **Positive blood culture and positive bacterial PCR with or without clinical correlation** | 26 | 17 | 0 | 0 | 5 |

to decide lumbar puncture [2]. The question arises whether we should perform LP in a clinically well baby on the basis of high CRP.

METHODS

A questionnaire based survey was acquired from General Paediatric consultants, Neonatologists and Paediatric specialty consultants who are working nationwide in all 3 levels of neonatal units or tertiary referral centers who look after neonates with sepsis. The questionnaire enquired about indications for lumbar puncture in clinically well neonates with raised CRP.

RESULTS

Response rate was 50% (n = 48 out of 96). Twenty-six general Paediatricians, fourteen Neonatologists and two Neurologists responded while 6 were anonymous. The results are shown in **Tab. 1**. Only seven of 42 clinicians base their decision on any form of international guidelines (as we do not have so far any national guideline) while 7 did not comment on this question. Only 8 clinicians recommend change in guidelines, while no suggestions are given by any clinician.

CONCLUSIONS

Most clinicians employ CRP as a complementary indicator to clinical decision rather than sole determinant of lumbar puncture in otherwise well babies. However many clinicians do use it sometimes to gear the decision. Absolute solution can only be yielded after outcome of lumbar puncture justifies the role of CRP, by conducting further audits.

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## ABS 18

## CHARACTERIZATION OF RESISTANCE PLASMIDS DURING A NOSOCOMIAL EPE-OUTBREAK USING OPTICAL DNA MAPPING

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INTRODUCTION

Resistance to antibiotic drugs increases worldwide and bacterial plasmids are extensively involved in the spread of resistant genes. Diagnostic tools that can trace the transmission of the plasmids may therefore be of great importance. We aimed to examine the plasmids carrying the resistance gene, in an outbreak of ESBL-producing *Enterobacteriaceae* (EPE) in a neonatal intensive care unit (NICU). The examination included how the plasmids evolved with time in each patient and the spread of the plasmids between different species of bacteria. We also aimed to evaluate the

use of optical DNA mapping as a diagnostic tool for tracing transmission of bacterial plasmids in a nosocomial outbreak.

METHODS

Plasmids originating from EPE-samples collected during an NICU outbreak and repeatedly two years after the patients' discharge were studied by optical DNA mapping in nanofluidic channels. This method reveals the number of plasmids in a sample, their size, the presence of resistance genes as well as a fingerprint that can be used for tracing and characterization of the plasmid.

RESULTS

Seventeen patients were colonized with EPE bacteria at the outbreak. Isolates from 16 of them were studied with the optical mapping method. All patients initially carried ESBL-*K. pneumoniae* that contained two plasmids, 80 kb and 220 kb. In all patients, the ESBL-gene was present on the 80 kb plasmid. The same two plasmids were identified also in follow-up samples and the ESBL-gene was still located on the 80 kb plasmids (**Fig. 1**). In follow up samples, some patients also carried an ESBL-*E. coli* that had a plasmid of size 130 kb. In this strain, the ESBL-gene was not present on the plasmid DNA, suggesting that it had been transferred to the chromosomal DNA.

CONCLUSIONS

We identified 3 main plasmids, in *K. pneumoniae* (2) and *E. coli* (1), during the EPE outbreak in our NICU. The optical mapping method showed that only in the *K. pneumoniae* strain was the resistance plasmid borne. Optical mapping showed to be a rapid and detailed method for detection of plasmids that carry antibiotic resistant genes in clinical samples.

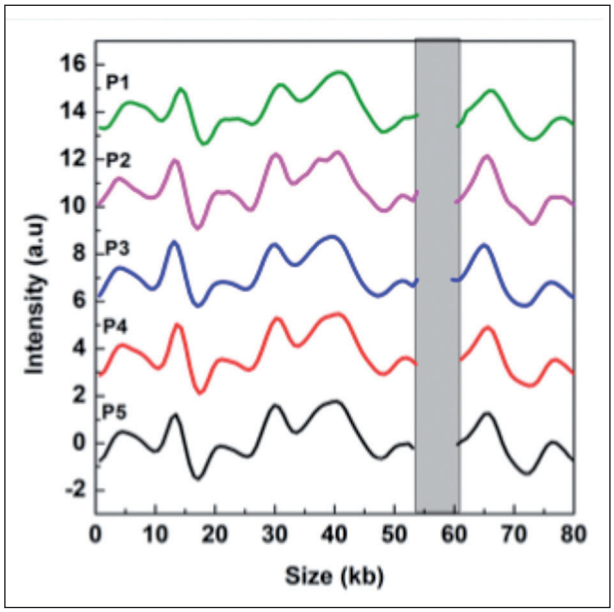


**Figure 1 (ABS 18).** Barcodes of the 80 kb plasmids from five of the patients where the grey area indicates the position cut by Cas9.

## ABS 19

## NEONATAL INTESTINAL COLONIZATION WITH ESBL-PRODUCING ENTEROBACTERIACEAE – A 5 YEAR FOLLOW UP STUDY

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INTRODUCTION

Our aim was to characterize *K. pneumoniae* isolates from a neonatal outbreak of ESBL-producing *Enterobacteriaceae* (EPE) and to determine duration of such intestinal colonization in affected subjects.

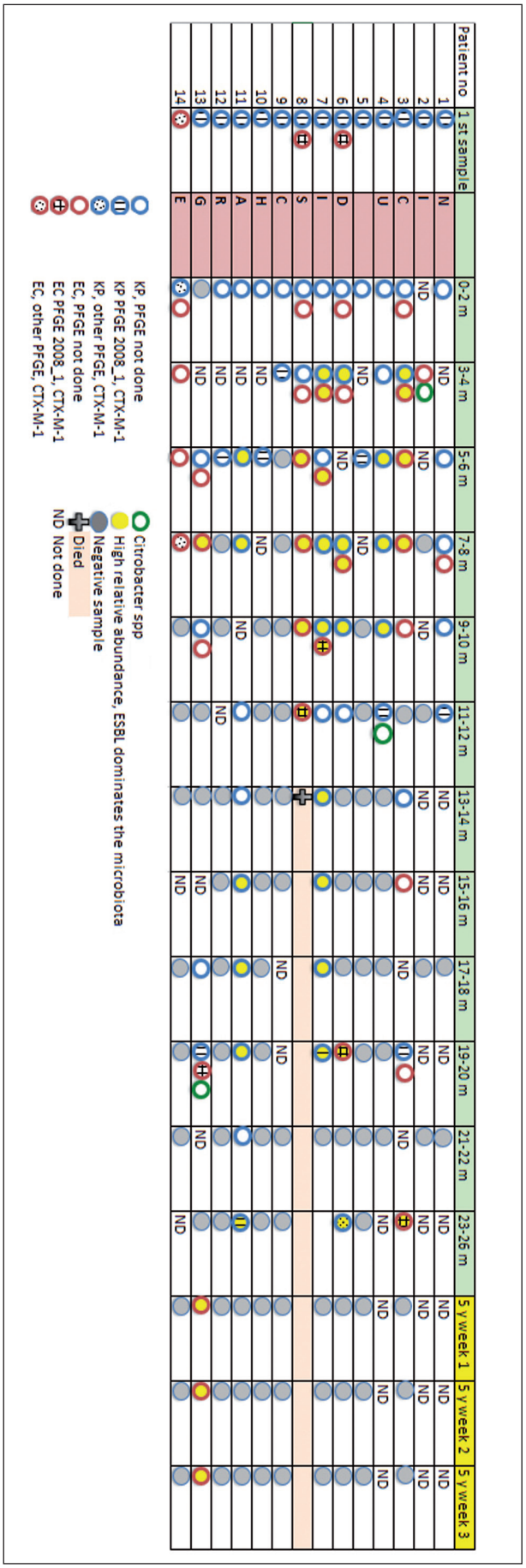
METHODS

A prospective cohort study of 14 neonates affected by an outbreak of ESBL-producing *K. pneumoniae* (ESBL-KP) in two neonatal intensive care units (NICUs). Whole genome sequencing (WGS), MLST and cgMLST, PFGE and molecular identification of blaCTX-M were performed on the first isolates of the outbreak. Stool cultures were performed every second month after discharge from NICU until two years of age and final cultures were performed at five years-of-age. The last positive samples were analysed with PFGE and blaCTX-M. The intestinal relative abundance of ESBL-producing Enterobacteriaceae was determined in each carrier.

RESULTS

In total, 13 patients were colonized with the same strain type of ESBL-KP, sequence type ST 101. This strain harboured the K29 capsule type and the blaCTX-M 15 gene. The virulence genes as irp1,

**Table 1 (ABS 19).** Colonization time of EPE.




irp2, iutA, kfu and mrk were detected in all isolates. The median length of colonization was 12.5 months (range 5-68). Three (23%) out of 13 children were carriers of ESBL-KP/ESBL-EC at two years of age. At five years of age one child was colonized with ESBL-EC. The colonization time of EPE and the relative abundance of the strains can be seen in **Tab. 1**. No child suffered from an EPE-infection during the follow-up.

## CONCLUSIONS

Three of thirteen children were still carriers of EPE two years after neonatal colonization and two of them carried the moderately virulent, highly resistant ESBL-KP strain ST 101. One child was still colonized with ESBL-EC at five years-of-age.

## ABS 20

## DNA VIRUSES: THEIR ROLE IN ACUTE RESPIRATORY INFECTIONS IN NEONATAL UNIT IN TUNISIA

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## INTRODUCTION

Acute respiratory infections (ARIs) in children and neonates are mainly caused by RNA viral pathogens. DNA viruses such as Adenovirus (AdV) and Bocavirus (BoV) are also defined in these infections. The aim of this study is to characterize ARIs induced by AdV and BoV in neonates from the Sousse area of Tunisia.

## METHODS

A total of 211 Tunisian neonates aged 0-28 days were enrolled. Patients were hospitalized for ARIs in the service of neonatology in Farhat Hached University-Hospital of Sousse from September 30, 2013 to December 31, 2014. Nasopharyngeal aspirates were collected by special physicians for the rapid diagnosis of respiratory syncytial virus (RSV) infection. The QIAsymphony Sp automated

and the QIAsymphony DSP virus/Pathogen Mini Kit (QIAGEN) were used for the total nucleic acids extraction according to the manufacturer's instructions. For the detection of respiratory agents the FTD Respiratory pathogens 21 Kit (Fast-Track Diagnostics) was performed which allows the identification of 21 pathogens including AdV and BoV.

RESULTS

AdV was detected in 10% of tested samples and was more prevalent in male cases with 57.1% from total infections. AdV infection in tested neonates was found to reach the third place after respiratory syncytial virus (RSV A/B) and rhinovirus (RV). In more than 2/3 of AdV infections, multiple detections were identified. Co-infections with AdV were described mostly with RSV A/B and RV (3 co-infections each). Mono-infection with AdV was detected in 5 neonates (23.3%). Considering BoV infection, 6 patients (2.84%) were positive in which only one of them was female. Multiple infections with BoV were detected in 50% of total BoV infections and 2 of them were co-infected with RV. AdV seasonality spreads in winter with a peak of infection between January and February 2014. On the contrary, BoV infection is fluctuating throughout the study period with 2 infections reported in the summer.

CONCLUSIONS

ARI caused by respiratory DNA viruses are important in neonates. AdV was found to be one of the most agents responsible for hospital admission. The difference of seasonality observed between AdV and BoV permits physicians to take further prevention and to avoid nosocomial transmissions between hospitalized neonates. Including clinical manifestations of the enrolled population and studying the association between viral infection and clinical profile of patients should be reported in perspectives.

## ABS 21

## OUTCOMES OF CONGENITAL CYTOMEGALOVIRUS DISEASE FOLLOWING MATERNAL PRIMARY AND NON-PRIMARY INFECTION

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INTRODUCTION

Maternal immunity to cytomegalovirus (CMV) prior to pregnancy cannot be viewed as protective in terms of CMV fetal damage and subsequent sequelae. Natural history and long-term prognosis of congenital CMV disease according to maternal primary versus non-primary infection are not clearly documented. The aim of this study was to investigate clinical, laboratory and neuroimaging features at onset and the long term outcome of congenitally CMV-infected patients born to mothers with non-primary infection compared with a group of patients born to mothers with primary infection.

METHODS

Consecutive neonates born from 2002 to 2015 were considered eligible for the study. Maternal infection was classified as primary or non-primary according to the results of CMV serological test performed prior and/or during pregnancy. Patients underwent clinical, laboratory and instrumental investigation, and audiologic and neurodevelopmental evaluation at diagnosis and during the follow up. Infants were included in the study in the presence of certain classification of maternal CMV infection, complete data at diagnosis and during the observation period, and if the follow up was > 1 year. Patients with other perinatal infections or other chronic concomitant diseases were excluded.

RESULTS

A cohort of 158 congenitally infected children was analysed. Ninety-three were born to mothers with primary CMV infection (Group 1) and 65 to mothers with a non-primary infection (Group 2). Eighty-eight infants had a symptomatic congenital CMV disease: 49 (46.2%) in Group 1 and 39 (60%) in Group 2. Maternal and demographic characteristics of patients of Group 1 and Group 2 were comparable, with the exception of prematurity and a 1-minute Apgar score less than 7, which were more frequent in Group 2 compared to Group 1. CMV-related clinical signs and symptoms at onset are reported in **Tab. 1**. Prevalence of neuroimaging findings did not significantly differ between the two groups. An impaired neurodevelopmental outcome was observed in 23.7% of patients of Group 1 and in 24.6% cases of Group 2. Similarly, the frequency of hearing loss did not differ between the two groups (25.8% versus 26.2%, respectively).

CONCLUSIONS

Neurodevelopmental and hearing sequelae are not affected by the type of maternal CMV infection. Our data point up that CMV prevention strategies should target both mothers not immune to CMV than those

**Table 1 (ABS 21).** Signs and symptoms of congenital cytomegalovirus (cCMV) infection at onset in 88 symptomatic patients divided according to the type of maternal CMV infection.

| Features | Group 1: maternal primary infection (n = 49) | Group 2: maternal non-primary infection (n = 39) | P |
|---|---|---|---|
| Severe onset | 42 (85.7) | 35 (89.7) | 0.5 |
| Microcephaly | 6 (12.2) | 11 (28.2) | 0.06 |
| Small for gestational age | 12 (24.5) | 11 (28.2) | 0.7 |
| Neurologic signs | 7 (14.2) | 13 (33.3) | 0.03 |
| Liver involvement with cholestasis | 11 (22.4) | 8 (20.5) | 0.8 |
| Skin signs/petechiae | 5 (10.2) | 8 (20.5) | 0.8 |
| Thrombocytopenia | 5 (10.2) | 11 (28.2) | 0.02 |
| Pathological newborn hearing screening test | 14 (28.6) | 15 (38.5) | 0.3 |
| Abnormal HUS [a] | 34/48 (70.8) | 30/38 (78.9) | 0.4 |
| Abnormal brain CT [a] | 28/46 (60.9) | 21/33 (38.7) | 0.8 |
| Abnormal brain MRI [a] | 27/44 (61.4) | 29/35 (82.8) | 0.06 |

Values are expressed as numbers and percentages.
[a] Not available in all cases.

with a preconceptional immunity, and raise the need of universal newborn screen as a major tool for a prompt diagnosis of congenital CMV infection.

## ABS 22

## LONG TERM FOLLOW UP OF HEARING DISORDERS IN PATIENTS WITH CONGENITAL CYTOMEGALOVIRUS INFECTION

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### INTRODUCTION

It is well known that children with congenital cytomegalovirus (cCMV) infection are at high risk for hearing impairment. Sensorineural hearing loss may present at birth, progress in severity, or develop later in cCMV patients. This means that a proportion of children with cCMV do not present hearing loss until after the newborn period. Aim of this study was to evaluate the long term audiological outcome of a large series of cCMV infected patients according to the presence or absence of symptoms at onset and according to antiviral treatment.

### METHODS

The study was conducted at the Perinatal Infection Unit of the University Federico II of Naples (Italy), a tertiary care hospital with a dedicated multidisciplinary team. All patients with a diagnosis of cCMV received periodical clinical and laboratory evaluation, fundoscopy, audiometry, and psychometric examination up to a patient age of 6 years. Patients underwent serial standard audiological evaluations to detect transmissive and sensorineural hearing loss, every 3-6 months until the age of three years, and every 6-12 months later. Hearing loss was defined as air conduction thresholds > 30 decibels (dB), in conjunction with normal middle-ear function and was considered as sensorineural, if the air-bone gap was less than 10 dB.

### RESULTS

168 patients (mean observation period 4.4 ± 2.5 years) were included: 110 symptomatic and 58 asymptomatic patients. Seventy-one symptomatic cases received antiviral therapy. 53/110 (39%) symptomatic patients had a monolateral or bilateral hearing impairment at onset. Treated infants had a higher prevalence of severe hearing loss compared to untreated patients. The overall prevalence of hearing impairment at last examination was 23%. Among symptomatic patients, hearing impairment was more frequent in treated compared to untreated patients (47% versus 18%; $p < 0.05$). None of 58 asymptomatic patients had hearing deficit at last observation. In only 3 (5%) of them we observed a fluctuating mild hearing impairment during the follow up. Time to negativization of urinary CMV DNA did not differ between patients with normal hearing and those with at least one pathological hearing evaluation (**Fig. 1**).

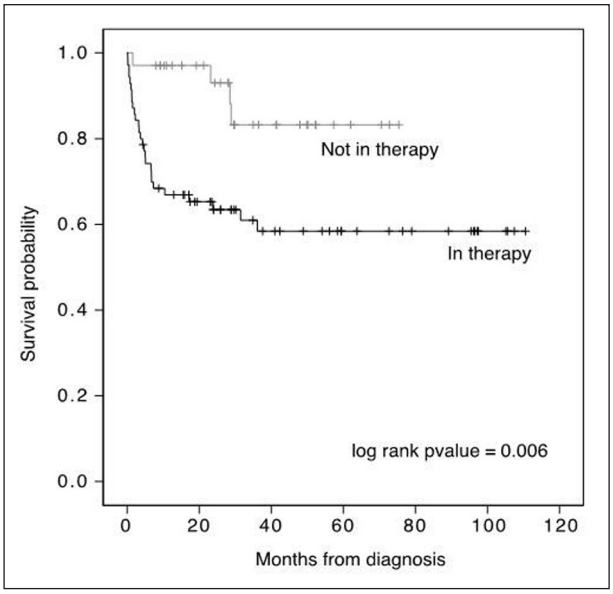


**Figure 1 (ABS 22).** Kaplan Meier curves showing the probability of remaining free from severe hearing impairment in patients with congenital CMV infection stratified by therapy.

CONCLUSIONS

Prevalence of hearing impairment in cCMV infection varies according to the study. Continued monitoring of hearing function is mandatory mainly in children with symptomatic cCMV infection and central nervous system involvement at onset. In case of symptomatic patients without neurologic involvement or in asymptomatic cases the risk to develop hearing loss seems to be very low.

## ABS 23

## REVIEW OF ADVERSE VACCINE REACTIONS IN AN IRISH NEONATAL UNIT

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INTRODUCTION

The primary immunisation schedule in Ireland at the time these babies were inpatients of our neonatal unit included 6 in 1 vaccine and PCV vaccine at two months of life. Since October 2016 the Men B vaccine and Rotarix oral vaccine are included in the schedule. In official Health service documents an adverse event following immunisation (AEFI) is defined as "any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease." Our neonatal unit admits babies from 26 weeks gestation. Babies who are inpatients at 60 days of life will receive their first childhood immunisations here.

METHODS

We looked at babies who received their first 6 in 1 and PCV vaccines in the neonatal unit between 2013 and 2015. Notes were analysed and the following were documented: birth gestation, birth weight, Apgar, gestation at vaccine, weight at vaccine. We reviewed medical notes for any adverse event documented, type of event and action taken. We were interested in identifying which babies had documented adverse reaction after first vaccines. We wanted to see if vaccines had been clearly prescribed and if administration of the vaccines had been clearly documented in the medical notes. We did a chart review to see if an adverse reaction had occurred and what steps were taken following identification of this.

RESULTS

16 babies were included. One baby had first vaccine administered at a different institution and was excluded. The birth gestation ranged from $24^{+6}$ to $29^{+5}$ weeks and birth weights between 650 g and 2.45 kg. Six babies had events post vaccination documented as adverse vaccine reaction (**Tab. 1**). Three of these babies had elevated temperatures secondary to vaccine documented. The highest temperature recorded was 37.7°C. Paracetamol was administered in all three cases. None of these babies had a septic work up (SWU) done. One baby had increased desaturations and bradycardias 11 hours post vaccine. He required SWU and IV antibiotics. A second baby had apnoea requiring IPPV which occurred 7 hours post vaccine. He was described as floppy, appeared septic looking. This baby had SWU done and was started on IV antibiotics. A third baby was described as lethargic 19 hours post vaccine and had a SWU and IV antibiotics.

CONCLUSIONS

Mild adverse reactions such as local reaction at injection site are common. There was no association found between weight and adverse reactions and no correlation between gestation and adverse event. Adverse events secondary to vaccine administration in this patient group are relatively uncommon. Vaccines were clearly prescribed. There was clear documentation in all 6 charts of babies with recognised adverse event and clear management plan. In 4 charts it was not documented in the

**Table 1 (ABS 23).** Characteristics of the six babies who had events post vaccination documented as adverse vaccine reaction.

| Patient | Birth gestation | Birth weight | Gestation vaccine | Weight at vaccinations | Required septic work up, y/n |
|---|---|---|---|---|---|
| 1 | $26^{+2}$ | 920 g | $36^{+2}$ | 2.8 kg | Y |
| 2 | $27^{+4}$ | 1.03 kg | $37^{+3}$ | 2.78 kg | Y |
| 3 | $24^{+6}$ | 670 g | $35^{+1}$ | 2.15 kg | N |
| 4 | $29^{+1}$ | 1.02 kg | $37^{+4}$ | 2.05 kg | N |
| 5 | $27^{+6}$ | 1.01 kg | $37^{+4}$ | 2.71 kg | Y |
| 6 | $27^{+1}$ | 1.07 kg | $35^{+3}$ | 2.32 kg | N |

doctors notes that vaccines had been administered. It is important to clearly identify babies which will be at increased risk of adverse reaction, particularly babies less than 28 weeks gestation and of note all 3 babies who required SWU were less than 28 weeks gestation. Best practice guidelines to be introduced to our unit to standardise management of babies with adverse event post vaccines.

## ABS 24

## DOES DURATION OF BLOOD CULTURE REPORTING IMPACT ON THE CARE OF NEONATES AT RISK OF EARLY ONSET NEONATAL SEPSIS?

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### INTRODUCTION

A large numbers of well babies are identified in our unit as having risk factors for early onset sepsis (EONS) as per NICE guidance. Although NICE recommends blood culture reporting within 36 hours we noted that this target was not being reached. In this study we planned to evaluate the mean time for blood culture reporting and identify reasons for the delay in blood culture reporting with an aim to reduce the duration of antibiotics and length of stay amongst term infants at risk of EONS.

### METHODS

Retrospective observational study of all neonates greater than $36^{+6}$ weeks gestation who were deemed to be at risk of neonatal sepsis, and were born between the 30/06/2014 and 27/07/2014 were included. Eligible neonates were identified through the postnatal ward paediatric and handover diaries, and BadgerNet. Data collection was performed using patient notes and ICE. Data was entered into an Excel® proforma, and then analysed.

### RESULTS

A total of 420 babies were born who were greater than $36^{+6}$ weeks gestation. 58 were assessed to be at risk of EONS, 3 were excluded due to incomplete data. Gestation at birth ranged from $37^{+0}$ to $42^{+2}$, and average birth weight was 3,467 g, (range 2,160-5,420 g). Results are displayed in **Tab. 1**. 60% of our cohort were deemed at risk of EONS but were eligible for their antibiotics to be discontinued at 36 hours; their average duration of antibiotics was 3 days, length of stay 4 days, and the time between taking and reporting BC results 48 hours. A 12 hour delay in BC reporting could partially explain the prolonged duration of antibiotics, and length of stay. Using the data from this study a business case was developed for a point of care (POC) BC machine to be installed within the neonatal unit, and the trust have approved the request.

### CONCLUSIONS

Neonates who are at risk of EONS but not septic, should have their antibiotics discontinued within

**Table 1 (ABS 24).** Results comparing duration of antibiotics, length of stay, and time between taking and reporting of BC in all neonates and those receiving antibiotics for less than 5 days.

| | All neonates | | | Those receiving antibiotics for < 5 days | | |
|---|---|---|---|---|---|---|
| | Mean | Median | Range | Mean | Median | Range |
| Duration of antibiotics (days) | 4 | 4 | 2-8 | 3 | 3 | 2-4 |
| Length of stay (days) | 5.7 | 5 | 3-23 | 5.3 | 4 | 3-23 |
| Time between BC being taken and report becoming available (hours) | 50.8 | 48 | 36-96 | 51.8 | 48 | 36-96 |

36 hours, to reduce antibiotic associated morbidity and expedite discharge. Delay in BC reporting prolongs both duration of antibiotics and length of stay. POC BC machines could reduce both of the above. We plan to re-evaluate the impact a POC BC machine has within our department once installed.

## ABS 25

## A *CANDIDA TROPICALIS* OUTBREAK DURING EL NIÑO IN A NEONATAL INTENSIVE CARE UNIT IN SOUTHERN PHILIPPINES

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### INTRODUCTION

During El Niño, the Philippines experiences prolonged dry periods. It affects epidemiological pattern of diseases, increasing the incidence of water borne, water washed and vector borne illnesses. On September 2015, El Niño commenced in the Pacific. On January 2016, the drought drained the main water source of Zamboanga City in southern Philippines. The drought had an impact on agriculture, food and water supply, sanitation and health conditions of residents. On March 2016, the Zamboanga City Medical Centre (ZCMC) water supply was affected. We report an outbreak of *C. tropicalis* fungemia in the hospital Neonatal Intensive Care Unit (NICU) during this period.

### CASE REPORTS

The setting of the outbreak is a 500 bed tertiary public hospital with a 40 bed NICU. With the onset of drought in the Zamboanga City, the hospital outsourced water delivered via trucks and stored in inflatable rafts as makeshift containers. On the first week of March 2016, an outbreak of diarrhea from rotavirus contaminated water supply killed 9 and affected 1,500 patients. On March 28, 2016, the initial case of culture proven *C. tropicalis* fungemia at the ZCMC NICU was detected. A full term 4,150 g newborn delivered via spontaneous vaginal delivery admitted for complications of asphyxia neonatorum. On assisted mechanical ventilation, the patient developed recurrent bouts of health care associated infections needing treatment with broad spectrum antibiotics. On the fourteenth day of life, the patient developed pallor, respiratory distress with platelet counts < 100,000/uL. The blood culture grew *C. tropicalis*. Despite treatment with fluconazole, the patient expired. Subsequently a total of eleven cases of culture proven *C. tropicalis* fungemia were documented. **Tab. 1** shows the case characteristics. The mean birth weight of cases was 1.66 ± 0.97 kilograms. The mean gestational age of the cases was 33 ± 4 weeks ranging from 28-40 weeks. Majority of cases were prematures with only three full term infants. The mean age from birth to onset of fungemia is 16 days. Thrombocytopenia was a constant feature among all the cases. Most of the cases underwent treatment with broad spectrum antibiotics, endotracheal intubation with assisted ventilatory support and umbilical vein catheter placement. All *C. tropicalis* growths were sensitive to fluconazole. All cases received intravenous

**Table 1 (ABS 25).** Characteristics of 11 cases of culture proven *C. tropicalis* fungemia.

| No. | Birth weight (kg) | Gestational age (weeks) | Days from birth to onset of fungemia | Use of broad spectrum antibiotics | Platelet count < 100,000/uL | UVC | ET | Antifungal treatment | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 4.15 | 40 | 14 | + | + | - | + | fluconazole | Expired |
| **2** | 2.78 | 40 | 16 | + | + | + | - | fluconazole | Expired |
| **3** | 1.2 | 32 | 15 | + | + | + | - | fluconazole | Survived |
| **4** | 1.4 | 34 | 24 | + | + | + | + | fluconazole | Expired |
| **5** | 1.14 | 32 | 26 | + | + | + | + | fluconazole | Expired |
| **6** | 1.29 | 32 | 32 | + | + | + | + | fluconazole | Expired |
| **7** | 1.34 | 32 | 20 | + | + | + | + | fluconazole | Expired |
| **8** | 1.08 | 32 | 13 | + | + | + | + | fluconazole | Expired |
| **9** | 1.06 | 28 | 8 | + | + | + | - | fluconazole | Expired |
| **10** | 1 | 28 | 7 | + | + | + | + | fluconazole | Expired |
| **11** | 1.89 | 38 | 10 | + | + | - | + | fluconazole | Survived |

UVC = umbilical vein catheter; ET = endotracheal intubatiion.

fluconazole. Supportive care, mechanical ventilation and platelet concentrate transfusions were provided. During this period, the NICU underwent cleaning and disinfection twice. Only two patients survived. Multiple environmental culture samples from patients' beddings, incubators, sinks, warmers, table tops, air ducts, ventilators, refrigerators, breast milk samples and staff hands were obtained but yielded no growth. The last documented case was on June 10, 2016. It coincided with the onset of rainfall and the restoration of the city water supply. To prevent recurrence a NICU contingency plan was developed including priority provision of safe water supply during crisis, regular cleaning and disinfection, active disease surveillance, antibiotic stewardship, breastfeeding support and hand washing.

CONCLUSIONS

El Nino is capable of magnifying all community health problems. The simultaneous rotavirus and *C. tropicalis* outbreaks highlight the correlation between fecal coliform water levels with levels of other disease agents including candida species. Immunocompromised NICU patients are very vulnerable to these agents. Appropriate measures should be developed to address this potential problem.

## ABS 26

## CONGENITAL CYTOMEGALOVIRUS INFECTION – NEONATAL ASPECT

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INTRODUCTION

Timing for diagnosis of congenital cytomegalovirus infection is one of the most important factors as positive CMV at birth or during the first 2 weeks of age confirms prenatal infection of the baby. CMV is detected by direct isolation of the virus in urine or saliva using electronic microscopy – the quickest and the most reliable method for early verification of this infection. Diagnosis can be confirmed by PCR method, as well. To recognize congenital CMV without previous information about the mother's infection is very difficult but yet possible for experienced clinical neonatologists. Aim of the study was to find out what are the most frequent clinical signs that were recognized at first clinical assessment in children later diagnosed as congenital CMV infection.

METHODS

It is a clinical study held at neonatal department of the Institute for Children and Youth Health care of Vojvodina in Novi Sad, Serbia during 10 years period.

RESULTS

There were 27 neonates with congenital CMV infection, meaning less then 1% of all hospitalized term newborn. All of them had been diagnosed after delivery. Clinical signs are very discrete. The most important signs are paleness or jaundice of the skin, rash, reduced fat tissue, reduced birth weight and length SGA, microcephaly, hepatomegaly, poor feeding, hypotonia, lack of spontaneous motility, lethargic behavior. The main reasons for serological and PCR testing were: jaundice, reduced fat tissue, poor gaining on weight and pathological neurological neonatal assessment. Clinical signs are very discrete. The most characteristic signs were: small for gestational age (100%), neonatal jaundice (88.88%) and hypotonia (85.18%). The leading clinical problem that induces their hospitalization was poor feeding and poor gaining on weight (74.07%).

CONCLUSIONS

It is of great importance to recognize discrete signs of illness as they can lead to proper differential diagnosis. If congenital CMV is diagnosed, then we should as soon as possible begin modern therapeutic approach toward baby and afterward follow up carefully psychomotor development, apply early treatment if necessary in order to prevent serious neurological problems and psychomotor retardation.

## ABS 27

## DIAGNOSTIC VALUE OF SERUM AMYLOID A IN NEONATAL BACTERIAL INFECTIONS AND ASSOCIATIONS WITH CIRCULATING HIGH DENSITY LIPOPROTEIN (HDL) AND CYTOKINE LEVELS

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INTRODUCTION

Early diagnosis of neonatal bacterial infections is of great importance. Studies in animals and human

adults have shown that serum amyloid A (SAA) is an acute phase protein predominantly produced by hepatocytes after induction by proinflammatory cytokines. It circulates as an apoprotein, complexed to high density lipoprotein (HDL). SAA has been proposed as an early marker of neonatal bacterial infections; however relevant studies are few with conflicting results. The aim of this study was to evaluate the role of SAA as a marker of neonatal bacterial infections and its associations with HDL and cytokine levels.

METHODS

SAA levels were determined by immunonephelometry in 98 term neonates (gestational age 38.5 ± 1.3 weeks, birth weight 3,148 ± 454 g) at 16.4 ± 6.7 days of life. Sixty five neonates presented with clinical signs and symptoms of sepsis, according to the diagnostic criteria of late onset sepsis for neonates with postmenstrual age of ≤ 44 weeks proposed by the European Medicines Agency in 2010. Thirty-three healthy neonates, of similar postnatal age and gender distribution to patients, consisted the control group. SAA levels were serially measured on days 1, 2, 3-5 and 7-10 of hospitalization in all patients, and once in controls. Associations of SAA with positive cultures for bacteria, as well as with serum CRP, IL-1b, IL-6, TNF-a and HDL levels were assessed.

RESULTS

Blood, urine and/or CSF cultures were positive for bacteria in 30/65 patients. Median ($25^{th}$-$75^{th}$) SAA levels (mg/L) were significantly higher in culture-positive group on day 1 (224.5 [102.0-405.0]), day 2 (239.0 [57.8-512.5]), day 3-5 (34.5 [10.1-151.4]) and day 7-10 (4.0 [4.0-5.6]) in comparison with culture-negative group (12.0 [4.5-38.2], $p < 0.0001$; 8.8 [4.0-46.2], $p < 0.0001$; 4.0 [3.5-9.0], $p < 0.0001$; 3.5 [3.5-4.0], $p = 0.023$; respectively] and controls (3.5 [3.5-4.0], $p < 0.001$ for days 1, 2, 3-5 and $p = 0.005$ for day 7-10). SAA levels on admission correlated positively with CRP ($rs = 0.885$, $p < 0.0001$), IL-6 ($rs = 0.622$, $p < 0.0001$) and IL-1b ($rs = 0.286$, $p < 0.05$), but negatively with HDL levels ($rs = -0.567$, $p < 0.0001$). ROC analysis of SAA levels resulted in significant areas under the curve (AUC) for detecting culture positive neonates on admission (AUC = 0.930 [95% CI 0.867-0.992], $p < 0.0001$).

CONCLUSIONS

SAA can be used as a diagnostic marker of bacterial infections in term neonates in routine clinical practice. At the acute phase of infection, SAA levels are positively associated with IL-6 and IL-1b, but negatively with HDL levels. Whether the results of this study are applicable to infants with early onset sepsis, or born prematurely, should be further evaluated.

## ABS 28

## CONGENITAL TUBERCULOSIS AS A RESULT OF DISSEMINATED MATERNAL DISEASE. IS CORRECT THE ACTUAL MANAGEMENT?

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INTRODUCTION

Although tuberculosis is highly prevalent worldwide, congenital tuberculosis is one of the least common manifestations of the disease. The diagnosis is usually difficult because of the non-specific clinical presentation.

CASE REPORT

Preterm infant born at $24^{+1}$ weeks of gestation to a mother with a severe case of disseminated tuberculosis who was treated from $24^{+6}$ weeks of gestation with first-line antituberculous drugs: ethambutol, pyrazinamide, isoniazid and rifampicin. A cesarean was practiced due to premature rupture of membranes and severe oligohydramnios. The newborn infant was transferred to the neonatal unit due to mild respiratory distress. Initially he was connected to continuous positive airway pressure and then nasal cannulas as respiratory support. He was immediately started prophylaxis with isoniazid. Cultures obtained and Quantiferon test were performed, both of them were negatives. At ten days of age he developed a severe respiratory distress with bilateral alveolar infiltrates and required mechanical ventilation. PCR was positive for *M. tuberculosis* in bronchoalveolar and gastric aspirate. He was treated with a four-drug regimen (isoniazid, rifampicin, pyrazinamide and amikacin) during 2 months and then completed 12 months with isoniazid and rifampicin.

CONCLUSIONS

Few cases have been reported of congenital tuberculosis and in preterm infants it is extraordinary. The clinical manifestations of our patient coincide with those reported in the literature [1]. Central nervous system involvement is variable but can be as high as 20%, in our patient it was negative. The diagnosis was confirmed with a positive PCR

for *M. tuberculosis* in bronchoalveolar and gastric aspirate. The recommended treatment includes a four-drug anti-TB regimen for the first 2 months, followed by a two-drug regimen to complete a total of 12 months. The disease should be suspected in neonates that present respiratory distress, fever and hepatomegaly in the first 3 months of life and with radiological studies revealing a familiar pattern in the lung and in the newborns born to mothers with active TB. The importance of this case is the bad evolution of the disease in this newborn in spite of the correct treatment with isoniazid and the lack of reliability of the Quantiferon test in this type of patients because of immaturity of their immune system.

REFERENCE

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## ABS 29

## NEONATAL SEPSIS: FREQUENCY, RISK FACTORS AND OUTCOME IN A LEVEL II NICU UNIT

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INTRODUCTION

Despite progress made in the care for newborn infants in modern neonatal intensive care units (NICUs), neonatal sepsis is still an important cause of morbidity and mortality among newborns and an important issue for public health care services. The spectrum of bacteria involved in the neonatal sepsis and their sensibility to antimicrobial therapy varies from country to country ant is continuously changing. Treatment possibilities are often limited by the rapid emergence of species resistant to antibiotic therapy.

METHODS

The aim of this paper is to analyze the bacteriological profile of neonatal infections in our unit, the risk factors for their onset, the diagnostic possibilities and outcome. We conducted a retrospective study on a three-year period; 1,080 newborn infants admitted to "Dominic Stanca Clinical Hospital" s NICU were investigated.

RESULTS

44 babies (8%) were diagnosed with sepsis; only 27 had positive blood cultures; *Pseudomonas spp.* and *E. coli* were the most frequently isolated bacteria. One case developed meningitis and 5 cases septic shock. The mortality rate was 4.5%. Male gender and gestational age below 31 weeks were the main risk factors.

CONCLUSIONS

Gram negative neonatal sepsis remain a major risk factor for neonatal morbidity and mortality.

## ABS 30

## LUMBAR PUNCTURE SUCCESS & FAILURE IN A TERTIARY NEONATAL UNIT – A PROSPECTIVE COHORT STUDY

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INTRODUCTION

Published success rates for neonatal lumbar puncture (LP) are 48-60%, and lower in certain subgroups. Unsuccessful procedures often necessitate repeat LPs, prolonged courses of antibiotics and extend hospitalisation.

METHODS

Demographic, procedural and laboratory data for LPs on neonatal and postnatal wards were collected prospectively over 54 days. Medical notes were reviewed for details of additional procedures and subsequent management/complications.

RESULTS

Forty-seven infants had 52 separate indications for LP, requiring 73 procedures, each involving up to 5 attempts. In comparison with 2010 audit data (pre-NICE guidance), we estimated that the number of LPs per year had increased by 27%. 81% of indications were 'raised CRP' (> 25 mg/L), and for 92%, antibiotics had started before the LP. A quarter of indications required > 1 procedure, and 48% of procedures involved > 1 attempt. During first LPs, CSF which was deemed interpretable (e.g. red cell count < 25,000) was obtained for 55% of indications, rising to 82% after multiple procedures. Success rates were lower when preterm or < 3 days old, but were not affected by doctor seniority. 44%

of LPs triggered altered antibiotic prescriptions. Babies with no/uninterpretable CSF samples were usually treated with 14-21 days' IV antibiotics, necessitating an additional length of stay in half of cases.

CONCLUSIONS

LP success rates were similar to those previously published. Methods to enhance LP success could potentially reduce unnecessary procedures, treatments, complications, and length of stay.

DECLARATION OF INTEREST

MS was a co-investigator on an investigator-initiated research grant from Pfizer (2012-2015). Other authors: none declared.

## ABS 31

## THE EARLY ONSET RISK CALCULATOR TO EVALUATE EARLY-ONSET SEPSIS IN INFANTS BORN ≥ 35 WEEKS GESTATION

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INTRODUCTION

Blood culture-proven early-onset sepsis (EOS) occurs in 10% of newborns who receive empiric antibiotics. We aimed to compare our current CDC 2010 risk-based guideline with the Neonatal Early Onset Risk Calculator (NEORC) [1] to determine if any cases of EOS in infants born ≥ 35 weeks' gestation would be missed and if the utilization of unnecessary antibiotics could be reduced.

METHODS

Retrospective audit of obstetric factors and clinical signs, investigations and antibiotic treatment in infants born ≥ 35 weeks' gestation from January-June 2016 at the Royal Women's Hospital, a tertiary perinatal centre with > 7,700 annual deliveries. The calculated NEORC score stratified infants into 3 risk groups (treat empirically, observe and evaluate, continued observation).

RESULTS

3,716 infants ≥ 35 weeks' gestation were born over 6 months, of whom 157 (4.3%) were evaluated for EOS (blood culture, FBE, CRP) and treated with empiric benzyl penicillin and gentamicin. GBS was isolated from one blood culture (EOS rate 0.34/1,000 live-births). Application of the NEORC would have resulted in only 58/137 (42%) being evaluated and treated for possible EOS, an absolute reduction of 58%.

CONCLUSIONS

Compared with a risk-based EOS guideline, the NEORC reduced the proportion of infants born ≥ 35 weeks' gestation treated with antibiotics by ~60%, without missing any cases of EOS. Implementation of the Neonatal EOS risk calculator should be considered in routine neonatal care.

REFERENCE

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## ABS 32

## HOSPITALISATION FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN PREMATURE INFANTS BORN IN MULTIPLE BIRTHS

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INTRODUCTION

Premature birth is a well-recognised risk factor for respiratory syncytial virus (RSV) hospitalisation (RSVH) in early childhood. It has also been reported that infants from multiple births are associated with a higher incidence of RSVH and higher healthcare costs. However, there is a recognised association between multiple births and prematurity, which confounds potential analysis in this area. This retrospective study aimed to provide novel data on the link between RSVH and multiple births, alongside trying to identify any influence that prematurity exerted in this relationship.

METHODS

Data from the Information Services Division (ISD) of the NHS National Services Scotland was utilised for this study, covering all National Health Service hospital care within Scotland. All live births from 2000-2011 were identified and included in the study. RSVHs within the first two years of life were assessed through the use of ICD 10 codes (J12.1, J12.8, J12.9, J18.0, J18.9, J20.5, J20.9, J21.0, J21.9, J22). Results were stratified by RSVH, the number of births in that pregnancy, and prematurity (< 37 weeks' gestational age [wGA] at birth). Rates per 1,000 live births were calculated.

**Table 1 (ABS 32).** Link between RSVH, gestational age and multiple births.

| | Premature with RSVH (n = 4,692) | Premature with no RSVH (n = 39,999) | Full-term with RSVH (n = 24,048) | Full-term with no RSVH (n = 555,002) |
|---|---|---|---|---|
| **Incidence rate of RSVH within premature and full-term groups (%)** | 10.5% | - | 4.2% | - |
| **Mean birthweight (g)** | 2,046 | 2,311 | 3,419 | 3,467 |
| **Mean gestational age at birth (weeks)** | 33 | 34 | 39 | 40 |
| **Rate per 1,000 (relative rate vs. respective no RSVH cohort)** | | | | |
| **Singleton** | 774.3 (0.99) | 784.3 (1.00) | 983.3 (1.00) | 985.4 (1.00) |
| **Multiple** | 225.7 (1.05) | 215.7 (1.00) | 16.7 (1.14) | 14.6 (1.00) |

## RESULTS

A total of 623,741 births were included of which 28,740 infants (4.6%) had a RSVH. As expected, the multiple birth rate was higher in the premature group than the full-term group (216.8 vs. 14.7 per 1,000). For infants with RSVH, however, the rate of multiple births was even higher than in their counterparts without RSVH whether born prematurely (225.7 vs. 215.7 per 1,000) or at full-term (16.7 vs. 14.6 per 1,000) (**Tab. 1**). Compared to full-term infants without RSVH, the rate of multiple births in premature infants with RSVH was 15 times higher. Premature infants with RSVH had lower mean birthweight (2,046 vs. 2,311 g) and GA at birth (33 vs. 34 wGA) than premature infants without RSVH.

## CONCLUSIONS

Higher rates of RSVH were found in infants born in multiple births irrespective of GA. This study demonstrates that multiple birth is a possible risk factor for RSVH in its own right, albeit there is a strong link with prematurity and other associated risk factors for RSVH.

## DECLARATION OF INTEREST

JC and RT have received research funding and/or compensation as advisor/lecturer from AbbVie. SB, BRG and JF, working for Strategen, have previously received payment from AbbVie for work on various projects. CM is an employee of ISD Scotland which received payment from AbbVie for data extraction and analysis.

## FUNDING STATEMENT

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## ABS 33

## ANTIBIOTICS FOR EARLY ONSET NEONATAL SEPSIS: AUDITING PRACTICE AND ANALYSING COST

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## INTRODUCTION

Early-onset neonatal sepsis (EOS) is associated with significant morbidity and mortality. Identifying sick neonates, initiating timely antibiotic treatment while avoiding overtreatment of those without infection, pose great challenge to health professionals. Based on NICE guidelines (NICE CG149), the Norfolk and Norwich University Hospitals NHS Foundation Trust (NNUH) Clinical Practice Guidelines on EOS, introduced in January 2016, provides a comprehensive guidance in the local context. The aim of our audit was to assess adherence to this guideline and to conduct a cost-analysis of current practice.

## METHODS

We conducted a single centre retrospective study of neonates born at ≥ 34 weeks' gestation and on antibiotics for EOS (< 72 hours of age) in the postnatal ward of a tertiary centre, over 6 months. The audit events were evaluated, based on the NICE audit tool, across 6 domains including risk factors for sepsis, septic screen prior to treatment, antibiotics given within 1 hour timeframe from diagnosis, appropriate choice of empirical antibiotics, appropriate blood tests, and stopping antibiotics in 36 hours in eligible neonates. Further, a cost-analysis was conducted using the bottom up/ingredients approach.

## RESULTS

Our cohort (n = 123) was predominantly male (56%), with a mean gestational age and birth weight of $38^{+4}$ weeks and 3.257 kg, respectively. Mean time for administration of antibiotics was 80 minutes after the decision to treat; with only 54% (67/123) having antibiotics within the recommended ≤ 1 hour. 72 (n) of the 123 neonates met the criteria for 36 hours'

antibiotics as per the guideline (NICE CG149). However, 61% (44/72) of the former actually had antibiotics for 36 hours while the remaining 39% (28/72) had their antibiotics for an average of ≥ 48 hours due to delays in stopping antibiotics. Of note, in neonates that only had 36 hours' of antibiotics, blood culture results were negative, and there was no death; but 3 of these babies had sepsis-related re-admissions. Cost analysis found delays in stopping antibiotics and prolonged admissions to represent a sizeable annual cost.

CONCLUSIONS

Management of EOS on the postnatal ward of a large, urban teaching hospital (NNUH) is suboptimal to the CG149 recommendations, resulting in unnecessary doses of antibiotics and prolonged hospitalisations. Educational interventions, comprehensive strategies, and a re-audit for improved performance; are required.

## ABS 34

## DYSFUNCTIONAL INFLAMMATION; THE SIGNIFICANCE OF TLR2 SIGNALING IN HYPOXIC NEONATES PREDISPOSED TO NEURAL ENCEPHALOPATHY

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INTRODUCTION

The Toll-like receptor-2 pathway has been implicated in neonatal brain injury in animal models. We aimed to investigate systemic Toll like receptor (TLR)-2 activation in infants with NE compared to neonatal controls.

METHODS

Neonatal controls, adult controls and infants with NE requiring therapeutic hypothermia were sampled. Whole blood was treated with LPS (10 ng/ml) and/or Pam3CSK4 (250 ng/ml) and compared to vehicle controls. Monocyte and neutrophil CD66b, CD15, CD11b, TLR2, and NOX were measured by flow cytometry. Reverse transcription polymerase chain reaction (RT-PCR) analysis was conducted on cDNA isolates of NE and neonatal controls patients for the following genes TRIF, IRAK4 and MyD88 using the AB7900 system. Results were expressed as the ratio of target gene cDNA to the internal control using the 2-ΔΔCT method.

RESULTS

LPS and Pam3CSK4 treatment stimulated neutrophil TLR2 and CD11b upregulation in NE samples. NE samples showed similar upregulation to that of adult and neonatal controls for the expression of NOX-2 protein. PCR analysis showed upregulation in NE samples of IRAK4, TRIF and MyD88 gene expression in comparison to control samples.

CONCLUSIONS

Infants with NE had systemic neutrophil TLR2 activation by both LPS and Pam3CSK4 as well as upregulation of IRAK 4, TRIF and MyD88 and may indicate dysregulated immune function in these infants with increased sensitivity to TLR2 agonists and Gram positive organisms.

## ABS 35

## NEONATAL THYMIC CHARACTERISTICS IN A RAT MODEL OF INTRAUTERINE GROWTH RESTRICTION

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INTRODUCTION

Intrauterine growth restriction (IUGR) induces a thymic atrophy due to massive apoptosis of thymocytes. IUGR is associated with a higher risk of infections in early life, due to altered immune response. We aimed to characterize the thymic phenotype in rats born after IUGR, with particular concern to medullary thymic epithelial cells (mTECs). The mTECs orchestrate the final processing of lymphopoiesis by eliminating autoreactive lymphocyte clones via the Auto Immune Regulator (AIRE) and selecting functional effector T cells via the major histocompatibility complex (MHC) I and II.

METHODS

Sprague-Dawley rats were exposed to normal or to low-protein diet (LPD, 9% casein) during gestation. At postnatal days (PND) 2 and 60, the

thymus was harvested and frozen. Slices were either stained with hematoxylin/eosin (measurement of the cortico-medullar ratio, CMR) or labeled with immunofluorescent (IF) antibodies directed against cytokeratins (CK) 5, 14 and 8+18 and MHC I and II and AIRE. The expression of AIRE was also quantified using Western blot technique on frozen and smashed thymus extracts.

RESULTS

At PND2, the CMR was significantly lower (3.00 vs. 3.49; p = 0.049) in thymic slices from newborn IUGR rats. The IF expression intensity (mean in arbitrary units ± SEM) of CK5 (9.88 ± 0.85 vs. 8.64 ± 1.31; p = 0.42), CK14 (15.55 ± 1.24 vs. 16.95 ± 1.11; p = 0.42) and CK8+18 (4.15 ± 0.48 vs. 4.43 ± 0.40; p = 0.67) was not significantly different between groups, neither was the expression of AIRE (14.26 ± 1.36 vs. 14.76 ± 1.88; p = 0.86), MHC I (13.57 ± 0.76 vs. 11.72 ± 0.30; p = 0.08) and MHC II (10.42 ± 1.37 vs. 7.99 ± 1.69; p = 0.33). At PND60, AIRE expression was significantly lower in IUGR group (IUGR vs. CTRL, mean in arbitrary units ± SEM: 0.58 ± 0.09 vs. 1.04 ± 0.06; p < 0.05).

CONCLUSIONS

Our findings confirm the abnormal morpho-phenotype of the thymus observed after exposition to IUGR, with a reduced CMR indicating the massive apoptosis of thymocytes in such context, and show a possible association between IUGR and the expression of AIRE. Further studies may address functional analysis of mTECs and thymic output to better understand the mechanisms of the short-term and long-term effects of IUGR on immune functions.

## ABS 36

## IMPACT OF MICROBIAL-ASSOCIATED INTRA-AMNIOTIC INFLAMMATION AND "STERILE" INTRA-AMNIOTIC INFLAMMATION ON SHORT-TERM NEONATAL OUTCOME IN WOMEN WITH PRETERM LABOR AND INTACT MEMBRANES

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INTRODUCTION

The earlier the symptoms of preterm labor with intact membranes (PTL) occur during pregnancy, the higher is the involvement of intra-amniotic inflammation (IAI) and/or infection in the physiopathology of spontaneous preterm delivery. Microbial-associated IAI (M-IAI) and "sterile" IAI have been related with an earlier gestational age (GA) at admission, at delivery and a shorter latency to delivery. The aim of this study was to evaluate the impact of M-IAI and "sterile" IAI on short-term neonatal outcome in women with PTL when other antenatal factors such as GA, antenatal steroids administration or antibiotics were considered.

METHODS

Prospective cohort study including women with PTL with an amniocentesis at admission to rule out infection. Clinical chorioamnionitis and multiple gestations were considered non-eligible. Subgroups were identified according to the presence of infection or IAI. Infection was defined based on amniotic fluid aerobic/anaerobic/genital *Mycoplasma* cultures. Culture results were available to individualize clinical management. However, information about IAI, based on interleukin (IL)-6 levels (≥ 13.4 ng/mL) was not. Pregnancy and short-term neonatal outcomes were compared among groups. The independence of infectious/inflammatory subgroups, GA and antenatal management to predict a worse neonatal outcome was evaluated in a multivariate analysis.

RESULTS

One hundred eighty six women were included. The prevalence of M-IAI and "sterile" IAI was 22% and in 54%, respectively. There were 3 women with infection but without IAI, they were excluded from the analysis. We observed significant differences on GA at amniocentesis and delivery among groups. The presence of M-IAI was found to be an independent predictor of early-onset sepsis (EOS) (Odds ratio [OR] of 5.03 with a 95% Confidence interval [CI] of 1.1-22.2). However, neither M-IAI nor "sterile" IAI were independent predictors of a worse neonatal outcome. GA was the main predictor of neonatal respiratory distress syndrome (OR 0.61, 95% CI 0.493-0.755), IVH grade III/IV (OR 0.757, 95% CI 0.579-0.991) and neonatal death (OR 0.485, 95% CI 0.316-0.744). In addition, the antenatal steroids

**Table 1 (ABS 36).** Main characteristics of the 3 groups.

| | Group A M-IAI n = 40 | Group B "Sterile" IAI n = 100 | Group C No-MIAC/ No-IAI n = 46 | p[1] | p[3] A vs. B | p[2] B vs. C |
|---|---|---|---|---|---|---|
| **GA at amniocentesis (weeks)** | 26.3 (23.3; 30.7) | 28.1 (25.0; 31.1) | 29.9 (26.5; 31.8) | < 0.001 | < 0.001 | < 0.001 |
| **Antenatal steroids** | 29 (94) | 82 (88) | 43 (93) | 0.495 | 0.052 | 0.387 |
| **Antenatal antibiotics** | 31 (100) | 59 (63) | 16 (35) | < 0.001 | < 0.001 | 0.002 |
| **GA at delivery** | 26.4 (23.3; 30.7) | 32.6 (28.2; 37.3) | 37.8 (36.5; 38.1) | < 0.001 | < 0.001 | < 0.001 |
| **Latency to delivery (days)** | 1 (0; 2) | 15 (2; 49) | 55 (31; 78) | < 0.001 | < 0.001 | < 0.001 |
| **Male gender** | 14 (45) | 45 (48) | 25 (54) | 0.713 | 0.836 | 0.591 |
| **Birthweight (g)** | 1,150 (775; 1,600) | 1,865 (1,311; 2,920) | 2,915 (2,465; 3,434) | < 0.001 | < 0.001 | < 0.001 |
| **Miscarriage < 24.0 w** | 10 (25) | 7 (7) | 0 | < 0.001 | < 0.001 | 0.098 |
| **Admission to NICU** | 29/30 (97) | 64/92 (70) | 12 (26) | < 0.001 | 0.007 | < 0.001 |
| **Early onset sepsis** | 8/30 (27) | 3/89 (3.4) | 1 (2.2) | 0.033 | 0.030 | 0.471 |
| **Neonatal respiratory distress syndrome** | 12/30 (40) | 13/91 (14.3) | 2/45 (4.4) | 0.466 | 0.466 | 0.370 |
| **BPD** | 5/30 (17) | 4/89 (5) | 0/45 | 0.810 | 0.807 | 0.998 |
| **ECN** | 0/30 | 1/90 (1) | 0/45 | 0.431 | 0.998 | 0.998 |
| **ROP** | 5/29 (17) | 8/85 (9) | 0/45 | 0.660 | 0.066 | 0.997 |
| **IVH ≥ grade III** | 4/29 (14) | 4/86 (5) | 0/45 | 0.800 | 0.803 | 0.998 |
| **Neonatal death** | 1/30 (3) | 8/92 (9) | 0/45 | 0.027 | 0.028 | 0.998 |

Continuous variables were compared using a nonparametric Mann-Whitney U test or Kruskal Wallis test presented as medians ($25^{th}$;$75^{th}$ percentile). Categorical variables were compared using Chi-square or Fisher exact tests and presented as number (%). Short-term neonatal outcome was adjusted for the amniotic fluid infectious/inflammatory phenotypes, gestational age at delivery, antenatal steroids and antibiotics. IAI: intra-amniotic inflammation; M-IAI: microbial-associated IAI.

administration was an independent protector factor of EOS (OR 0.065, with 95% CI of 0.009-0.484). Results are presented in **Tab. 1**.

CONCLUSIONS

GA was more determinant of the short-term neonatal outcome than the presence of M-IAI or "sterile" IAI. Amniocentesis is a key tool in the management of these patients, since it allow us to identify those women at high risk of giving birth in the following days and better advise to the family. Strategies such as steroids, neuroprotection, transfer to referral hospital or targeted antibiotic treatments can be considered according to this information.

## ABS 37

## VARIABILITY IN IMMUNOLOGICAL RESPONSE TO OROPHARYNGEAL COLOSTRUM ADMINISTRATION IN PRETERM NEWBORN BASED ON SEX

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INTRODUCTION

Very low birth weight (VLBW) newborns have an immature immune system and also disrupted defense natural barriers. Human colostrum provides higher concentrations of secretory IgA, growth factors, lactoferrin, anti-inflammatory cytokines and other protective components as compared with mature human milk. Oropharyngeal colostrum administration (OCA) stimulates the immune system (IS), developing the protective immune barrier. Aim: To evaluate the immunologic effects of OCA to VLBW infants, regarding sex, in their first two weeks of life, by assessing IgA, lactoferrin, interleukin-6 (IL-6) and interleukin-10 (IL-10) serum levels evolution up to one month of life.

METHODS

We conducted an interventional, non randomized, controlled trial recruiting newborns ≤ $32^{+6}$ gestational weeks and/or < 1,500 g at birth. 86 newborns were enrolled from April 2014 to July 2016. Subjects received 0.2 ml of their own mother colostrum every 4 hours, starting in the first 24 hours of life, and for a 15 days period. IgA, lactoferrin, IL-6 and IL-10 serum levels were measured at birth (M1), 3 (M2),

15 (M3) and 30 (M4) days of life using a panel Luminex xMAP technology. Perinatal data for the first month of life were registered. Differences were considered significant at $p < 0.05$.

RESULTS

40 newborns were enrolled in the colostrum group (24 males, 16 females) and 46 in the control group (26 m, 20 f).

Males group (n = 50):

- Higher serum levels of IgA in colostrum group at M3 (31.06 μg/ml vs 23.92 μg/ml, $p = 0.33$) and M4 (46.20 μg/ml vs 31.19 μg/ml, $p < 0.01$).
- Lower levels of IL-6 in colostrum group at M3: IL-6 7.50 pg/ml vs 13.97 pg/ml, $p = 0.04$.
- Higher serum levels of lactoferrin (921.29 ng/ml vs 693.12 ng/ml, $p = 0.04$) and IL-10 (17.16 pg/ml vs 12.09 pg/ml, $p = 0.015$) in colostrum group at M4.

Females group (n = 36):

- Higher levels of IL-10 in colostrum group at M3: 14.50 pg/ml vs 11.16 pg/ml, $p = 0.04$.
- Lower levels of IL-6 in colostrum group at M4: 6.84 pg/ml vs 11.51 pg/ml, $p = 0.03$.

When comparing serum IgA between males and females in intervention group at 15 and 30 days of life, boys showed significant higher levels: M3, 31.06 μg/ml vs 20.75 μg/ml, $p < 0.01$; M4, 46.21 μg/ml vs 37.11 μg/ml, $p = 0.027$.

CONCLUSIONS

Our data show that OCA might facilitate the development of IS in males and females preterm babies at one month of age, by increasing IgA, lactoferrin and anti-inflammatory cytokines (IL-10) serum levels and decreasing pro-inflammatory cytokines (IL-6). Regarding sex, the most noteworthy result is a higher serum IgA in males who received oropharyngeal colostrum. This result suggests a different immune response to OCA depending on newborn sex.

## ABS 38

## PCT, IL-6 AND IL-8, BUT NOT HA ARE USEFUL FOR DIAGNOSTIC UTILITY IN NEONATES AT RISK THAT FULFILL THE NORWEGIAN CONSENSUS DEFINITION OF NEONATAL SEPSIS

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INTRODUCTION

Clinical signs and biomarkers of early-onset neonatal sepsis (EONS) are unspecific. The aim of this study was to assess the diagnostic utility of procalcitonin (PCT), interleukin (IL)-6, IL-8, and hyaluronic acid (HA) in a) newborn infants, and b) human umbilical cord blood (HUCB) from pregnancies with chorioamnionitis versus healthy, in predicting EONS. In neonatal sepsis these biomarkers were compared with C-reactive protein (CRP), white blood cell count (WBC) and platelets.

METHODS

Blood were collected from term infants with EONS (group 1, n = 15); healthy term infants (group 2, n = 15); the umbilical vein from pregnancies with suspected chorioamnionitis (group 3, n = 7); and from healthy pregnancies with no signs of infection (group 4, n = 15). Regression analysis to show the extent to which a routinely used predictor (e.g. CRP, WBC, or platelet count) was correlated with an alternative biomarker was performed.

RESULTS

Neonatal plasma PCT and IL-8 showed good predictive value (90 and 83%, respectively) for EONS, and the combination of IL-6 or HA with PCT increased predictability from 73 to 87% and 43 to 90%, respectively. Any other combination of PCT, IL-6, IL-8 or HA did not improve predictability. PCT, IL-6, IL-8, and HA was 8.1-, 4.6-, 3.7- and 1.9-fold higher when compared with non-infections neonates. PCT, IL-6 and IL-8 in HUCB predicted chorioamnionitis and fever in the delivering mother (91, 91 and 86%, respectively). HA was a poor predictor but in combination with PCT, IL-8 or IL-6 increased predictability in both EONS and HUCB. In HUCB from chorioamnionitic deliveries IL-6, IL-8 and PCT were 23-, 16- and 3-fold higher when compared to control HUCB. There was no correlation between CRP, WBC or platelet count, and PCT, IL-6, IL-8 or HA.

CONCLUSIONS

In neonates that fulfilled the Norwegian consensus definition of neonatal sepsis, PCT, IL-6 and IL-8, but not HA, have the potential to improve our management of neonates at risk. Except for PCT and IL-8, both with a high predictability, combinations of the biomarkers increased predictability for EONS and chorioamnionitis.

## ABS 39

## THE ANTISECRETORY FACTOR IN RELATION TO PRETERM BIRTH AND INFLAMMATORY RESPONSE

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## INTRODUCTION

Antisecretory factor (AF) is an endogenous protein with a role in the innate regulation of secretory and inflammatory processes. Inflammation contributes to the onset of preterm labour and complications of prematurity, such as bronchopulmonary dysplasia and necrotizing enterocolitis. AF in plasma and breast milk can be increased by an AF-inducing diet and dietary supplements. We have previously described significantly lower levels of AF in preterm placental tissue compared to term placenta and hypothesized that this would be reflected in infant plasma following birth. The objective was to determine AF in serial plasma samples from preterm and term infants in relation to inflammatory markers.

## METHODS

Infants born preterm (< 30 weeks gestation) and term control infants were recruited at the Karolinska University Hospital Huddinge, Sweden. Plasma samples were collected from cord blood at delivery, from the infant at approximately 1 week and at 12 weeks postnatal age. A sandwich ELISA using catching and detecting antibodies, was performed to determine the level of active AF in plasma. A panel for multiple serum protein analysis (Proseek®, Olink AB, Uppsala) was used and known inflammatory markers identified. Here we report specifically on the protein RAGE (Receptor for Advanced Glycation Endproducts) and Pentraxin 3 (PTX3, a soluble pattern recognition receptor), both previously described mediators of fetal cell injury and inflammation-induced preterm birth.

## RESULTS

A total of 215 samples from 81 infants (52 preterm with mean gestational age 27 weeks + 3 days, and 20 term) were analysed. Results showed lower AF levels in cord blood (0.23 ± 0.30 vs 0.44 ± 0.31, mean ± SD) and plasma at one week postpartum (0.60 ± 0.74 vs 1.20 ± 0.86) after preterm birth compared with term birth ($p < 0.01$ ANOVA, Mann Whitney U-test). AF-levels increased with postnatal age in both term and preterm infants, and were significantly higher at 12 weeks postnatal age compared with levels in cord blood and one week of age (p 0.05). A negative correlation was shown between levels of AF and the plasma proteins RAGE (Spearman's rho = -0.34, $p < 0.01$) and PTX3 (Spearman's rho = -0.41, $p < 0.001$).

## CONCLUSIONS

Following preterm birth, the plasma levels of AF appears to be lower than after term birth, and increase with postnatal age. Low levels of AF is associated to high levels of several proteins suggested as important mediators of cellular injury and inflammation in relation to preterm birth, i.e. RAGE and PTX3. This novel finding indicate that AF has a role in the inflammatory response induced by preterm birth and may be a target for intervention.

**ABS 40**

# NEONATAL INVASIVE CANDIDIASIS: STUDY OF 108 CASES COLLECTED IN NEONATOLOGY DEPARTMENT OF SOUSSE (TUNISIA)

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## INTRODUCTION

Invasive candidiasis (IC) in the neonatal period is a real problem because of their high morbidity and mortality. The aim of this work is to study risk factors, clinical, biological, therapeutic and prognostic aspects of CI in the newborn.

## METHODS

This is a retrospective study of 108 cases of IC, 81 cases of confirmed IC and 27 cases of catheter IC (probable CI), over a 14-year period (January 2000 to December 2013) in newborns hospitalized in the Neonatology Department of the F. Hached Hospital in Sousse. The identification of the different species was made at the Laboratory of Parasitology-Mycology of CHU F. Hached.

## RESULTS

In our series, infection was most often nosocomial (93.5% of cases). The main risk factors identified

were: preterm birth, found in 73.14% of cases with a term below 28 weeks in 12% of cases, very low birth weight (7 days in 58.3% of cases, broad spectrum antibiotherapy prescribed in 94.4% of patients and exclusive parenteral nutrition in 37% of cases. 81.84% of the patients benefited from the placement of an umbilical or central venous catheter. The clinical presentation was very polymorphic with variously associated signs, sometimes explaining the delay in diagnosis. The non-specific biological assessment was not very contributory in the diagnosis of IC. Thrombocytopenia was the most frequent manifestation (25%), however, isolated hyperleukocytosis, positive CRP or stagnation of CRP were found. The classification of neonatal IC showed candidemia in 56.48% and candiduria in 36.11%. Secondary sites were present in 4.63% of cases. *C. albicans* was by far the most frequently isolated species (80%), followed by *C. tropicalis*, *C. parapsilosis* and *C. glabrata*. Isolation of two different species of candida in blood culture was noted in two newborns. In two other newborns, two different species were isolated at two different sites. The study of the sensitivity of *Candida spp.* to antifungals showed no resistance to fluconazole and amphotericin B and a low resistance to itraconazole. An antifungal treatment was undertaken in 71 newborns (66%). Fluconazole was the main treatment used. Amphotericin B was used in only 4.63% of cases. The evolution was fatal in 50% of the cases.

CONCLUSIONS

Candidiasis infection in hospitalized newborns remains a major problem due to difficulty of diagnosis and management of the newborn. A better understanding of the risk factors is needed in order to propose an appropriate prevention strategy.

## ABS 41

## HERO AS A TOOL FOR PREDICTING MORBIDITY AND MORTALITY IN PRETERM INFANTS WITH LATE ONSET SEPSIS ADMITTED TO TERTIARY LEVEL NEONATAL UNIT

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INTRODUCTION

The Heart Rate Characteristics Index was developed to use pathophysiologic changes of decreased heart rate variability and heart rate decelerations to predict an imminent clinical deterioration occurring due to late onset sepsis in preterm infants. This is represented as an hourly cotside "HeRO score". The score represents the fold-increased risk of morbidity or mortality within the next 24 hours. Aims: to determine the impact of HeRO in babies with proven culture positive sepsis on mortality, PVL, IVH, NEC and BPD.

METHODS

A retrospective cohort study was undertaken to include three years pre-introduction of HeRO and three years post-introduction of HeRO on the Neonatal Unit at the Liverpool Women's Hospital. We identified all cases of late onset sepsis (LOS) in both time periods using the Badgernet system. We compared the mortality, significant IVH, BPD, PVL and NEC rates for both populations. We then conducted subgroup analysis for the following groups:

1. VLBW infants (< 1,500 g),
2. CONS sepsis,
3. Non-CONS sepsis.

RESULTS

The median gestational age at birth and birthweight were similar in both cohorts (see **Tab. 1**). The total number of infants in the pre-HeRO cohort was 83 and post-HeRO 70. The total mortality rate for the pre-HeRO cohort was 22% and for post-HeRO cohort 24%. There was no statistical significance. (p 0.7627). The difference for CONS and non-CONS culture positive sepsis was also not statistically

**Table 1 (ABS 41).** Pre-HeRO and Post-HeRO comparison data: gestational age and birthweight (**A**), mortality and morbidity (**B**).

**A.**

| Pre-HeRO | Median | Interquartile range |
|---|---|---|
| Gestational age at birth | 26 | 25.28 |
| Birthweight | 860 | 670; 1,080 |
| **Post-HeRO** | **Median** | **Interquartile range** |
| Gestational age at birth | 26 | 24.28 |
| Birthweight | 827 | 642; 1,027 |

**B.**

| | Pre-HeRO | Post-HeRO | p-value |
|---|---|---|---|
| Overall mortality | 22% | 24% | 0.7627 |
| Mortality from Cons | 30% | 39% | 0.8845 |
| Mortality from Non-cons | 19% | 17% | 0.82 |
| Total % VLBW infants | 93% | 91% | 0.758297 |
| Mortality in VLBW infants | 23% | 27% | 0.662 |
| BPD | 71% | 66% | 0.52 |
| IVH | 59% | 39% | 0.76 |
| PVL | 18% | 7% | 0.045 |
| NEC | 30% | 40% | 0.2 |

significant in the two cohorts (p 0.229). There was no statistical difference in mortality between infants with CONS sepsis in the pre and post-HeRO cohort, nor in the non-CONS sepsis groups. In addition, there was no any statistical difference in IVH, BPD or NEC in the two cohorts. However, there was a statistical difference in outcome of PVL (p 0.045).

CONCLUSIONS

This retrospective study has shown that the introduction of HeRO into our tertiary level neonatal unit has not shown any statistically significant reduction in mortality rates in preterm infants diagnosed with late-onset sepsis.

## ABS 42

## NEWBORN SCREENING TESTS IN INFANTS WITH CONGENITAL ZIKA VIRUS SYNDROME AND MICROCEPHALY

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INTRODUCTION

Zika virus infection during pregnancy causes congenital brain abnormalities including microcephaly. Since the Zika outbreak started in Puerto Rico in 2016, there have been 3,678 pregnant women with confirmed infection. The first newborn with microcephaly secondary to congenital Zika virus infection was admitted to our neonatal service in April 2016. It is known that infants with abnormal brain development are at risk for hypothalamic dysfunction leading to pituitary insufficiency. Thyroid function test is included in the universal newborn screening in Puerto Rico. The objective of our study is to determine if congenital Zika virus syndrome is associated to abnormal newborn screening tests.

METHODS

Newborn screening tests results were reviewed for all infants with microcephaly associated to maternal Zika virus infection during pregnancy who were admitted to the Puerto Rico University Pediatric Hospital (UPH) Neonatal Intensive Care Unit or referred for follow-up to the UPH High Risk Clinics. Screening was performed for galactosemia, biotinidase deficiency, phenylketonuria, hypothyroidism, congenital adrenal hyperplasia, hemoglobinopathies, cystic fibrosis and severe combined immune deficiency.

RESULTS

Twelve newborns with congenital Zika syndrome and microcephaly were screened from April 2016 to April 2017. One newborn (7%) had an initial test suggestive of hypothyroidism but two repeated samples were normal. One newborn was a carrier for sickle cell disease. No other positive screening tests were reported.

CONCLUSIONS

Infants with congenital Zika syndrome and microcephaly did not show abnormal newborn screening tests. Efforts should continue to better describe the spectrum of anomalies associated to congenital Zika virus syndrome.

## ABS 43

## CAN ENDOCAN PREDICT LATE NEONATAL SEPSIS?

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INTRODUCTION

Endothelial cells have an important role in the pathogenesis of sepsis. Endothelin-releasing endocan (endothelial cell-specific molecule 1) has been shown to elevate significantly in adult sepsis studies. It has also been proven that endothelial dysfunction is a good marker for multiorgan failure and sepsis survival. Our aim was to determine the predictive value of endocan level in late neonatal sepsis (LOS).

METHODS

Premature infants with gestational age ≤ 32 weeks and LOS diagnosed were included in the study prospectively. Sepsis was diagnosed by the presence of two or more clinic presentations plus the presence of significant elevations in C-reactive protein (CRP) or interleukin-6 (IL-6) levels. Blood culture positivity was defined as proven sepsis. Blood samples were taken to determine leukocyte count, CRP, IL-6, and endocan levels immediately after the sepsis diagnosis and on days 3 and 7.

RESULTS

A total of 102 premature infants, including 52 late neonatal sepsis (21 proven, 31 clinical sepsis) and 50 controls were included in the study. Mean

**Table 1 (ABS 43).** Comparison of endocrine, CRP, IL-6 and WBC levels in clinical and proven sepsis with control subjects.

| | Sepsis | | | Control | |
|---|---|---|---|---|---|
| **Parameters** | **Clinical sepsis n = 31** | **Proven sepsis n = 21** | **p [a]** | **n = 50** | **p** |
| **Baseline** | | | | | |
| **Endocan** | 12.9 ± 2.48 | 14.6 ± 1.43 | 0.003 | 6.53 ± 1.93 | < 0.001 [b,c] |
| **CRP** | 51.0 ± 33.0 | 59.4 ± 30.7 | 0.365 | 2.39 ± 1.89 | < 0.001 [b,c] |
| **IL-6** | 1,310.8 ± 1,799.7 | 1,674.2 ± 1,902.2 | 0.448 | 14.24 ± 14.83 | < 0.001 [b,c] |
| **WBC** | 17,171 ± 3,498 | 18,446 ± 5,193 | 0.295 | 9,586 ± 1,853 | < 0.001 [b,c] |
| **72nd hours** | | | | | |
| **Endocan** | 9.0 ± 4.08 | 10.93 ± 3.47 | 0.086 | | |
| **CRP** | 33.3 ± 26 | 41.4 ± 34.6 | 0.337 | | |
| **IL-6** | 155.8 ± 282.5 | 181.8 ± 302.3 | 0.753 | | |
| **WBC** | 1,475 ± 2,998 | 13,603 | 0.238 | | |
| **120th hours** | | | | | |
| **Endocan** | 7.0 ± 3.88 | 10.23 ± 4.84 | 0.017 | | |
| **CRP** | 14.9 ± 15.6 | 13.3 ± 10.8 | 0.701 | | |
| **IL-6** | 28.3 ± 30.1 | 70.1 ± 185.0 | 0.221 | | |
| **WBC** | 10,975 ± 2,211 | 10,694 ± 2,612 | 0.678 | | |

All values are given as mean ± SD.
CRP: C-reactive protein; IL-6: interleukin 6; WBC: leukocyte count.
p: comparison of 3 groups; [a] comparison of clinical and proven sepsis; [b] comparison of the control group with clinical sepsis; [c] comparison of the control group with proven sepsis.

baseline leukocyte count, serum CRP, IL-6 and endocan levels were significantly higher when compared with healthy controls ($p < 0.001$). There was no significant difference in CRP and IL-6 levels between proven and clinical sepsis at the beginning of LOS and following controls; endocan levels were significantly higher in the proved sepsis group on the first and 7th day ($p = 0.003$, $p = 0.017$, respectively) (**Tab. 1**). Cut-off level of endocan for predicting GNS was found 9.2 ng/ml (Sensitivity: 94.2%, Specificity: 94%, PPV: 94.2%, NPV: 94%) (AUC: 0.986, 95% CI: 0.970-1.000, $p < 0.001$).

CONCLUSIONS

The combination of endocan levels with acute phase reactants such as CRP and IL-6 has a high sensitivity and specificity in the diagnosis and follow-up of LOS.

## ABS 44

## UMBILICAL CORD CARE AND OMPHALITIS IN NEWBORNS OF NORTHERN PORTUGAL: A MULTICENTRIC RETROSPECTIVE STUDY

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INTRODUCTION

Although the incidence of neonatal omphalitis is still high in low-income countries, in high-resource countries, as ours, the incidence of neonatal omphalitis has decreased and is now rare. These different realities have resulted in divergent recommendations for cord care by World Health Organization (WHO), published in 2013, which advocates dry cord care for infants born in a hospital or in settings of low neonatal mortality and application of chlorhexidine for all others. With this study, we intend to review the characteristics of the newborns admitted with omphalitis, as well as the umbilical cord care method used and its relation with the time of umbilical cord fall and omphalitis.

METHODS

A retrospective study was performed, with the analysis of clinical data from newborns admitted to three northern Portuguese hospitals with the diagnosis of omphalitis, between 1-01-2008 and 31-12-2016. Patient charts were reviewed and those

who didn't meet the criteria for omphalitis (purulent or malodorous discharge, periumbilical erythema, periumbilical edema or tenderness) were excluded. Data regarding age at diagnosis, sex, gestational age, provenience, admission diagnosis, cord care method, time of umbilical cord fall, physical examination at admission, cultural exam from umbilical exudate, antibiotherapy and disease evolution were recorded. The data were analyzed with the program IBM® SPSS® statistics (v. 24), significance level < 0.05.

RESULTS

83 newborns met the criteria for omphalitis (51.8% male). Median age at diagnosis was 7 days (2-28). Median gestational age was 39 weeks (27-41). The cord care method was known in 45 newborns: 59% alcohol; 29% dry care; 9% chlorhexidine. No correlation was found between cord care method and time of umbilical cord fall. There was a significant decrease in the number of cases of omphalitis in 2010 (n = 3), and an increase in 2015 (n = 12). The most common finding in newborns was umbilical malodorous discharge (79.5%), followed by umbilical erythema (77%) and edema (7.2%); none had fasciitis. In 66%, cultural exam from umbilical exudate was requested and the commonest pathogens were *St. aureus* in 56.3% and *E. coli* in 40%. Intravenous antibiotics were instituted in 90% (36% flucloxacillin plus gentamicin; 30% ampicillin plus gentamicin), with favorable outcome in all cases.

CONCLUSIONS

Our results are in accordance with the existing data in the literature. Although omphalitis remains rare, being aware of the first signs of omphalitis is crucial for an early treatment, avoiding severe consequences. In the future, a prospective study should be made to access how the umbilical care method could influence the risk of omphalitis.

## ABS 45

## CENTRAL LINE ASSOCIATED INFECTION IN NEWBORNS ADMITTED TO A PORTUGUESE NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION

Central lines (CL) are an important part of neonatal patient management. Nevertheless, CLs have been linked to many complications, sepsis being the most serious of them. Prevention of such infections should be a priority for all neonatal intensive care units (NICUs). The aim of this study was to describe the use of CL and to find potential risk factors for CL-associated bloodstream infection (CLABSI) in newborns admitted in a level III Portuguese NICU.

METHODS

A retrospective single-centre cohort study was performed, where all infants with any CL (UAC, UVC, PICC and Broviac) admitted between Jan 2015 and Dec 2016 were included. CLABSI refers to a bloodstream infection or a clinical sepsis (symptoms or signs for sepsis and no organism detected in blood) in the presence of a CL or within 48 h of its removal. For infection rate purposes all CLABSI were included and for the remaining variables only the 1st CLBSI was analysed. The sample was selected from Portuguese infection surveillance database and the medical records were reviewed. The $\chi^2$ test for categorical variables and the Mann-Whitney U test for continuous variables were used. Differences in the CL time length before CLABSI were analysed using Kaplan-Meier survival curves.

RESULTS

A total of 373 CLs (48 UAC, 110 UVC, 201 PICC, 14 Broviac) were placed in 215 of the 1,030 newborns admitted to the NICU. CL utilization rate was 27.3/100 patient days. 100 CLABSIs occurred (7.1/1,000 patient days; 25.9/1,000 catheter days). CLABSI mortality was 1.4% and 1/1,000 catheter days. Infection-free CL probability was 94.6% at day 5 and 65.5% at day 10 for UVC; for PICC it was 73.4% at day 10 and 39.7% at day 20. There were no differences in CLABSI regarding birthweight, gestational age and prior parenteral nutrition duration. Age at CL insertion (median 3 vs. 1 days; p = 0.001), age at enteral trophic nutrition onset (median: 5 vs. 3 days; p = 0.001), prior antibiotic use > 5 days (28.3% vs. 15.6%; p = 0.004) and length of NICU stay (median 47 vs. 28 days; p = 0.001) were higher in patients with CLABSI.

CONCLUSIONS

CLABSI rate described in our study is higher than other centers. The potential risk factors described, namely age at CL insertion, age at trophic nutrition onset, prior antibiotic duration and CL time length should be a target for CL bundle strategies focusing in CLABSI rate reduction. The expected outcome of these measures would be not only a lower CLASBI rate but also a decrease on NICU length of stay.

## ABS 46

## NEONATAL INFECTIONS AT PREMATURE AND AT TERM NEWBORN

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### INTRODUCTION

Neonatal infections are infections that affect newborn in first 28 days of life. Neonatal infections can be transmitted transplacentally, during child-birth by crossing the birth canal and after the childbirth. Infections in the uterus can be transmitted transplacentally anytime before childbirth from a maternal infection obvious or subclinical. The consequences on the fetus depend on the infectious agent, but also of gestational age. The reduction of neonatal and perinatal mortality, as well as subsequent morbidity, represents one of the essential objectives both gynecologists and neonatologists.

### METHODS

This study is a retrospective study of neonatal newborns diagnosed with neonatal infections in the Neonatology Section of Bega Obstetrics and Gynecology Clinic. The study was conducted in 2016 on a batch of 66 newborns with neonatal infections from all 2,587 childbirth. I collected the following data: fetal parameters (sex, gestational age, birth weight, APGAR score), date of birth and the onset of onset infection, the leukocyte count, the value of reactive C protein (CRP), blood culture, other cultures (cultures from bronchial aspiration, nasal exudate, pharyngeal exudate, catheter peak cultures, crops from a tegument fragment, cultures of conjunctival secretion, CRL cultures), DST, treatment, disease progression, and maternal infectious antecedents during pregnancy.

### RESULTS

In this study, the incidence of neonatal infections is 3%. Only neonates with neonatal infections confirmed by microbiology test were included in the study. In the batch of patients studied, 74% of newborns with infections were premature and 26% were newborns. It has also been noticed that early onset infections are made in 47% of term neonates, and 57% of preterm. Late onset infections are developed by premature babies in 94% and newborns in term only of 6%. In early-onset infections, the most common etiologic agents were: *S. aureus* MRSA in 18% of cases, followed by *S. aureus* MSSA, *group Streptococcus B*, *E. coli* and *Klebsiella spp.*, each having a 12%. In late-onset infections the order was this: *A. baumannii* in 17% of cases, followed by *K. pneumoniae* with 15%, by *S. maltophilia* with 9% and *Coagulase negative Staphylococcus* and *C. albicans* with 7%.

### CONCLUSIONS

27% of newborn mothers have experienced at least one infection during pregnancy. 23% of newborns with infections had a birth weight of less than 1,000 grams. The most common gram positive bacterium was *S. aureus* (MRSA) in percentage of 21%. The most frequent gram negative bacterium was *A. baumannii* (26%). Evolution under treatment was favorable in 89% of cases.

## ABS 47

## PROSTAGLANDIN E2 URINARY METABOLITE IN PRETERM INFANTS. A BIOMARKER FOR INFLAMMATION?

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### INTRODUCTION

Cardiorespiratory disturbances are the major presenting symptoms of neonatal infections. Our previous study on cerebrospinal fluid (CSF) suggests prostaglandin E2 as a biomarker for respiratory dysfunction during infectious events [1]. Measuring PGE2 in CSF is not reasonable in daily neonatal care and PGE2 in blood is rapidly metabolized. However, the urinary metabolite of PGE2 (u-PGEM) is a stable and noninvasive biomarker for inflammation in children [2]. We aimed to investigate the normal distribution of u-PGEM in preterm infants and term infants, as well as levels during inflammation and respiratory dysfunction with the goal to evaluate u-PGEM as a biomarker for inflammation in newborns.

### METHODS

10 preterm infants (mean gestational age, 26 ± 5 weeks) and 48 full-term infants (mean gestational

age 39 ± 3 weeks) from a level 3 neonatal intensive care unit and the general maternity neonatal ward were enrolled retrospectively and a subgroup was enrolled prospectively (6 preterm infants, mean gestational age, 27 ± 3 weeks). Infants with a condition that can cause secondary apnea were excluded. u-PGEM levels were analyzed on day 1, 3 and 7, followed by week 2, 4, 6, 8 and 12 after birth and correlated to gestational age, inflammatory parameters and respiratory support requirement. Parents had to give informed consent and ethical approval was granted.

RESULTS

u-PGEM levels depended on gestational age. Preterm infants exhibited higher levels of u-PGEM compared to full-term infants ($p < 0.05$). Levels of u-PGEM decreased during the first week of life in preterm as well as term infants ($p = 0.05$ and $p < 0.05$). Additionally, a correlation between u-PGEM concentrations and another inflammatory marker, white blood cell count (WBC), was found ($p < 0.05$). Analyses are still ongoing for u-PGEM in relation to cardiorespiratory disturbances and inflammatory conditions such as infection and necrotizing enterocolitis (NEC).

CONCLUSIONS

u-PGEM levels are elevated in preterm infants compared to full-term. Both exhibit a decrease of u-PGEM during the first week of life. In term infants there might be a correlation to high levels of u-PGEM and apneic events during the first days of life, higher u-PGEM levels also seen in premature infants perhaps rendering them more prone to apnea. However, analyses need to be finalized before u-PGEM feasibility as a biomarker is concluded.

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## ABS 48

## COLONISATION WITH GRAM-NEGATIVE BACTERIA (GNB) IN INFANTS IN A TERTIARY NEONATAL UNIT

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INTRODUCTION

Infection is a major issue in the care of hospitalised neonates and its prevention remains a cornerstone of good neonatal care. Multi-resistant Gram-negative bacterial infections and outbreaks are of particular concern in the neonatal units (NNUs) and increasing globally. In order to devise strategies to prevent and control these infections in our Neonatal Unit we reviewed our data on colonization and invasive infection.

METHODS

Aiming to define the epidemiology of neonatal colonisation with resistant Gram-negative bacteria (RGNB) and the risk of developing invasive infection we analysed our data over the last 4.5 years. Screening samples (ear, throat rectal) were collected on admission and then weekly for all babies admitted to NNU. All identified Gram-negative bacteria (GNB) were subjected to antibiotic susceptibility testing using BSAC methodology [1]. RGNB were defined as isolates resistant to at least one of the antibiotic classes.

RESULTS

Overall 20,293 screening swabs were collected from 3,422 infants during the study period and of those 1,363 (6.7%) were positive. 765/1,363 samples, from 408 infants, were positive for GNB. Of the Gram-negative organisms 57.1% were RGNB. The majority (553, 72.3%) were *Enterobacteriaceae* with *E. coli* accounting for 49.5% (274/553) followed by *Enterobacter spp.* (140/553, 25.3%). Median age at the time of colonisation was 12 days (IQR: 5-22). There were 27 cases of GNB bacteraemia during the same period. *E. coli* and *Enterobacter spp.* were the most frequent bacteraemia causing pathogens accounting each for 33.3% of the cases and followed by *Klebsiella spp.* (14.8%). Overall association between colonisation and invasive infection with the same organism is shown in the **Tab. 1** below. For most of the invasive cases (11, 40.7%) screening for colonisation was negative.

CONCLUSIONS

Of 1,363 positive swabs, 765 grew GNB; of those, 57% were RGNB. Only in 25% of the invasive cases screening was positive prior to infection. 40.7% of GNB bacteraemias had a negative screening suggesting other transmission modes.

**Table 1 (ABS 48).** Association between colonisation and invasive infection with Gram-negative bacteria (GNB).

| Different combinations | No. | Comments |
|---|---|---|
| No. of cases with positive swab before GNB BSI | 7 | 2 infants had repetitive +ve BCx |
| No. of cases with positive swab on same day as GNB BSI | 6 | |
| **No. of cases with GNB BSI and negative swabs** | **11** | **1 infant had repetitive +ve BCx** |
| No. of cases with positive swab after GNB BSI | 2 | |

GNB: Gram-negative bacteria; BSI: bloodstream infection.

Our study highlights the importance of GNB screening to recognise local epidemiology and guide antimicrobial treatment. More work is needed to define RGNB transmission in NNU and its relationship to invasive infections.

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## ABS 49

## APPLICATION OF EVIDENCE-BASED MEDICINE METHODS TO DIAGNOSE EARLY NEONATAL SEPSIS

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INTRODUCTION

The lack of clear clinical and paraclinical symptoms of infectious inflammation in infants in the first two days of life makes it difficult to diagnose these conditions and prevents optimizing the treatment of this pathology.

METHODS

The objective of our study was to determine the diagnostic value of clinical and paraclinical indices in infants with suspected infectious inflammation in the first two days of life. A comprehensive clinical and laboratory examination of 100 newborns has been carried out. The findings were analyzed by applying the methods of biostatistics, using the principles of clinical epidemiology.

RESULTS

The examination complex proved, that none of the standard clinical and paraclinical indices had sufficient sensitivity and specificity to verify the diagnosis. Determining the rate of "inflammatory" interleukins 6 and 8 showed that the examined newborns mostly had low concentrations of these interleukins, which do not have sufficient independent diagnostic value to diagnose early neonatal infection. Assessing the diagnostic value for determination of C-reactive protein in serum provided its excess is above 10 mg/L, which is traditionally considered to be a discriminant as to the infection in infants, was characterized by the indices presented below. Sensitivity: 65%, specificity: 79%, positive predictive value: 66%, negative predictive value: 78%, positive likelihood ratio: 3.0 and a negative likelihood ratio: 2.3. Depending on the point of distribution, the diagnostic value of these acute phase indices of inflammation was determined to confirm the neonatal infection in infants in the first two days of life. The high rates turned out to be specific (IL 6 > 60 pkh/ml: 85%; IL 8 > 70 pkh/ml: 70%; CRP > 60 mg/L: 74%) but insensitive markers of infectious inflammation and they were accompanied by falsely negative results in 59-79% of cases. Assessing the diagnostic value of low results of inflammation to deny neonatal infections (IL 6 < 20 pkh ml: 48%; IL 8 < 20 pkh/ml: 69%; CRP < 10 mg/L 94%) was accompanied by falsely positive results in 42-68% of cases.

CONCLUSIONS

The findings give reason to believe that, currently, there is no clinical or paraclinical indices, which could be used to detect early neonatal infection reliably and fast as well as there is no such indices to deny it.

## ABS 50

## NEONATAL BRONCHIOLITIS: CLINICAL PRESENTATION, MANAGEMENT AND PREVENTION

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INTRODUCTION

Bronchiolitis is a common and serious lung infection among children under the age of two. Its treatment is purely symptomatic or better

preventive particularly since certain risk factors of severity have been identified. Our study aims to describe the epidemiological, clinical and therapeutic features of neonatal bronchiolitis in a Neonatal Resuscitation and Intensive Care Unit.

METHODS

A retrospective descriptive study of patients admitted in our Neonatal Resuscitation and Intensive Care Unit over a one-year period (from April 2016 to March 2017).

RESULTS

Our study included 46 patients, 22 male and 24 female. 16 patients were born prematurely. 22 patients were exposed to passive smoking. The median age at admission was 25 days. 43 patients had congestion. Polypnea was found in 42 cases, retractions in 27, difficulty feeding in 28, cyanosis in 12 and apnea in 4 cases. 9 patients had fever. RSV was found in 7 nasopharyngeal specimens from the 13 performed. 43 patients had chest x-ray: normal in 10 cases. Secondary bacterial infection occurred in 17 cases. 10 patients needed mechanical ventilation. We used inhaled epinephrine in 38 cases, aerosolized corticosteroids in 33 and aerosolized anticholinergic agent in 29 cases. Hypertonic saline was used in 2 cases. Chest physiotherapy was performed in 28 cases. The median length of hospital stay was 6 days. 3 patients died: 2 by acute respiratory distress syndrome and one due to trisomy 13.

CONCLUSIONS

Bronchiolitis represents a growing public health problem despite prevention companions. Newborns are particularly vulnerable to this disease. Authors focus on the risk factors and outcome of neonatal bronchiolitis. Despite a lack of supporting evidence, many interventions continue to be used excessively, prompting efforts to curb unnecessary testing and treatments. Prevention remains the best treatment.

## ABS 51

## SHOULD WE LUMBAR PUNCTURE TERM BABIES BASED ON CRP CRITERIA SET BY NICE?

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INTRODUCTION

NICE recommends considering a lumbar puncture if the baby: (1) has a C-reactive protein (CRP) concentration of 10 mg/L or greater, (2) has a positive blood culture or (3) does not respond satisfactorily to antibiotic treatment. We audited LPs performed in term babies in a tertiary neonatal unit.

METHODS

Babies who had CSF sent between 01/01/15 and 31/12/15 were identified. The Badger.net electronic patient record and hospital results systems were reviewed to collect data.

RESULTS

80 babies between $37^{+0}$ and $42^{+3}$ gestation had their CSF analysed. 70 LPs were indicated by a raised CRP (range from 17.2 to 167). Median CRP was 64.9. Four LPs were indicated by a positive blood culture (GBS and *E. coli*). In all of these cases, the CRP was high. Six LPs were prompted by seizures and in three of these cases the CRPs were normal. Two cases of meningitis were managed based on the CSF microscopy. In both cases the CSF culture showed no growth. These LPs were prompted by a raised CRP of 54.8 and 86.6. Treatment included 14 days of cefotaxime. Meningoencephalitis was diagnosed in one case based on clinical presentation, EEG and MRI findings. CSF microscopy, culture and PCR were negative. Treatment included 7 days of cefotaxime/amoxicillin and 21 days of aciclovir.

CONCLUSIONS

The main indication for LPs was a raised CRP. Despite using a higher threshold than the NICE recommendations, only 2 cases of meningitis were identified and in both cases the CRP was greater than 40. In the absence of other clinical indicators, an LP can be considered at higher CRP threshold.

## ABS 52

## MENB (BEXSERO®) IMMUNISATION IN NICU: EXPERIENCE IN A UK TERTIARY NEONATAL UNIT POST INTRODUCTION OF VACCINE

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INTRODUCTION

The UK on 01 September 2015 became the first country to introduce Meningococcal B

(MenB) vaccine (Bexsero®) into the national infant immunisation programme. Bexsero® is recommended for all infants as part of their routine vaccinations at ages 2, 4 and 12 months alongside other regular vaccines. Bexsero® is highly immunogenic and is estimated to protect against 73%-88% of MenB strains causing invasive meningeal disease (IMD) in England and Wales. Objective: We retrospectively evaluated tolerability of Bexsero® vaccine on preterm babies in our neonatal intensive care unit.

METHODS

Retrospective observational study comparing tolerability of the vaccines in the two time periods, before (Period 1, n = 13) and following (Period 2, n = 13) the introduction of the new vaccine (Bexsero®) in September 2015. We inspected the clinical status 48 hours prior to and 48 hours post immunisation to evaluate vaccine tolerance during these two time periods.

RESULTS

Before introduction of Men B vaccine, there were convincingly low levels of side effects in our babies following routine immunisation. After introduction of MenB vaccine, 46% (6/13) of babies became unwell within 24-48 hours of immunisation; 30% (4/13) needed escalation in respiratory support. 15% (2/13) needed rescue ventilation after Bexsero® vaccination.

CONCLUSIONS

We hypothesized that all babies immunised with Bexsero® alongside regular vaccines will remain clinically stable and will tolerate the vaccines without any appreciable side effects. 46% of our babies became unwell following the combined MenB programme, raising speculations about safety profile of the Bexsero® in preterm infants. Precautionary monitoring following vaccination is recommended. Larger studies are needed to ensure safety of Bexsero® vaccine in preterm babies.