

Ethics and limitations to care

NEONATAL ETHICAL DILEMMAS BEYOND EUROPE, A CASE REPORT (202)

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### Introduction /Case Report

There are several agreed ethical principles that are widely accepted in the neonatal practice. However, fundamental variations exist and they hugely influence the plans of management.

In the Middle East and Arab World, there is an ethical framework that governs the process of decision making in the Neonatal Intensive Care (NICU). This framework is primarily drawn from the interpretation of Islamic rules.

### Case Report

A preterm baby (32 weeks gestation) who was known antenatally to be growth restricted with oligohydramnios, cleft lip and palate, bilateral renal pelvic dilatation and echogenic bowel. The parents declined offers for antenatal karyotype testing. At birth, it became clear that he has more dysmorphic feature than the previously detected ones. The baby was unable to maintain his airways. Therefore, he was eventually intubated and ventilated. Few days later, an attempt at extubation was unsuccessful. Karyotype result confirmed the diagnosis of Trisomy 13. The family has opted for the withdrawal of intensive care. The case was submitted to the Hospital Ethic Committee to be specially considered for withdrawal of intensive care and instating palliative care. The Committee has unanimously rejected the proposed plan. The decision was based on the fact that the law of United Arab Emirates (UAE) does not allow for this.

After a very painful and highly emotional time in our NICU, He was air lifted to India where the withdrawal of intensive care could be carried out. He died a week after he left us.

### Conclusions

This case represents the difficulties that are facing families and healthcare professionals in dealing with such a situation. In UAE, the Medical Liability Law (Law No.10 of 2008) has a clear cut stand on these circumstances. In its Article (9), it states that "Patients' life may not be ended for whatsoever reason even upon their request or their guardians or custodians'." There are increasing calls upon lawmakers to revisit this specific issue.

Picture



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## PROFESSIONAL ETIQUETTE AT NICU: A BRIDGE OR OBSTACLE TO AN EFFECTIVE DOCTOR-PARENTS COMMUNICATION? (478)

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### Introduction /Case Report

Debates about etiquette or good manners for many people sound old-fashioned or anachronistic. On the other hand, there is well confirmed that patients' satisfaction with health care services depends not only on the quality of medical care received (related to caregivers' technical expertise) but also on the quality of doctor-patient communications. Etiquette could be considered a tool for expressing mutual courtesy, respect, honest and civility during such a communication. There is to be emphasized that: (i) etiquette norms are culture-dependent and time-changeable and (ii) remains unclear whether stressful situation (expected at NICU) enhances/diminishes the role of etiquette.

### Patients and Methods

A questionnaires were developed to survey both parents of newborn babies hospitalized at NICU (NICU-parents, n=50: 34 mothers and 16 fathers) and health care professionals who work at this ward (n=47: 9 doctors and 38 nurses/46 females and 1 male). Parents were asked to determine how important is for them doctors' (female/male) and nurses' adherence to standards of behavior and issues related to their appearance (e.g. hairstyle, nails length, intensity of perfume/eau de cologne, presence of visible tattoos etc.). Health care professionals (doctors and nurses) were asked about their opinion about how important are for NICU-parents above indicated issues related to etiquette. An adequate statistical analysis was performed.

### Results

This preliminary study shows ( $p \leq 0,05$ ) that NICU-parents are much more focused on health care professional appearance than doctors and nurses believe they are. It is particularly true with regard to nurses appearance. It is to be emphasizes that NICU-parents pay particular attention to health care professional fresh breath/no cigarette smell. On the other hand, generally speaking, health care professionals overestimate the role of certain behaviors (e.g. maintenance high standards of confidentiality during doctors/nurses communications with NICU parents).

### Conclusions

Health care professionals who work at NICU seem to be focused on they behavior and verbal communication. Doctors/nurses underestimate the role of they appearance which, as different studies show, plays a vital role to the successful communication. It is postulated to introduce issues related to professional etiquette to the curricula of medical (doctors/nurses) education. The role that etiquette-based medicine has to offer to medical practice is still to be discovered.

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## SOCIAL CONTEXT OF THE CONCEPT OF FUTILE THERAPY: BIOETHICAL CONSIDERATIONS (219)

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### Introduction /Case Report

Though the concept of medical futility finds its roots in the Greek Antiquity, undoubtedly, this idea exploded in 1980s and 1990s. It is to be emphasized that one of the central theme of this feverish debate, which took place in the last decades of the 20th century, was the problem of the utility of the treatment (mainly cardiopulmonary resuscitation) of very low birth-weight babies. Nonetheless the concept of futile treatment has entered into the common use not only in research articles, but first and foremost in the guidelines aimed at defining best practice standards for, among other, NICU treatment, there is still lack of agreement how this concept should be defined.

### Patients and Methods

This study is based on a literature review. The PubMed database was browsed. All ethical consideration were undertaken within the context of four principles approach to bioethics (commonly known as principlism) and coherentism, as the proper method of this approach to bioethics, was used to justify conclusions.

### Results

An attempt, observed especially in guidelines defining the correct course of the treatment in different medical wards, including NICU, to define futile treatment in purely biomedical terms and leaving decisions (and responsibility) in hands of doctors should be considered as the expression of a backdoor reentry of medical paternalism. Purely biomedical (“physiological”) definitions of medical futility not only fail in providing value-neutral understanding of the concept, but also seem to be intrinsically discordant with the principle of respect for autonomy. To demonstrate righteousness of the above formulated judgment, four problems are considered: (i) the role of parents in making decision, (ii) duties that family members have towards one another, (iii) socially constituted meaning of “resuscitation”, and (iv) the responsibility of the members of the therapeutic team.

### Conclusions

The way toward explaining the concept of medical futility should not be limited to strictly medical consideration, moreover it seems that there is not enough to extend such considerations by taking into account (bio)ethical reasons. The understanding of the concept of medical futility needs to be founded on consideration undertaken in the context of (broadly understood) philosophy of medicine.

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MORBIDITY AND MORTALITY IN INFANTS AT THE LIMIT OF VIABILITY IN A LEVEL 3 PERINATAL HOSPITAL, IN LISBON, PORTUGAL (596)

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### Introduction /Case Report

Over the past decades, advances in neonatal care have increased the rates of extremely preterm birth, decreased preterm mortality rates and lowered the limit of viability, the level of maturity below which survival without severe deficits is unlikely.

It is essential to have local data on infant survival after extremely preterm birth in order to assess care services, clinical guidelines and parental counseling. Our aim with this study is to evaluate rates of survival and neonatal morbidity to discharge, among extremely preterm infants admitted to a tertiary Neonatal Intensive Care Unit (NICU), in Lisbon, Portugal.

### Patients and Methods

A retrospective chart review of all extremely low gestational age infants (23-26 weeks), who were born alive, between January 1, 2012 and December 31, 2014. Collected data included neonatal morbidity and mortality, and associations between perinatal interventions and survival. Severe neonatal morbidity was defined as the presence of at least one of these: peri- and intraventricular haemorrhage grade III and/or infarction (Volpe), cystic periventricular leukomalacia (de Vries et al), retinopathy of prematurity stage  $\geq 3$  (International Committee for the Classification of Retinopathy of Prematurity), moderate or severe bronchopulmonary dysplasia (requirement for supplemental oxygen and/or mechanical respiratory support at 36 weeks PMA), or necrotizing enterocolitis Bell's stage  $\geq 2$ .

### Results

Eighty six extremely preterm infants were included. Early neonatal death occurred in 34.9% (from 85.7% at 23 weeks to 10.0% at 26 weeks), including 9 cases of delivery room death. Survival rates for live born infants at 23, 24, 25 and 26 weeks' gestation were 17.7%, 33.3%, 55.6% and 90.0% respectively. Of the 77 infants admitted to NICU, 47 (61.0%) survived to discharge and within this group 65.9 % developed severe neonatal morbidity, with infants at the lowest gestational age at greater risk. Between 23 and 26 weeks there was a marked increase in the rates of prenatal steroid use (47.0% and 96.7%, respectively) and caesarean delivery (0% and 73.3%, respectively). In contrast, a decrease was observed in multiple pregnancy (70.6% and 26.7%, respectively), chorioamnionitis (58.9% and 20.0%, respectively) and assisted reproductive techniques (52.9% and 16.7%, respectively).

## Conclusions

Of the 86 extremely preterm infants born alive, 54.6% survived. Global survival (17.7% and 90.0%, respectively) and survival without major short neonatal morbidity (0% and 51.9%, respectively) increased between 23 and 26 weeks.

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### SOLIDARITY WITH DISABLED SURVIVORS BORN EXTREMELY PRETERM – A SURVEY AMONG THE SWISS POPULATION (538)

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## Introduction /Case Report

Moderate to severe overall disability rates among children born extremely premature ( $\leq 28$  weeks) range between 25 and 30%. Alongside the individual impact of extreme prematurity there are also considerable costs at the societal level. Yet very little is known about society's attitudes. Although the burden on babies, family and doctors are frequently described the burden on society is deemed controversial. The financial and structural solidarity provided by society to disabled people may influence decision-making about treatment options for infants born extremely preterm. Therefore, we designed a population survey among residents living in Switzerland to assess their level of solidarity.

## Patients and Methods

We conducted a nationwide representative anonymous telephone survey. 1210 Swiss residents aged 18 or older were interviewed. We asked 13 questions regarding extreme prematurity such as initiation, withholding and withdrawal of intensive care, setting an upper financial limit to intensive care and aspects of decision-making. Three specific questions pertained to the solidarity of the interviewed person, of the personal environment and of the society at large towards people with disabilities. Statistical analysis was performed using IBM SPSS Statistics 22 (Armonk, NY, USA). The results were weighted with regard to the three language areas to allow for nationwide generalisation of the results.

## Results

36% of the respondents believed that intensive care must not be withheld from extremely preterm infants with an expected poor quality of life, 29% agreed to this option, while 27% found themselves in between the two positions, and 8% did not know. When asked if an upper financial limit was justified for the treatment of extremely preterm infants with an uncertain future quality of life, 32% of the population were against such a limit, 34% were in favour, and 27% were deliberating. 89% rated their own solidarity towards disabled people as high; the solidarity of their personal environment and of the society at large was estimated as high by 79% and 49%, respectively. The question whether the readiness to provide support to disabled people had changed over the last 10 years was answered as follows: very improved 11%; rather improved 48%; remained equal 26% and rather decreased 10%.

## Conclusions

This survey reveals that the majority of the Swiss population rated their solidarity as high. This finding may alleviate some pressure on parents and health care providers in the decision-making process of extreme preterm infants. According to our respondents' solidarity with disabled people encompasses the right to life with a handicap resulting from extremely preterm birth independent of quality of life or costs.

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BORN AT THE VIABILITY CUSP: TO CARE OR PLEAD SILENCE? (647)

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## Introduction /Case Report

In an era where clinical and ethical debates are swirling around resuscitation and life-support treatments for infants born at the "cusp of viability", it is imperative to determine survivability and health outcomes in this population so as to influence decisions.

While large epidemiologic studies such as EPICure 1 and 2 have shown improved survivability, but not health outcomes in periviable babies.

This study was done with the intent of retrospectively determining the survival rate and short term health outcomes in 23 to 23+6 week deliveries at a Level III neonatal intensive care unit in the UK.

## Patients and Methods

This is a retrospective study based on the record analyses of infants born between 23 0/7 and 23 6/7 weeks gestation, in the Neonatal Intensive Care Unit of Norfolk and Norwich University Teaching Hospital, UK; between January 2008 and April 2015.

Data from our perinatal database was abstracted and analyzed. For each patient, data was abstracted using 5 domains, namely Demographic, Maternal, Perinatal, Clinical and Survivor, characteristics respectively.

Descriptive statistics, Independent t-test and Mann-Whitney test, were built accordingly. A p-value  $\leq 0.05$  was considered statistically significant. The primary outcome, survival, was defined as discharge from neonatal intensive care.

## Results

A total of 32 neonates born between 23 0/7 and 23 6/7 weeks fulfilled the criteria. 15(46.9%) of these neonates were girls and 17 (53.1%) - were boys. The mean birthweight and median gestation were 572.22g and 23+4 weeks respectively. Overall, 12/32 (38%) of the neonates survived to the time of NICU discharge (survival rate 0.38; 95% CI 0.20, 0.56). All the survivors developed RDS/chronic lung disease during their NICU course, out of which 6/12(50%) did not require supplemental oxygen at discharge. Of the 12 surviving infants, 7 (58.3%) did not have significant neonatal morbidity (Retinopathy of Prematurity  $\geq 3$ , Bronchopulmonary dysplasia and severe brain damage) at discharge (P= 0.004).

## Conclusions

Over an 8 year period, more than one third of infants delivered at 23 0/7 and 23 6/7 weeks' gestation survived to be discharged from NICU. Our study indicates that more than half of the infants who survived

did remarkably well at discharge without substantial morbidity. Although long term outcome evaluation is warranted in this population, our study is well poised to inform parental counselling and short term outcome prognostication.

Table

Table 1: Summary of short term outcomes among infants born between 23+0 and 23+6 weeks at Norfolk and Norwich University Teaching Hospital from 2008 to 2015

Outcomes	Number (%)
<b>Showed Signs of Life at birth</b>	32(100)
<b>Admitted to NICU, No. (%)</b>	32(100)
<b>Died before NICU Discharge</b>	20(62.5)
<b>Survived to NICU Discharge</b>	12(37.5)
<i>Survived with Significant Morbidity</i>	5(41.7)
<i>Survived without Significant Morbidity</i>	7(58.2)

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ARTIFICIAL NUTRITION: HUMANE SYMPTOM RELIEF OR PROLONGING THE PROCESS OF DEATH? (228)

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### Introduction /Case Report

Provision of basic nutrition and hydration is considered a basic human need. This is especially pertinent in neonates who are entirely reliant on others for this provision. Whilst the administration of artificial nutrition and hydration is viewed as a medical intervention, its withdrawal remains controversial. Infants born with some life limiting conditions may not have the physical ability to feed naturally without intervention. Do we have an obligation to intervene or are we only prolonging the infant's life with painful, invasive procedures?

### Case Report

We present a case of a term infant with an antenatal diagnosis of Edwards Syndrome, Tetralogy of Fallot and oesophageal atresia. Infants born with Edwards Syndrome survive for a median of 2-14.5 days, with a 1 year survival rate of 5-10%(1). Following antenatal diagnosis at 20 weeks the parents declined termination of pregnancy. They did, however wish for comfort care and requested no active resuscitation at birth. Comfort care encompasses provision of basic human needs including managing hunger. Fluids and nutrition can therefore be considered as essential care and not instituting basic nutrition viewed as "starving" the infant. If oesophageal atresia is confirmed postnatally in our case, nutrition for hunger control would involve insertion of a gastrostomy tube with intravenous fluids being commenced pending surgery. This could all be viewed as active medical management inflicting pain with potential additional complications. Is this an ethical option if the ultimate aim is to provide symptom relief? Prior to delivery there was a meeting between the clinical team, the ethics committee and the parents to make a plan for delivery. The baby girl was born at 37 weeks by spontaneous vaginal delivery. She was given IV fluids pending initial investigations. Her oesophagus was found to be not patent and her parents declined surgical intervention. She was transferred to a local hospice at 24 hours of age where she died in the arms of her parents.

### Conclusions

Availability of advanced medical and surgical care does not readily translate to their provision in infants with limited life expectancy. Effective and empathic communication between the medical and surgical teams, ethics committee and parents provided a cohesive and humane management plan in this infant.

Other / Quality improvement and Safety and Error Preventio

A QUASI EXPERIMENTAL STUDY: IMPACT OF INSERTION AND MAINTENANCE CHECKLISTS ON CENTRAL VENOUS CATHETER INFECTION IN A NEONATAL INTENSIVE CARE UNIT. (178)

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Introduction /Case Report

Central venous catheters (CVC) are lifesaving devices, especially for sick and extremely preterm infants. However, infection is a major complication of these catheters. Every incidence of HAI in ELBW infants increases the risk of neurodevelopment impairment;

41% of infants with an infection will develop one adverse neurodevelopment outcome at 18-22 months of corrected age. There is an abundance of literature describing numerous strategies to reduce and prevent infection in CVCs. In neonates, checklists have successfully enabled the introduction of bundles of interventions to reduce catheter infections.

Patients and Methods

A quasi experimental study, over 24 months, utilising a pre-post design to determine if an insertion, daily maintenance and line access checklists reduces confirmed and suspected infections in central venous catheters in the neonatal unit.

Results

Following the introduction of checklists definite CLABSI significantly reduced from 14 ( $\pm 6.4$ ) to 6.6 ( $\pm 4.5$ ) /1,000 catheter-days per month, a reduction of 7.5 (95% CI of 2.6 to 12.4),  $p=0.005$ . Total CLABSI also significantly reduced from 22.8 ( $\pm 11.5$ ) to 13.2 ( $\pm 5.3$ ) /1,000 catheter-days per month after introduction of the checklist, a reduction of 9.7 (95% CI of 1.8 to 17.6),  $p=0.019$ . Checklist compliance for insertion mean ( $\pm$ SD) was 74.6 ( $\pm 9.48$ ) and compliance for daily maintenance mean ( $\pm$ SD) and 67.4 ( $\pm 4.3$ ).

Conclusions

Introducing checklists of evidence based interventions reduce infection rates and increases the survival time of the central line. Catheter related infections are expensive and impact adversely on long term outcomes and survival. Checklists are an economical way to reduce infection and improve outcomes.

## Ethics and limitations to care

### A CONVERSATION ANALYTIC STUDY OF PARENTAL INVOLVEMENT IN NEONATAL CRITICAL CARE DECISION-MAKING (697)

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## Introduction /Case Report

The RCPCH (1) recommend that parents should be involved in decisions regarding the redirection of care for their baby. The extent to which parents are involved has been studied retrospectively with the use of interviews and surveys (2). What remains unknown though, is ultimately what the decision making process looks like in practice. The aim of the study was to explore the decision-making process between doctors and parents of babies in the neonatal unit, and who are faced with decisions about the redirection of care from full intensive care to palliative care. We address this issue through the transcription and analyses of real life decision making conversations.

## Patients and Methods

Thirty one families were recruited from a single neonatal intensive care unit in England, where a discussion around the redirection of care was a possibility in the future. All formal conversations between the doctor and parents were audio recorded. Recordings were then transcribed and analysed using the method of Conversation Analysis (3). Decision-making sequences were analysed in terms of the patterned ways in which decisions were introduced and the implications for what participants did next. The study was funded by a NIHR Programme Development Grant and approved by the East London REC.

## Results

Fifteen conversations were identified (eight families; five consultants) in which redirection of care was discussed. Three infants had severe perinatal asphyxia, four infants were born extremely preterm with neurological complications, and one infant was born with a lethal congenital anomaly. Two distinct communicative approaches to decision-making were used by doctors: 'making recommendations' (n=10) and 'providing options' (n=5). Different trajectories for parental involvement in decision-making were afforded by each design, as well as differences in terms of the alignments, or conflicts, between doctors and parents. 'Making recommendations' led to misalignment and reduced opportunities for questions and collaboration; 'providing options' led to an aligned approach with opportunities for questions and fuller participation in decision-making.

## Conclusions

The analysis provides a unique evidence base that will be important in the development of communication skills training for doctors. Findings also undermine the communication guidance currently provided by professional bodies, showing that the best way to identify what works is through evidence-based analysis.

The results have important implications for improving the experiences of parents who are faced with these life changing decisions.

NEONATAL STROKE - CASE STUDY (192)

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Introduction /Case Report

Perinatal stroke in neonates is not rare. It is an important precursor of long-term neurological disability, including congenital hemiplegia, seizures, and cognitive disorders. In contrast to the more diffuse perinatal brain insults that cause cerebral palsy, cerebral infarction is associated with obstruction of large vessels and typical focal damage in otherwise intact brain. In most cases clinical recurrent focal seizures are the only clinical manifestation. Neonatal seizures of non-vascular causes are often multifocal or myoclonic. Determination of the etiology of seizures in a newborn is necessary because treatment and clinical results vary, depending on the underlying condition.

Case Report 1

The child was born in the referral hospital at 36 weeks of gestation by cesarean section, due to failure of tocolysis. The birth weight was 3050 g, length 51 cm, Apgar score 10/10. Immediate postnatal adaptation was without complications. At the age of 3 hours apnea with cyanosis occurs, requiring ventilation with bag and mask. Subsequently the child was transported to our department. The course of hospitalization was complicated with accumulation of apneic spells requiring mechanical ventilation. Ventilation setting was low with FiO<sub>2</sub> 0.21. Simultaneous amplitude-integrated EEG (aEEG) revealed convulsive background of apnea, therefore we started anti-convulsant therapy with phenobarbital. Convulsions on aEEG persisted in spite of the treatment that is why we changed it - seizures resolved on levetiracetam treatment in combination with midazolam. Prophylactic antibiotics therapy was terminated at the age 48h, after exclusion of infection etiology. CSF analysis and culture were negative. Inflammatory, toxic or metabolic etiology of the convulsions has not been established. Implemented MRI examination at DOL 18 revealed image of extensive extraaxial pseudocysts supratentorially, intra-axially, fronto-temporo-parietally on the left, with partial septa of size 65 x 26 mm without perifocal edema. Consulting radiologist concluded the finding as a perinatal stroke attack in term child of overcome perinatal vascular attack. In the next course of hospitalization the child was breathing spontaneously, without seizure activity seen neither clinically nor per aEEG. Thromboembolic evaluation (factor II, factor VIII, antithrombin III, protein S and protein C activity) were all within normal limit for age. Genetic testing was negative for mutations for factor V Leiden. There was no need for surgical intervention of the brain. At the time of discharge in neurological findings dominated mild hypotonia, physical therapy was started. The child was discharged without anticonvulsant therapy.

Case report 2

The child was born at 40 weeks of gestation by vaginal delivery assisted with fundal pressure. The birth weight was 3500 g, length 50 cm. The child had perinatal asphyxia (Apgar score 7/8, pH 7.13, pCO<sub>2</sub> 9, BE - 7), immediate postnatal adaptation was without complications. At the 3rd day of life (DOL) clonic convulsions of hands and legs developed, lasting about 3 minutes, with opisthotonus and deviation of eyes. Phenobarbital was administered with good response. Cerebral function monitoring with amplitude-integrated EEG was started. aEEG had normal pattern. However, approximately 24 hours after the initiation of the treatment with phenobarbital, we saw clonic seizures, therefore we added midazolam to the

treatment. Inflammatory, toxic or metabolic etiology of convulsions was excluded. CSF analysis and culture were negative. Ultrasonography of the brain was normal. MRI at 13 DOL revealed signal and structural changes in the white matter and cortex fronto-parieto-occipital-temporally on the right, corresponding with ischemia at chronic stage, healing with glial scars and postmalatic pseudocyst changes with atrophy of cortical zone and residual deposits of hemosiderin / ferritin after petechial hemorrhages. At the time of discharge in neurological findings dominated mild hypotonia, physical therapy was started. The child was discharged without anticonvulsant therapy.

Both children are followed closely by a neurologist so that early referrals for rehabilitative or educational services can be made.

## Conclusions

Seizures, apnea, and depressed level of alertness may be the main clinical features of perinatal stroke in the neonatal period. Symptoms after birth lead us to neuroimaging, such as ultrasound, Doppler sonography, computerized tomography (CT) scan, CT angiography, and multimodal MRI, where usually an insult of vascular origin is recognized.

CEREBRAL WHITE MATTER INJURY FOLLOWING GRAM NEGATIVE BACTERIAL SEPTICAEMIA IN NEONATES  
(696)

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Introduction /Case Report

BACKGROUND

Gram negative bacterial sepsis and meningitis remains a significant cause of neonatal mortality and long term morbidity (1, 2).

AIM

We report two neonatal cases with gram negative bacterial septicaemia and meningitis who had multifocal cerebral lesions.

METHODS

We retrospectively analysed the case notes, electronic neonatal and radiological databases at our neonatal intensive care unit to get patient information.

Case Report 1

A preterm neonate born at 27 weeks of gestation with a birth weight of 960 grams colonized with *Serratia marcescens* clinically deteriorated on day 16 of life. She was screened for infection and commenced on antibiotics with serratia sensitivity. She had raised C- reactive protein and low white cell count. She grew *Serratia marcescens* in both blood culture and cerebrospinal fluid. On day 17, cranial ultrasound showed echogenic lesions in the right parietal area. Repeat scan on day 18 showed extensive bilateral fronto-parietal cerebral echogenic lesions with effaced sulci and midline shift suggestive of multifocal abscesses. In view of the multi-systemic deterioration with non-responsive status epilepticus and extensive cerebral abscesses, palliation was instituted and she died on day 19 of life.

Case Report 2

A term neonate with birth weight of 2800 grams presented after discharge on day 3 of life with jaundice, poor feeding and weight loss. There were no known risk factors for sepsis. He rapidly deteriorated by the following day requiring ventilatory support and anticonvulsive therapy for status epilepticus. The infective markers were raised with positive blood culture growing *Enterobacter cloacae* and significantly raised cerebrospinal white cell count indicative of meningitis. The cranial ultrasound scan done on day 4 showed bilateral fronto-parietal cerebral echogenic lesions with infarction which rapidly progressed in subsequent scans. MRI on day 11 confirmed extensive haemorrhagic ischaemic fronto-parietal cortical, basal ganglia and thalamic lesions with evolving cystic encephalomalacia. Intensive care was withdrawn and the baby died in a hospice on day 30 of life.

## Conclusions

These cases illustrate that gram negative bacterial septicaemia and meningitis can lead to rapidly progressive cerebral lesions. Though uncommon, brain abscess is a serious complication of meningitis. Close monitoring with serial bedside cranial ultrasound imaging helps to identify these lesions. The outcome of extensive cerebral abscess can be poor in neonates despite treatment.

## Brain & Development / Early developmental care

### CODE32 (427)

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### Introduction /Case Report

Highly specialized care, centered on infant development, during the first minutes of life of preterm infants < 33 weeks of gestation, can facilitate their transition to extrauterine life and prevent medium and long-term health complications. Additionally, proper attention to the family can help them to adapt to this stressful experience and favour bonding between parents and the child.

### Patients and Methods

Multidisciplinary meetings among a specialized team of neonatologists, obstetricians, neonatal nurses, nurses assistants and midwives started in July 2012, in order to develop a guide to improve the medical attention given to preterm babies during the first minutes of their life. The goals of such meetings were to 1) implement evidence-based interventions (control body temperature, oxygen delivery, respiratory management with continuous positive airway pressure (CPAP), and developmental care measures), 2) improve coordination between the staff involved and 3) carefully attend to the family role during the overall process.

To improve the quality of care in the delivery room for babies born at less than 29 weeks of gestational age, a neonatal nurse was also incorporated into the team.

### Results

During a two years period, the multidisciplinary team helped develop key materials (checklists, tables of tasks to define the role of each member of the staff) to guide the attention and care given to premature babies < 32 weeks during the first minutes of life (CODE 32 Guide). This guide includes: prenatal information given to the family, ethical issues related to limits of viability, prevention of hypothermia, respiratory management with continuous positive airway pressure (CPAP with binasal prongs), and baby's position and environment measures (light, noise, odor, etc).

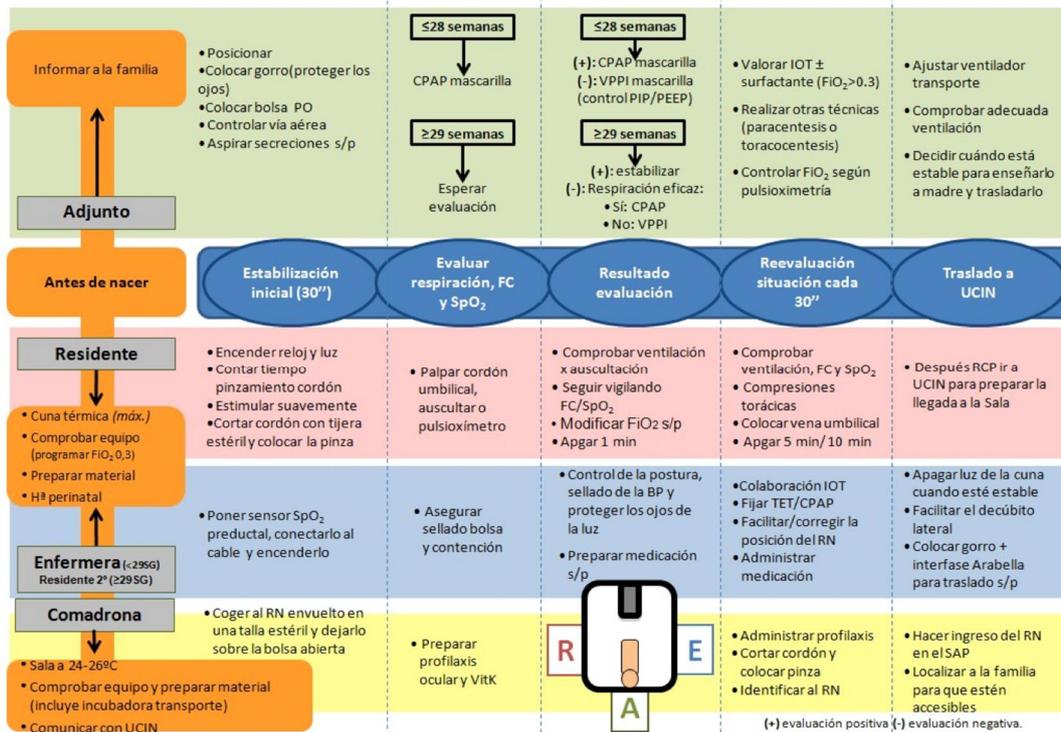
Neonatal nurses were trained in neonatal cardiopulmonary resuscitation. The staff involved (midwives, nurses assistant, neonatal nurses and pediatricians) attended small-group sessions with a slide show and participated in some multidisciplinary simulation training workshops.

The process was completed in July 2014.

## Conclusions

Highly specialized attention given to premature infants born at less than 33 weeks of gestational age at the delivery room and during their first hours of life requires a multidisciplinary team. Such team need to coordinate work in order to carry out properly the most beneficial interventions for the welfare of the baby. This process requires highly specialized staff members coupled with their continued and specific training.

Table



Picture



Brain & Development / Structural and Functional Brain Imaging

NEWBORN WITH ARACHNOID CYST-CASE REPORT (633)

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### Introduction /Case Report

Primary arachnoid cysts are present at birth and are result of developmental abnormalities in the brain or spinal cord that arise during the early weeks of gestation. They can occur anywhere including interhemispheric fissure, posterior fossa, quadrigemine cisterna, ventricles, suprasellar cisterna. They can be diagnosed by ultrasound in the fetal period or after birth. Arachnoid cysts may occur together with anomalies of the corpus callosum, skeletal and vascular malformations. Only 20% of patients have symptoms that may present with headache, signs of obstructive hydrocephalus, focal neurology or seizures.

The aim of this report is to present a newborn with arachnoid cyst.

### Case Report

Clinical, neurological, ultrasound examination, MRI, total blood cells, glycemia, C –reactive protein, ELISA on TORCH and Epstein-Barr virus (EBV).

Clinical Cases or Summary Results: The newborn is from the second pregnancy of a 30 year old women. In sixth month mother had sinusitis with high fever, and was treated with antibiotics. We found Candida in vaginal smear at ninth month of pregnancy. Delivery was finished by cesarean section due to central placenta previa. The female newborn had BW 2700g, BL 51cm, head size 32cm, Apgar score was 8/9, 37/38 weeks of gestation. Newborn was vital, paler skin color, hypotonic, with other normal clinical findings. Endocranial ultrasound was done in the second day of life, showing presence of a cystic formation in right lateral ventricle level, with normal sized ventricles. Endocranial MRI: Arachnoid cyst in right venticle trigone (8x7,5mm) with mild lateral ventricle displasment. Other ventricular system parts were normal size and configuration.

Neurological exam shows generalized hypotonia.

All laboratory test were within normal values. ELISA of child blood samples on TORCH and EBV shown elevated levels of IgG to CMV, HSV1, EBV and T.gondii, IgM negative.

### Conclusions

The localization and size of the arachnoid cyst determine symptoms and their manifestation period. Significance of ultrasonographic monitoring of cysts and measuring their size through the first year of life, lies in the possibility of their dilatation and symptom manifestation. Neurosurgical treatment is conducted only in case of neurological deficit progression or hydrocephalus development.

Brain & Development / Placenta and prenatal factors

## PERIVENTRICULAR LEUKOMALACIA IN A PRETERM NEONATE WITH EARLY ONSET CAPNOCYTOPHAGA SEPSIS (316)

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### Introduction /Case Report

Capnocytophaga is an opportunistic, slow-growing, capnophilic, facultative anaerobic, gram negative fusiform bacilli residing in oropharyngeal cavity of mammals. In humans, it causes localized periodontal infections, sporadic invasive infections in immunocompromised persons and rarely neonatal infections. Chorioamnionitis and perinatal infection with Capnocytophaga is infrequent and is generally of lower morbidity risk in fetus and neonates. We describe a case report of early-onset neonatal Capnocytophaga sepsis with culture negative meningitis associated with development of early cystic periventricular leukomalacia, which has been reported rarely in literature.

### Case Report

A 1.39kg male infant was born vaginally at home to a 16 year old single mother. Mother did not receive any prenatal care or antenatal steroids. The mother reported no evidence of fever, rash or foul smelling vaginal discharge and there was no evidence of clinical chorioamnionitis. She did not undergo any dental procedures during the pregnancy and her dental hygiene was good. There were no pets at her home and no history of animal bites or scratches. The mother started having contraction at home, followed by rupture of membrane and delivery of baby on the bed. The cord was cut and placenta delivered by paramedical staff at 10 minutes of life. Baby had spontaneous cry at birth and he required initial support with bag and mask for respiratory distress. Baby was scored to be of 32 weeks gestation by modified Ballard's scoring.

In neonatal intensive care unit, baby was placed on continuous positive airway pressure support for 12 hours and later debronged to room air uneventfully. He did not receive any inotropic support and clinical examination was unremarkable except mild respiratory distress. Chest X-ray was suggestive of mild respiratory distress syndrome.

Complete blood count done on admission was unremarkable and baby was started on first line antibiotics of intravenous penicillin and gentamycin. Initial blood culture showed no bacterial growth but later grew Capnocytophaga sputigena on day 5. Antibiotic was changed to cefotaxime and it was continued for total 21 days. The lumbar puncture was suggestive of leukocytosis (WBC 60 cells). CSF and repeat blood culture was negative.

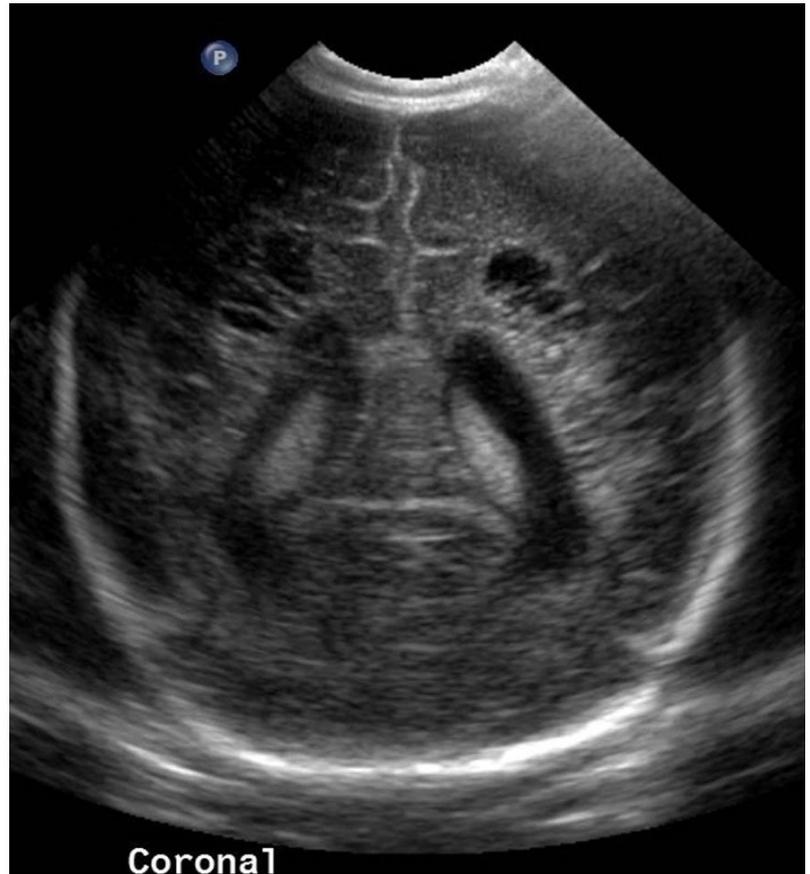
Cranial ultrasound scan done on day 3 showed bilateral grade I intraventricular hemorrhage. Repeat scan done 2 weeks later showed tiny cystic spaces in the periventricular white matter bilaterally, suggestive of periventricular leukomalacia.

Baby was started on total parenteral nutrition and he reached full enteral feeds by day 14. His metabolic screen, ophthalmological examination and hearing test were normal and he was discharged well at 1 month of age.

## Conclusions

Capnocytophaga infection is probably under-reported due to its fastidious nature causing subclinical infection in mother. This case reminds that though Capnocytophaga neonatal septicemia and meningitis are rare, the organism is more virulent in neonates with possibility of periventricular leukomalacia. We recommend serial neuroimaging of preterm neonates with Capnocytophaga sepsis to evaluate for possibility of neurodevelopmental morbidities.

## Picture



Brain & Development / Early developmental care

SKIN-TO-SKIN AND RELATIONALITY - A QUALITATIVE IN DEPTH EXPLORATION OF THE SKIN-TO-SKIN PROSESS IN THE RELATIONSHIP BETWEEN THE MOTHER AND THE NURSE. WHAT PROMOTES AND INHIBITES SKIN-TO-SKIN CONTACT AND PARENTAL INVOLVEMENT? (376)

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### Introduction /Case Report

In a Scandinavian single room NICU are the parents invited to stay 24/7 with their preterm infant. Consequences of separation between preterm infants and parents have been discussed in many aspects. Skin-to-skin care has become a common practice in Scandinavian NICUs. Resent research show that the physical environment and access to the preterm infant are the two most important factors for promoting parental involvement and skin-to-skin contact (SCC) between the parents and the infant. Several studys emphasize the important role of the nurse/parents relationship. The study will explore this relationship regarding what promotes and inhibites skin-to-skin contact (SCC) and parental involvement.

### Patients and Methods

A qualitative observational in-depht study of three nurse-mother interactions will be conducted in a Norwegian single-room NICU. The observations are planned to be conducted during the first week of admission to the NICU. The observation will be followed by a separat semi-structured interview with the nurse and the mother at the same day or the following day.

The preterm infant must be between 28-32u GA at birth and in a health condition that allows the infant to be cared for skin-to-skin with the mother.

### Results

The results will be available at the time of the conference. Data from the observation and interview regarding the nurse–mother–infant dyads will be presented and discussed. The results will contribute to new knowledge about the interpersonal interaction process between the mother and the nurse, due to the actual performing of skin-to-skin care (SSC) and the relational aspects.

### Conclusions

This new knowledge will contribute to an increased understanding of the nurse-parents relationship. And it may be important both for the parents in NICU and the professionals who wants to increase the incidence of SSC in the future.

Other / Quality improvement and Safety and Error Preventio

Cranial Ultrasounds: An audit of compliance in a tertiary neonatal centre (818)

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### Introduction /Case Report

Routine cranial ultrasound imaging is undertaken on many neonatal intensive care units with the aim of identifying abnormalities in order to inform treatment decisions, prognosis and monitoring for later complications. There are medico legal implications related to the timing of brain injuries that the ultrasound scan might identify. Our imaging guideline is similar to those suggested in a commonly used textbooks. We audited our current cranial ultrasound imaging guideline to assess adherence to it and implement a quality improvement initiative.

### Patients and Methods

We audited a sample of 14 cases that were selected from the admissions to our tertiary surgical neonatal intensive care unit from July to December 2014. Acknowledging that some infants had head scans at other timings, we still reviewed the notes strictly against our current guidance of scanning babies born below 33 weeks or below 1500g. Standards were based on timing of USS from date of delivery (<3hr, 7 days, 14 days, 21 days, 28 days and every two weeks following this). On the weekly scans we allowed a variation of +/- 1 day for the audit. We aim to record information on haemorrhage, ventricles and parenchyma with 10 images on each scan. This was strictly assessed per patient. We aim to document our findings on a reporting form and on an electronic discharge system.

### Results

We audited 14 patients. Nine patients met both the weight and gestation criteria, 2 met only weight criteria and 3 met only gestation criteria. Compliance was poor. 7% of patients had an ultrasound within 3 hrs of birth, 50% of patients received an ultrasound on day 7, 21% received an ultrasound at day 21, 27.5% received an ultrasound at day 28, 14% of patients received an ultrasound every two weeks subsequent to this until discharge. For all the scans for a given patient, information on haemorrhage, the ventricles and the parenchyma was recorded in 50%, 43% and 50% of cases respectively, with all scans comprising of 10 images in 43%. The imaging was documented correctly as per our guideline in 65% and each scan was documented on the electric discharge summary in 36% of cases.

### Conclusions

This audit provides evidence that we are not following out local guidance fully. This is likely to be multifactorial. There may be related workload issues, infrastructure issues (guidance, image storing) and a need for simplifying and updating the guidance. Following this audit we will institute a quality improvement project and reaudit in the next 4 months. No adverse outcomes were noted relating to deviation from the guidance.

Other / Quality improvement and Safety and Error Preventio

NEOMATE: A SMARTPHONE APP TO IMPROVE ACUTE CARE FOR SICK NEONATES (368)

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### Introduction /Case Report

Centralisation of neonatal intensive care to large tertiary centres has delivered huge improvements in neonatal care over the past decade. However, an important disadvantage is the diminished experience of staff in smaller hospitals at managing sick and extremely premature infants, resulting in errors and inadequate management as a consequence of avoidable human factors.

NeoMate is a smartphone app that has been created in response to this problem, to help neonatal staff provide the best possible care for all unwell babies, in every hospital. This free app offers drug and fluid calculations, concise checklists and information to help guide acute neonatal care.

### Patients and Methods

Systematic reviews of prescribing errors often cite factors such as memory lapses, lack of experience, fatigue and stress. NeoMate attempts to address these factors by providing checklists for acute care, and drug calculators to ensure prescribing accuracy, even in difficult situations.

A working group of neonatal transport staff created checklists for common neonatal problems. Such checklists are short, precise and easy to use, providing reminders of only the most critical steps that are dangerous to skip, but often overlooked nevertheless.

Drug calculations used an established London Neonatal Transfer Service formulary, and were checked by two neonatal pharmacists and automated testing.

The app was created for iPhone and Android, and has received MHRA Class I device approval.

### Results

The app was officially launched in February 2015 and has already been installed on over 12,000 smartphones, with users from over 130 countries. Feedback from users has been excellent and has already led to the development of several new features. An interesting development is the popularity of the app in countries like India, Mexico and Peru, where a more resource-poor environment means this app could be particularly valuable.

### Conclusions

NeoMate is an app for smartphone that has experienced a rapid uptake and enthusiastic initial welcome from the neonatal community. Anecdotally, the app appears to help neonatal staff perform more consistently in stressful situations, providing assistance with difficult drug calculations and offering

checklists to remember critical steps in acute management. Formal studies are required to quantitatively assess its utility.

Picture



# NeoMate

grams ✕

## ↶ Intubation

ETT Tube Size	3.0
ETT Length at Lips	7.0 cm
<b>Morphine bolus</b> (100mcg/kg)	133 micrograms by slow IV push
<b>Suxamethonium</b> (2 mg/kg)	2.7 mg by slow IV push
<b>Atropine</b> (10 mcg/kg)	13.3 micrograms by slow IV push
<b>Curosurf</b> (200mg/kg 1st dose, 100mg/kg 2nd dose)	<b>First dose:</b> 265 mg, <b>Second dose:</b> 133 mg (if indicated) Practical note: use whole vial closest to calculated dose.

## ♥ Cardiac Drugs

### Information and Disclaimer

Other / NICU design and Family centres care

## TRANSITIONAL CARE – ARE WE PICKING THE RIGHT PATIENTS? (476)

K. Pettinger, A. Fonfe, Y. Gargani, N. Sammons, T. Lau, A. Manou

Leeds Teaching Hospitals Trust

### Introduction /Case Report

Transitional care (TC) provides a useful place for medically supported care of the baby by the mother when baby needs more than routine post-natal care.

It prevents mother - baby separation, reduces neonatal unit burden and reduces stress on postnatal wards (PNW).

The admission to PNW in LTHT is determined by a Standard Operating Procedure: babies must be over 37 weeks gestation and between 2.3-4.5 kg. This means many 'well babies' are admitted to TC, or in case of capacity issues to special care, contributing to term baby admission to the neonatal unit.

We present the application of a low dependency work intensity score aiming to make admission to TC more dynamic.

### Patients and Methods

A standardised workload score proforma was devised, to quantify how much work each baby generated for their nurse or midwife. It covered aspects of care including: social, feeding, monitoring and medications. It was revised following a first run of the project, and updated with feedback from the multidisciplinary team.

### Results

Over 300 'baby days' were analysed.

Median Workload scores were higher on TCU [PNW: 4 (range 0 - 12) TC: 8 (range 0 – 22)]

Feeding support generated the highest workload intensity.

Monitoring scores were significantly higher on TCU.

Gestation did not correlate with workload intensity.

### Conclusions

Babies on TC have higher workload scores, largely skewed by routine observations, which could be undertaken on PNW.

Whilst there remains specific clinical need for admission of near term and term babies to TC, this should not be routine.

TC admission should be on the basis of clinical assessment, and could be facilitated by predicted workload scores.

The workload scores could potentially provide an insight into staffing needs.

Other / Miscellanea

## OVERVIEW OF DERMATOLOGICAL DISORDERS OF NEONATES IN A CENTRAL REGIONAL INTENSIVE CARE UNIT IN HUNGARY (846)

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### Introduction /Case Report

The immaturity and vulnerability of the skin and the epidermal barrier function, and the frequent iatrogenic complications following diagnostic and therapeutic procedures are often associated with various skin manifestations among infants in Neonatal Intensive Care Units (NICUs). The aim of our current survey was to investigate the dermatological disorders among neonates in our NICU.

### Patients and Methods

A prospective, cohort study was carried out in the NICU at the Department of Pediatrics at the University of Szeged between January 2012 and January 2013. All term and preterm infants hospitalized in the NICU underwent whole-body skin examinations, and all dermatological disorders and treatment modalities were recorded.

### Results

Among the 211 neonates admitted to the NICU, 89 different dermatological conditions were detected in 64 infants. These conditions were accompanied by a wide spectrum of clinical symptoms among the preterm and severely ill term infants. A considerable proportion of the disorders that were seen were results of the immaturity of the skin and various iatrogenic complications.

### Conclusions

Dermatological disorders are frequent among neonates requiring intensive care. The prevention, early detection and optimal treatment of these disorders with modern, standardized skin care management strategies can result in significant improvements in the barrier function and in the integrity of the skin, and can therefore increase the overall efficacy of neonatal intensive care.

Other / Miscellanea

## A CASE REPORT OF NECROTIZING ENTEROCOLITIS AFTER OCTREOTIDE TREATMENT IN A PRETERM NEWBORN WITH IDIOPATHIC CONGENITAL CHYLOTHORAX (735)

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### Introduction /Case Report

Chylothorax is defined as accumulation of lymph in the pleural space and it is the most common cause of pleural effusion in newborns with respiratory distress. In the literature, necrotizing enterocolitis (NEC) secondary to octreotide use has been reported. However, to our knowledge, this is the first case of NEC caused by octreotide in a preterm infant with idiopathic congenital chylothorax.

### Case Report

A male infant was born prematurely at 34th weeks, via caesarian section from a 28 years old mother, G3P3. Pregnancy was complicated by polyhydramnios and bilateral pleural effusion. Neonate's APGAR score was 4/7. Since the spontaneous breathing trials were unsuccessful, newborn was intubated and monitored in Neonatal Intensive Care Unit (NICU). In chest X-ray, bilateral pleural fluid was observed for which bilateral chest tubes were placed followed by 150 cc fluid drainage. Pleural fluid analysis was as follows: LDH 97 U/L, cholesterol 28 mg/dl, triglycerides 9 mg/dl, leukocyte count 1500/mm<sup>3</sup> with 100% lymphocytes. After the pleural fluid was drained, newborn was able to get extubated with improved ventilation and at postnatal 2nd hour and was placed on nasal CPAP. Oral feeding with 20 cc/kg/day breast milk was initiated at postnatal 6th hour. Nasal CPAP was discontinued at postnatal 16th hour. Feeding was optimized gradually. Right chest tube was removed in postnatal day 3. On postnatal day 4, 10 cc chylous fluid was drained from the left chest tube. Pleural fluid analysis yielded triglyceride level at 368 mg/dl, leukocyte count at 14900/mm<sup>3</sup> with 82% lymphocytic predominance. Oral feeding was replaced by middle chain triglyceride containing formula. Patient was further surveyed and dysmorphic features were not observed and the subsequent chromosomal analysis was normal. Cranial and abdominal ultrasounds were both normal. Cardiac echocardiography was normal and viral panel including rubella, toxoplasma, herpes simplex, cytomegalovirus and parvovirus was normal as well.

On postnatal day 6, left chest tube continued to drain 40 cc chylous fluid so patient was started on 1 mcg/kg/h intravenous octreotide which was subsequently followed by decreased drainage. At the 90th hour of the therapy, patient was noted to have abdominal distention and tenderness and started having bilious emesis. Upright abdomen film revealed pneumatosis intestinalis in the right lower quadrant and air was seen in the intrahepatic portal vein (Fig 1). Simultaneously, abdomen ultrasound was performed which showed dilated bowel loops with minimal free fluid in the pelvis. Patient was diagnosed with NEC and oral nutrition was stopped. He was initiated on orogastric decompression and was then started on antibiotics. Octreotide was stopped and TPN was initiated. On postnatal day 11, PA chest X-ray revealed accumulation of right-sided pleural effusion and 50 cc chylous fluid was drained. Three days following cessation of octreotide treatment, abdominal distention decreased. Medium-chain triglycerides (MCT) including formula feeding was initiated on postnatal day 17, which was followed with full oral feeding in 6 days. During his following hospital course, chylothorax did not recur. Patient was discharged on postnatal day 30 and no further problems were encountered in 2 month follow up clinic visit.

## Conclusions

Somatostatin analogue - octreotide has effective treatment potential in management of chylous pleural effusion. Octreotide treatment is commonly used in treatment of chylothorax in those patients who don't respond to the conservative treatment before surgical options are considered. Newborns that are at high risk for NEC should be carefully monitored for signs and symptoms of NEC during octreotide treatment.

## Other / Organization of perinatal care

### Language barriers and the evaluation of translation tools in Neonatology (873)

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## Introduction /Case Report

Communication with relatives of our patients is essential in daily clinical practice. It has been shown, that language barriers can have negative effects on treatment and outcome. Patiel and Davies and Börner et al found that online translation tools can be an alternative in the absence of professional interpreters. The aim of our study was to investigate the presence of potential language problems and to assess the performance of various online translation tools.

## Patients and Methods

223 paper-pencil-questionnaires were sent out to doctors, nurses and social workers at a large university hospital in Berlin, Germany. 61,6% were completed and returned.

## Results

50% reported to encounter "frequent" to "very frequent" language problems in daily clinical routine, 3% reported to "never" have such problems. In 50% of the time the staff employed relatives of patients for translation; in 39% professional interpreters were requested. Medical staff and electronic translation tools were used less frequently. The most popular online translation tools were Google Translate und Leo.org. Both were mostly used for single-word translation only. The staff rated Leo.org better than Google Translate. 40% of the staff reported improved communication using electronic translations tools, 39% did not find the above tools useful.

## Conclusions

Our study shows that language barriers are a commonly encountered problem in daily clinical practice. Currently electronic translations tools are not commonly used. This may be attributed to limited quality and the lack of specific vocabulary of current available tools. We are therefore developing a catalogue of sentences containing central information, which can be translated into defined foreign languages without misinterpretation or loss of information.

## Other / Miscellanea

### A Case of Severe Type of Cerebro-Costo-Mandibular Syndrome in an Infant (160)

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## Introduction /Case Report

Cerebro-costo-mandibular syndrome (CCMS) is a rare disorder, with only about 75 cases described in literature till today. This syndrome is characterized with association of specific multiple rib defects and micrognathia. It is accompanied with mental deficiency in considerable number of cases, and sometimes with some other anomalies and problems: spine deformities, feeding difficulties, delayed psychomotor development, growth impairment. Depending on severity of deformities and consecutive respiratory insufficiency, in about 35-50% CCMS cases death occurs during the first year of life.

## Case Report

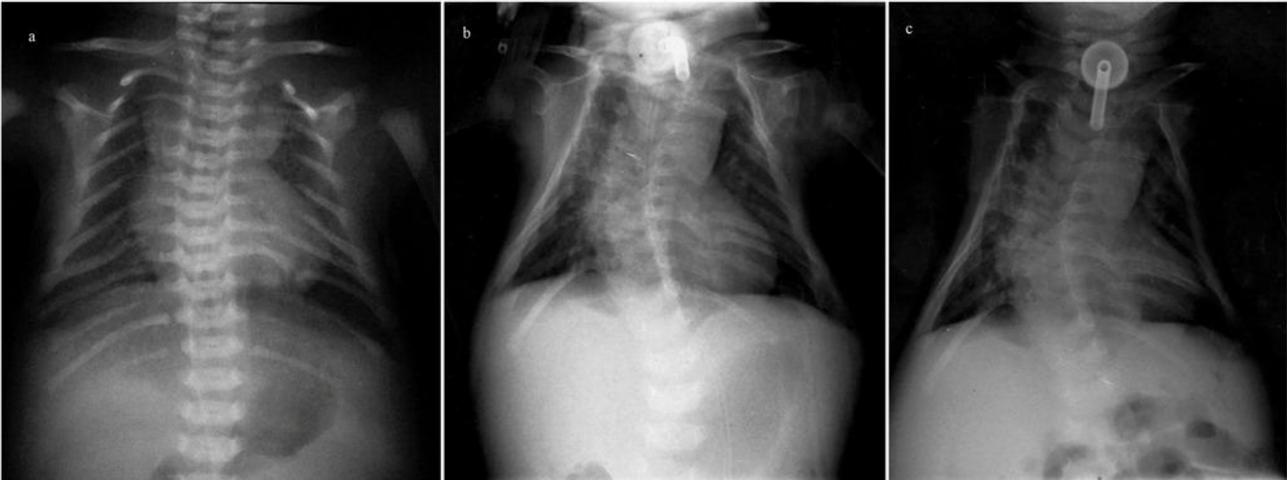
In this paper we present a female infant with severe type of CCMS. Diagnosis was established soon after birth, based on dyspnea, micrognathia and specific findings on the chest X-ray. Chest X-ray taken on first day of life showed narrow thorax with eleven pairs of ribs, with rib gap defects of posterior parts of 2nd – 9th rib on both sides. In subsequent chest X-rays, chest deformity was more and more pronounced. Also, scoliosis of the spine was noticed, which progressed over time (Figure 1). Some other malformations were also observed: retromicrognathia, high arched palate, hypertelorism, low set, malformed ears, narrow chest, redundant skin, muscle hypotonia.

Progressive, severe respiratory insufficiency caused by chest and air-way deformities and exacerbated by episodes of pneumonia, led to respiratory failure and death at the age of 7.5 months.

## Conclusions

CCMS should be considered in every newborn with dyspnea at birth, micrognathia and rib gap defects on chest X-ray.

Picture



## Other / Miscellanea

### TOLERANCE OF YOUNG INFANTS FED A PARTIALLY HYDROLYZED, WHEY PROTEIN-BASED INFANT FORMULA (053)

M.W. Borschel

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#### Introduction /Case Report

Partially hydrolyzed infant formulas (pHF) are widely available. Because of modifications of ingredients including protein type and form, as well as carbohydrate (CHO) and fat blends, young infants may tolerate these formulas differently than standard formulas. Differences may include feeding acceptance, changes in stool patterns, incidence of spit-up and/or vomiting, and intolerance symptoms. The purpose of this study was to evaluate the gastrointestinal tolerance of infants fed an experimental pHF. The primary variable was mean rank stool consistency (MRSC) of infants fed pHF during the study.

#### Patients and Methods

A randomized, double-blind, parallel study was conducted in healthy, formula-fed term infants fed 6 experimental whey-based pHFs. Results of 1 of the formulas with a CHO blend of 80% maltodextrin, 20% sucrose and galactooligosaccharide (GOS, 1.5 g/L) and palm olein-free fat blend later commercialized (Similac® Total Comfort®, Abbott Nutrition, Abbott Laboratories, Granada, Spain) are presented. Daily intake and stool records, assessment of weight and length at each visit, and questionnaires at 28 d of age were completed. MRSC was calculated from records (1=watery, 2=loose/mushy, 3=soft, 4=formed, 5=hard). Visits occurred at 0-8, 14, and 28 d of age. Stool patterns, intake, % of feedings with spit up and/or vomiting, and parental responses to questionnaires were collected.

#### Results

270 infants were enrolled; data from 46 infants on the study formula of interest are presented. MRSC was  $2.51 \pm 0.09$  during the study. Most stools were soft (40.8%) with the remaining loose/mushy (37.7%), watery (11.9%), formed (9%), and hard (0.6%). Parental responses to questionnaires showed that 92% of the infants consuming the formula rarely or never had stools that were too hard. Most infants (74%) rarely or never appeared to be constipated. Ninety-two percent of parents were very satisfied or somewhat satisfied with the formula. Twelve percent of feedings were associated with spit-up and/or vomiting during the study. Weight gain was in the expected range at  $40.2 \pm 1.9$  g/day. Based on adverse event review, there were no safety concerns with the formula. This is consistent with post-marketing safety surveillance data collected on this product.

#### Conclusions

The results demonstrated that this whey-based pHF was safe and well tolerated by healthy term infants. Parental satisfaction with the formula was high. (Supported by Abbott Nutrition, Abbott Laboratories).

Other / Quality improvement and Safety and Error Preventio

## RAPID VERSUS SLOW REWARMING OF HYPOTHERMIC NEWLY BORN INFANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS (102)

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### Introduction /Case Report

Despite efforts at preventing heat losses in newly born infants, hypothermia (temperature  $<36^{\circ}\text{C}$ ) at NICU admission still occurs in a large percentage of neonates, particularly the very preterm infants. Rewarming strategy (rapid vs. slow) of hypothermic neonates could influence neonatal outcomes. A systematic review was conducted to examine the effects of rapid versus slow rewarming on clinically important outcomes in infants namely; mortality, need for respiratory support, occurrence of apnoea, hypoglycaemia, major bleeding episodes, short and long term neurodevelopmental outcome.

### Patients and Methods

Trials on rewarming of hypothermic infants were identified by searching MEDLINE, EMBASE, CINAHL, all of Cochrane Library and other supplementary sources. Selected studies included randomised studies, studies with concurrent controls or with historical controls with one of the following outcomes: mortality, need for respiratory support, apnoea, major bleed/haemorrhage, hypoglycaemia, short and long term neurological outcome. Studies to be included were selected by two reviewers who also assessed the risk of bias of each trial. Data extracted and analyses were independently performed by two reviewers. All data were analysed using RevMan 5 and GRADEpro.

### Results

Data on rewarming strategy for treatment of hypothermic neonates is limited and dated. Two RCTs and 2 observational studies were identified. Results from pooled data of 2 observational studies involving 94 patients (very low quality of evidence, downgraded for very serious risk of bias, serious risk of indirectness and imprecision) suggest that mortality rate is lower in hypothermic infants rewarmed rapidly ( $>$  or equal to  $0.5^{\circ}\text{C}/\text{hour}$ ) with OR 0.23 [95% CI 0.06 - 0.83], but a RCT including 30 patients did not show any difference (RR 0.88 [95% CI 0.36 - 2.10]). Evidence from systematic review showed no difference in terms of episodes of convulsions, apnoea, hypoglycemia, major bleeding events in hypothermic infants managed on rapid compared with slow ( $<0.5^{\circ}\text{C}/\text{hour}$ ) rewarming strategy. No evidence was available on the need for respiratory support from all studies.

### Conclusions

There is insufficient evidence to recommend either rapid or slow rewarming of hypothermic neonates following hospital admission. The best strategy for rewarming of hypothermic neonates merits further investigation. For more meaningful evidence-based decision on treatment strategy, attempts should be

made to study a more homogenous patient population with specific inclusion criteria stratified by gestational and postnatal age, severity of hypothermia on admission, and common outcome measures.

Table

Rapid rewarming compared to slow rewarming for hypothermia in newborns and infants (Trevisanuto D, Yeo C. L. 2015)											
Bibliography (systematic reviews): Trevisanuto D, Yeo C. L. 2015											
No of participants (studies) Follow-up	Quality assessment					Overall quality of evidence	Summary of findings				
	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias		Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With slow rewarming	With Rapid rewarming		Risk with slow rewarming	Risk difference with Rapid rewarming
<b>Mortality (Tafari, 1974, 595)</b>											
30 (1 RCT)	very serious $\downarrow$	not serious	serious $\downarrow\downarrow$	serious $\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	6/16 (42.9%)	6/16 (37.5%)	RR 0.88 (0.36 to 2.10)	Study population 429 per 1000	51 fewer per 1000 (274 fewer to 411 more)
<b>Mortality, observational studies (Sofer, 1986, 211; Racine, 1982, 317)</b>											
98 (12 observational studies)	very serious $\downarrow$	not serious	serious $\downarrow\downarrow$	serious $\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	19/61 (31.1%) $\downarrow$	5/33 (15.2%) $\downarrow$	OR 0.23 (0.06 to 0.81)	Study population 311 per 1000 $\downarrow$	217 fewer per 1000 (285 fewer to 43 fewer)
<b>Apnoea (Motil, 1974, 546; Tafari, 1974, 595)</b>											
66 (2 RCTs)	very serious $\downarrow\downarrow$	serious $\downarrow\downarrow\downarrow$	serious $\downarrow\downarrow$	serious $\downarrow\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	2/38 (5.3%) $\downarrow$	1/28 (3.6%) $\downarrow$	RR 0.44 (0.04 to 4.32)	Study population 53 per 1000 $\downarrow$	29 fewer per 1000 (51 fewer to 175 more)
<b>Hypoglycaemia (Motil, 1974, 546) (assessed with: Blood glucose &lt;30mg%)</b>											
36 (1 RCT)	very serious $\downarrow$	not serious	not serious	serious $\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	8/24 (33.3%)	0/12 (0.0%)	RR 0.11 (0.01 to 1.83)	Study population 333 per 1000	297 fewer per 1000 (130 fewer to 270 more)
<b>Hypoglycaemia (observational study) (Sofer, 1986, 211) (assessed with: Blood glucose &lt;40mg%)</b>											
56 (1 observational study)	very serious $\downarrow\downarrow$	serious $\downarrow\downarrow$	serious $\downarrow\downarrow$	serious $\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	4/38 (10.5%)	0/18 (0.0%)	OR 0.21 (0.01 to 4.06)	Study population 105 per 1000	81 fewer per 1000 (104 fewer to 218 more)
<b>Convulsions (Tafari, 1974, 595)</b>											
30 (1 RCT)	very serious $\downarrow\downarrow\downarrow$	serious $\downarrow\downarrow\downarrow$	serious $\downarrow$	serious $\downarrow\downarrow\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	2/14 (14.3%)	2/16 (12.5%)	RR 0.88 (0.14 to 5.42)	Study population 143 per 1000	17 fewer per 1000 (123 fewer to 611 more)
<b>Haemorrhage (Tafari, 1974, 595)</b>											
30 (1 RCT)	very serious $\downarrow\downarrow\downarrow$	serious $\downarrow\downarrow\downarrow$	serious $\downarrow$	serious $\downarrow\downarrow\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	2/14 (14.3%)	3/16 (18.8%)	RR 1.31 (0.25 to 6.76)	Study population 143 per 1000	46 more per 1000 (107 fewer to 823 more)
<b>Haemorrhage (observational study) (Racine, 1982, 317)</b>											
38 (1 observational study)	very serious $\downarrow\downarrow$	serious $\downarrow\downarrow$	serious $\downarrow\downarrow$	serious $\downarrow\downarrow$	none	$\oplus\oplus\oplus\oplus$ VERY LOW	7/23 (30.4%)	1/15 (6.7%)	OR 0.16 (0.02 to 1.50)	Study population 304 per 1000	239 fewer per 1000 (206 fewer to 92 more)

1. supportive measures differ within the same study between comparative groups
2. supportive measures differ within the same study between comparative groups and also between studies
3. heterogeneity in the samples
4. small sample size with low event rate
5. simply pooled (combined without being weighted)
6. limited study subjects
7. patients randomised in sequential order with no consideration for BWT, weight on admission or duration of hypothermia
8. single study with limited numbers enrolled in groups within the study
9. no indication of time at which blood glucose was monitored in both groups
10. patients enrolled in random sequential order with no consideration for BWT, Wt on admission, duration of hypothermia and cause of hypothermia
11. haemorrhage reported as terminal event

## Other / Miscellanea

### A NANOSTRUCTURED, ELECTROCHEMICAL BIOSENSOR FOR DETECTION OF GBS DNA IN PREGNANT WOMEN (462)

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## Introduction /Case Report

Group B Streptococcus (GBS) is a neonatal pathogen with high mortality rate in infected neonates. Prevention of neonatal GBS disease involves penicillin chemoprophylaxis during labor of mothers who have urogenital colonization. Mothers with no screening (preterm labor or missed antenatal testing) need a rapid and reliable screening test beyond bacterial culture to detect vagino-rectal GBS. Rapid diagnostic methods for maternal GBS exist, but the technology has reduced sensitivity and high false positives. Thus, we fabricated an electrochemical biosensor to detect DNA of GBS during pregnancy.

## Patients and Methods

We used anodized aluminum oxide (AAO) filtration membranes with 200 nm pores as the platform for a DNA-based biosensor. Biosensors have functionalized gold-coated AAO membranes with attached single-stranded GBS DNA probes (pathogenic DNA sequences of GBS – *lytR* and *fbsA*). These locked nucleic acids (LNAs) achieved highly efficient DNA hybridization with single-stranded DNA of GBS recovered from bacterial cultures or maternal vagino-rectal swabs.

## Results

The biosensor was detect as a GBS bacteria/mL or a 10<sup>-18</sup> M concentrations of GBS DNA. Binding was specific because there was minimal probe interaction with DNA isolated from non-group B streptococci or other bacteria. Using highly effective *lytR* probe, isolated GBS DNA in vagino-rectal swabs taken at 35-37 weeks of gestation showed 100% concordance with four positive and 10 culture negative cultures taken concurrently from the same pregnant women. Four hours was required to detect GBS DNA in the vagino-rectal swabs (area under curve: .88, 95% confidence interval (.51, 1.0).

## Conclusions

Cyclic voltammetry using a novel DNA-based biosensor detected GBS colonization of pregnant women; additional refinements are underway to detect GBS DNA and to reduce processing time.

## Other / Medical Education and Training

Scratching our heads while we wait for cytogenetics for the answers? A case study of a neonate with microcephaly (798)

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### Introduction /Case Report

We present the case of a neonate with severe microcephaly. Congenital microcephaly is due to reduced proliferation of glial and neuronal cells in utero (Hagmann & Rennie 2012). Aetiology may be classified as metabolic, infective and genetic. CGH microarray, revealing a 7q deletion in this case, with other known associations, may imply a greater role for gene testing in the assessment of microcephaly. However, with increasing sophistication of genomic analysis available, the pressure for clinical diagnosis and traditional process of pattern recognition will become seemingly obsolete. Mindful of this, we must maintain our clinical acumen alongside these technologies in neonatal medicine.

### Case Report

A male infant, C, was born to a primiparous mother, and phenotypically normal parents at 37 weeks gestation following an induction of labour for faltering fetal growth. The maternal and paternal ages were 18 and 21 years respectively. There was no history of maternal smoking, alcohol intake or recreational substance misuse and medications. Antenatally, growth concerns had been noted, with faltering growth and in particular small cephalic dimensions at 35+4 weeks (Biparietal Diameter (BPD) 73.5mm, Occipitofrontal Diameter (OFD) 95.7mm and Head Circumference (HC) 265.8mm. There was no evidence of placental disease. No structural brain abnormality was noted in late pregnancy views and further invasive antenatal investigations were declined.

C was born by emergency Caesarian Section for failure to progress, requiring a brief period of facial oxygen to establish respiration. Chest X-ray revealed 13 pairs of ribs, with no evidence of cardiorespiratory pathology. C remained on the Neonatal Unit for ten days in order to fully establish bottle feeds

Clinical examination revealed microretrognathia, with no evidence of cleft palate. An Occipitofrontal Circumference (OFC) of 28.5cm, (<SD below the mean) with a birth weight of 2220g (0.4th centile). In addition, thick upper lips and gums were noted, as well as shortening of all four limbs. The genitalia were abnormal, with inguinal testes palpable bilaterally, hooded prepuce and micropenis. Ophthalmological assessment revealed no abnormalities. Hearing screening included both Automated Oto-Acoustic Emissions (AOAE) and Automated Auditory Brainstem Response (AABR) and showed no clear OAE response in the right ear, although the test was otherwise normal. A full metabolic and viral screen was sent, to exclude known causes of acquired microcephaly such as anaemia, and congenital CMV infection. Early karyotyping studies, revealing a normal diploid complement of chromosomes. A full CGH microarray subsequently however, later revealed a 23 Mb terminal deletion from the long arm of chromosome 7 at band 7q33q36.3.

Literature search through the database, OMIM identifies more than 700 conditions involving microcephaly. Genetic causes can be sub-classified into chromosomal disorders, such as trisomy 13, 18 and 21, and less common mutations, identified in comparative genomic hybridisation (CGH) microarray studies. There are deletions and other mutations causing known conditions, such as Cri-Du Chat Syndrome, which involves a

terminal deletion of the short arm of chromosome 5. Deletions of 7q are associated with various morbidities including holoprosencephaly, Currarino Syndrome (Sacral dysgenesis and pathognomonic anorectal malformation (Currarino et al 1981) ), Long QT Syndrome 2 and glycogen storage diseases of heart muscle, although there was no established link with microcephaly. Interestingly, several of the clinical features of this child, including microcephaly, full lips, and small jaw overlap with phenotypic features of Williams syndrome (Morris 2010), which is normally associated with deletions at significantly further away, at 7q11.23, (Nickerson et al 1995).

## Conclusions

These findings support the role for CGH arrays in genetic testing as part of the work-up for microcephalic newborn infants, as well as the need for clinical pattern recognition so that these skills do not become obsolete by relying on the technical advances of gene testing to solve such mysteries. Our brains may be restricted in size, but this shouldn't limit the scope of our diagnostic efforts as clinicians.

Other / Miscellanea

## VESICULAR LESIONS IN A NEONATE: WHAT'S YOUR DIAGNOSIS? (867)

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### Introduction /Case Report

Incontinentia pigmenti (IP) is a rare genodermatosis transmitted as an X-linked dominant trait with variable expressivity, occurring in 1:50000 newborns. It is frequently lethal in males. Skin manifestations evolve through 4 stages: vesicular (evident at birth or within the first few postnatal weeks, with linear erythematous streaks, plaques, pustules or vesicles, that follow Blaschko lines); verrucous; hyperpigmented (the hallmark of IP) and hypopigmented stage. In 50-80% of the cases there is extracutaneous involvement: alopecia (80%), dental (80%), central nervous system (30%) and ocular (10%). A skin biopsy and/or molecular study confirms the disease.

### Case Report

A female newborn was admitted to neonatal intensive care unit for vesicular skin lesions. She was the third daughter of a 30-year old mother (who had a previous miscarriage of a male fetus). Gestation was complicated with menace of preterm delivery at 34 weeks. Maternal serologic screening was negative. She was born by eutocic delivery after a 39-week pregnancy and the Apgar score was 9/10 at 1 and 5 minutes, respectively. Somatometry was adequate for the gestational age. The newborn was hospitalized in the first 12 hours of life with multiple vesicular lesions. The remaining physical findings were normal and clinically she was a well-appearing newborn. Given the suspicion of neonatal herpes, acyclovir was started after laboratory evaluation. Detection of Herpes simplex virus (types 1 and 2) by culture and polymerase chain reaction was negative (blood and skin lesions). In this phase, the mother revealed that she had some kind of “water bubbles” at birth and the older daughter had been hospitalized in the neonatal period with a “skin disease”. The newborn was evaluated by dermatologist in the second day of life, presenting then, vesicular and hyperpigmented linear skin lesions and their distribution over lines of Blaschko, evoking Incontinentia Pigmenti diagnosis. Ophthalmologic observation in the first and second day of life showed no abnormalities. Neurosonography was normal. Genetic testing for mutations in NEMO/IKK-gamma was proposed to confirm the diagnosis.

### Conclusions

IP is a rare disease and a high level of suspicion is necessary. Differential diagnosis of IP varies according to the stage of the disease. First stage occasionally can be confused with Herpes simplex and early treatment with acyclovir should be started until definitive diagnosis. IP prognosis is generally good, but a periodic assessment by a multidisciplinary team should be taken to rule out visual, motor or intellectual impairment.

Other / Quality improvement and Safety and Error Preventio

TOYS IN INCUBATORS ...WHAT IS ENGLAND UP TO? A STUDY INTO CURRENT PRACTICE AMONGST NEONATAL UNITS IN ENGLAND (602)

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Introduction /Case Report

It has long been postulated that the presence of non medical items in the incubators of pre term babies may serve as a source of nosocomial infection. This project aims to discover the current practice among neonatal intensive care units in England with regards to non medical items in incubators.

Patients and Methods

Level 3 neonatal intensive care units were identified from the National neonatal unit audit programme in England database. All level 3 units were contacted by telephone and a pre designed questionnaire was asked of nursing staff. The questionnaire asked about the current practice of the unit with regard to the acceptance of toys inside incubators as well as the washing and swabbing of the toys. The telephone questionnaire took no longer than 5 minutes to complete. Units were contacted at various times of day throughout the week from March to April 2015.

Results

77% (34/44) neonatal units in England participated in the survey. Of these 88% allowed non medical items in the incubators of patients. 47% allowed non medical items in incubators regardless of gestation. 87% of units required items to be cleaned in some way prior to placing in the incubator. Of those requiring preparation of non medical items 42% of units relied on parents to enact this policy. None of the units surveyed routinely swabbed the non-medical items. This survey revealed that units, linked by neonatal networks and geographical proximity often did not have similar policies with regards to non medical items in incubators. Of the 21 neonatal networks in England, only 2 networks had similar policies with regards to non medical items within incubators.

Conclusions

Multiple studies have proven that non medical items in incubators readily become colonised with bacteria, however a causal link between these objects and nosocomial infection has not been established. As a result of this study we have changed our unit policy and no longer allow non medical items inside our incubators. This study highlights the wide variation in practices across England, between hospitals and within local neonatal networks.

Other / Miscellanea

Variable Presentations of Congenital Epulis of Newborn (638)

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### Introduction /Case Report

Congenital Epulis, otherwise known as congenital granular cell tumor is a rare benign tumor in neonates. The incidence of congenital Epulis has been described to be 0.0006%. Commonly, Epulis arises from the maxillary alveolar ridge, rather than from the mandibular alveolar ridge. Due to its rare presentation, antenatal diagnosis is not common. The female to male incidence ratio is 8:1. Treatment is by surgical resection, which is curative and the long term prognosis is excellent, with no relapse.

### Case Report

We report two term born neonates with dissimilar presentation of Congenital Epulis. Both neonates were females. The first neonate presented at birth with an extensive tumorous mass arising from the mandibular alveolar ridge. There were no other clinical abnormalities. The mass consisted of several sarcois lobules with superficial erosions, which caused persistent oozing. Initial treatment consisted of admission to NICU, observation, regular volume therapy and antibiotic therapy to protect against bacterial infection. Due to its appearance, the differential diagnosis of Epulis of the mandibule was initially considered. The differential diagnosis of a haemangioma was debated following a preoperative MRI, which showed high signal on STIR and intermediate T1-weighted signal with intra-lesional areas of high T2-weighted signal. However, ultrasound of the mass suggested a soft tissue tumor with increased vascularity, not typical for haemangioma. Following complete surgical excision of the mass, histopathology showed positive cell stain for vimentin and negative for S-100. These tissue results were confirmative for Congenital Epulis. Following surgery breast feeding was established with no difficulty and follow up of the patient was unremarkable.

A second term born neonate presented with the classical presentation of Epulis, a pink, sessile tumorous mass of 2\*2cm arising from the maxillary alveolar ridge. The Epulis interfered neither with respiration nor with the breast feeding, hence conservative management was adopted and the child is currently being followed up.

### Conclusions

Only about 200 cases of Epulis are to date found in the literature. Our two cases, their clinical presentation and the two different management regimes will contribute towards building a knowledge base for the management of this rare disease entity.

Picture



Other / Miscellanea

## TEMPORAL ARTERY THERMOMETER MEASUREMENTS IN NEONATES (006)

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### Introduction /Case Report

Accurate monitoring of body temperature is important in caring for preterm and critically ill neonates. Axillary temperature measured with an electronic thermometer is the clinical standard for assessing core temperature in many neonatal units. Axillary thermometers are thought to be sufficiently accurate and safer than rectal thermometers for infants. However, axillary temperature measurement disturbs the patient and may alter the thermal environment because the infant must be unwrapped to expose the axilla. Infrared temporal artery temperature measurement offers an appealing alternative, as it is less disturbing for the patient and more efficient for the provider.

### Patients and Methods

The present study was undertaken to examine the accuracy of a commercial infrared temporal artery thermometer in neonates. We measured temporal artery, axillary, and rectal temperatures of 52 infants in the nurseries of the University of Iowa Children's Hospital. With the infants supine, temperature was measured simultaneously or in quick succession at the temporal artery (Tta) using an infrared temporal artery thermometer (Exergen TAT-5000), in the axilla (Tax) with a digital electronic thermometer, and 5 cm into the rectum (Tr) with a vinyl-covered thermistor probe. Tr was considered the "gold standard." The difference between rectal and temporal artery temperatures was compared with the difference between rectal and axillary temperatures for each infant.

### Results

The mean temporal artery, axillary, and rectal temperatures were 37.16 (SD 0.36) °C, 36.61 (SD 0.30) °C, and 36.82 (SD 0.30) °C, respectively. The measurements by these methods were all significantly different. The mean Tr-Tax was 0.21 (SD 0.26) °C, and the mean Tr-Tta was -0.34 (SD 0.37) °C, indicating that Tax was closer statistically to Tr than was Tta ( $P < 0.0001$ ).

### Conclusions

The infrared temporal artery thermometer was not as accurate as the axillary thermometer in neonates. The temporal artery thermometer read, on average, 0.13°C farther from rectal temperature than did the axillary thermometer. This difference may not preclude clinical use of the temporal artery thermometer in neonates, provided the user understands that temporal artery temperature, unlike axillary temperature, overestimates core temperature.

## Brain & Development / Neurodevelopmental Outcome

Psychomotor development depending on the dynamical level change sICAM-1 and sVCAM-1 in early neonatal period. (827)

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## Introduction /Case Report

He role of inflammatory markers in perinatal hypoxic –ischemic encephalopathy has been determined.

The aim of this study to determine psychomotor development of baby is exposed to hypoxic brain damage.

## Patients and Methods

For this purpose 77 infants were examined at 1st year of life by Denver 2 scale.The level sICAM-1 and sVCAM-1 was detected by Uscn (Life Science Inc., USA) kits in 1st-3rd and 5th-7 th days. The Studentt-test and the Mann-Whitney test were used for comparison of parametric and non-parametric parameters.

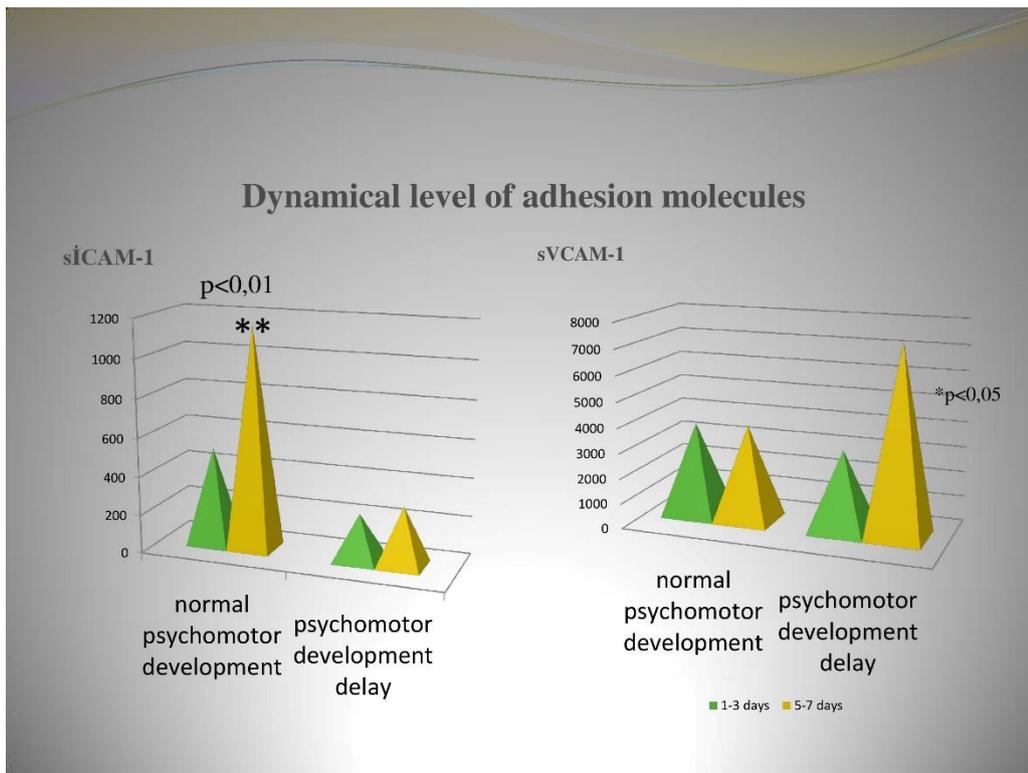
## Results

Psychomotor development delay observed in 14 babies, which sVCAM-1 adhesion molecules levels were increased more than 2 times ( $p<0,05$ )and sICAM-1 level increased less than 1.5 times( $p<0,05$ ) in 5-7 days of life.

## Conclusions

Dynamical change of adhesion molecules in neonatal period may reflect of brain injury severity and helpfull predictor for the psychomotor development.

Picture



## Other / Miscellanea

### Fetal hydrops : Retrospective analysis of our casuistry (217)

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### Introduction /Case Report

The fetal hydrops still remains to be a neonathological diagnostic challenge . It consists in an abnormal accumulation of fluid in soft tissues and serous cavities which entails several clinical complications . Etiology may be multifactorial and is associated with a high neonatal morbimortality, which justifies the comprehensive study of this entity in order to get to know the underlying cause.

### Patients and Methods

Analyze the casuistry of the last six years of newborns admitted to our unit with the diagnosis of fetal hydrops. At the same time, identify potential risk factors associated with higher mortality.

Retrospective descriptive Study of newborn with fetal hydrops dianotsic hospitalized in the period of time between January 2008-October 2014 analyzing epidemiological, clinical and etiological variables.

### Results

13 cases:

average gestational age 31 (94% PTNB),

84% prenatal diagnosis

70% cesarean (6 elective, 3 urgent), average weight: 2500g (74%> p95)

Apgar 1 minute of life. Median 3

85% type IV resuscitation.

Overall mortality rate 46%

variables associated with clinical severity:

vasoactive drugs 8

Mechanical ventilation 12

-PPH (Primary pulmonary hypertension) 5

-blood products 10

-drainages 8

-antibiotherapy 10

-peritoneal dialysis 5

etiology:

autoimmune 1

fetal arrhythmia (flutter) 1

Idiopathic 5

severe anemia 1

congenital anomaly 1

chylothorax1

viral (VZV, CMV)

metabolic (hemochromatosis)

### Conclusions

a multidisciplinary approach is essential for the perinatal handling and etiological study of this entity. In our casuistry predominates idiopathic cause, remaining the uncertainty of not being able to clarify the etiological diagnosis despite of the battery of complementary tests performed.

The prognosis and mortality of fetal hydrops, besides ethiology, depends on the prematurity and clinical outcome within the first hours of life.

## Other / Miscellanea

### A SURVIVAL BOY WITH MOSAIC TRISOMY 18: PHENOTYPE CHARACTERIZATION AND MANAGEMENT (176)

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#### Introduction /Case Report

Trisomy 18 (T18) is characterized by multiply malformations, high frequently of heart defects (HD), severe retardation, high incidence of mortality (from publications only 5-10% patients survival up age 1-year). Mosaic forms displayed remarkable variability of phenotype's expression.

We presented the 1,5 years old boy with mosaic T18: phenotype, cytogenetics, genetic counseling, management.

#### Case Report

41 years old pregnant, counseled due to age-related genetic risk refused from invasive diagnostics. Screening's results were normal (risk<360). Pregnancy complicated by fetoplacental insufficiency, intrauterine growth retardation; labor was at 33 weeks by cesarean section. Proposita – newborn underwent for genetic examinations due to prenatal hypoplasia (weight 915r., length 37cm, OFC 26cm), dysmorphism, neurological disturbances, HD (perimembranous ventricular septal defect, tricuspid valve's insufficiency, foramen ovale, pulmonary vein dilatation, pulmonary hypertension). Renal, brain defects were not found by US, MRI studies. The infant suffered from respiratory distress syndrome, pulmonary hypertension, bronchopulmonary dysplasia, feeding difficulties, anemia. The infant received the exogenous surfactant drug poractant-alpha in the first hours. Growth, motor, mental retardation was detected by follow-up. Karyotype: 47,XY,+18[9]/46,XY[10].

Patient's management: symptomatic treatment; cardiac surgery at 10 months old, regular cardiovascular evaluations; nutrition, growth, mental development follow-up.

#### Conclusions

HD is frequent sign of T18, main cause of morbidity and mortality. The survival patient's database may be important for the medical care improving.

Other / Miscellanea

## NEONATAL MCCUNE-ALBRIGHT SYNDROME WITH SYSTEMIC INVOLVEMENT (032)

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### Introduction /Case Report

McCune-Albright syndrome (MAS) is a rare sporadic disease characterized by fibrous bone dysplasia, café-au-lait (CAL) skin spots and variable hyperfunctional endocrinopathies. MAS is caused by somatic postzygotic activating mutations in the GNAS gene that produce a broad spectrum of effects.

### Case Report

We report a case of MAS with multi-organic manifestations in the neonatal period. A newborn preterm girl was referred to our Neonatal Intensive Care Unit (NICU) at the age of 17 days for suspected extra-hepatic cholestasis. On clinical examination she presented growth restriction, jaundice, hypertension, marked hypotonia and CAL spots on the back and lower limbs. Abdominal ultrasound excluded extra-hepatic causes of cholestasis but revealed bilateral serpiginous adrenal hyperplasia. These clinical findings suggested a diagnosis of MAS with multi-organic involvement. Laboratory data confirmed ACTH-independent Cushing syndrome, hyperthyroidism, cholestasis and elevated transaminases. Ventricular hypertrophy was demonstrated by echocardiography. The girl underwent medical treatment of Cushing's syndrome with metyrapone which was followed by a rapid recovery. A mosaic activating GNAS gene mutation was found on DNA extracted from a buccal swab sample. However, she died at 4 months due to a respiratory infection.

### Conclusions

In the neonatal period the diagnosis of MAS depends on having a high index of suspicion and CAL spots may be the clue for the diagnosis. It is possible that the poor outcome of Cushing syndrome in this age group reflects a greater burden of mutation-carrying cells.

Picture



Other / Medical Education and Training

PREMATURE BABY VACCINATION; COULD IT BE DONE ON TIME AND EFFECTING FACTORS ? (372)

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### Introduction /Case Report

Premature babies have an increased risk for vaccine-preventable infectious diseases. But vaccination of this group often delayed due to various concerns. In this study the aim is to investigate vaccination status during hospitalization and factors that effects this situation in babies followed in outpatient clinics.

### Patients and Methods

The study is cross-sectional; all babies gestational age  $\leq 32$  weeks admitted in high risk newborn outpatient clinic between October-December 2013 included. Babies divided in 2 groups according to hospital that gave care. Group 1 was our hospital, Group 2 was external center. Demographic features, hospitalization time, gestational weeks, weight and vaccination status at discharge recorded.

### Results

Sixty-seven babies included in study. 22 babies were in group 1 and 45 were in group 2. There were no statistical significance in gestational age, hospitalization time and demographic features between groups. First dose hepatitis B vaccine was delayed in 6 babies. and 5 of them were in group 2. Reasons for delay were clinical instability in 2 babies, transfer to outpatient follow-up in 2 babies, neglect of family in 2 babies. First dose combination vaccine was delayed in 42 (62.7%) babies. Reasons for delay were clinical instability in 21 babies, doctor's not recommended in 13 babies, neglect of family in 6 babies and fever of baby in 2 cases. 50% of babies delayed in group 1 and 68.9 % of babies delayed in group 2. 33 of cases had hospitalization longer than 60 days and 29 (74.3%) of them had delay in first dose of combined vaccine. This delay was 61.5% in group 1 and 80.7% in group 2.

### Conclusions

Healthy premature and low birthweight newborns should be vaccinated according to vaccination schedule at recommended chronological age for term babies. However in daily practice, these proposal can not be fully achieved. We suggest that with educational programs to care givers and families vaccination rates can be increased.

## Other / Miscellanea

### UTILITY OF MASS-TANDEM SPECTROMETRY (MS/MS) IN THE DAILY PRACTICE OF A 1ST LEVEL MATERNITY IN ROMANIA (EXPERIENCE BETWEEN 2009-2014). CASE PRESENTATION (674)

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## Introduction /Case Report

Newborn Screening Program (NBSP) in Romania for Phenylketonuria (PKU) and Congenital Hypothyroidism (CH) is available in all counties since 2012. There are five screening centers (Bucharest, Iași, Cluj-Napoca, Timișoara, Târgu Mureș) and a 6th under development (Arad) using Delfia method for CH and fluorometric method for PKU. Low financial resources, lack of staff are impediments of plans to expand NBSP. Mass-tandem Spectrometry (MS/MS) is available in Romania (Cellular Biology Dept., Univ. of Medicine – Iași, a privat laboratory and National Institute of Endocrinology in Bucharest since 2012/2014), but is not yet included in NBSP as a routine screening method.

## Case Report

The 1st level maternity of Marghita (15 bed, 416 newborn babies in 2014) is included in NBSP since more than 25 years (NBSP in Romania began in 1979 as a pilot study). We are surrounded to Cluj-Napoca screening centre. We are sending dry-blood spots on Schleicher&Schuell 903 type filter paper to screening center by post. In the case of a positive test parents are announced in a letter by screening center to present with their child for a fresh-blood gas chromatography confirmation test. In the period 2007-2014 there were totally 3950 newborns screened (100% of all live borns) and there were 12 newborns (known by us) with hyperphenylalaninaemia (hyper-Phe) at PKU screening (from which 1 was confirmed as PKU, 1 case we lost due to bad maternal compliance, 10 cases were considered transitory hyper-Phe) and 1 newborn with confirmed CH. Most of the families were without adequate financial and logistic possibilities to travel to the screening center (Cluj-Napoca). Because screening center accepts only MS/MS as an alternative confirmation method, we appealed to the help of a foreign MS/MS laboratory (Szeged, Hungary since 2009) by sending dry-blood spots on the same filter paper used in our country for NBSP. We also performed extended metabolical screening (aminic acids, acyl-carnitines, organic acids profile) for other well selected cases by MS/MS in the period 2009-2014. We tested totally up to 5 cases/year between 2009-2014. We can demonstrate in the following cases the utility of MS/MS technique in clarifying some problematic situations met in our daily practice.

In a pair of 1st grade full-term born, eutrophic cousins (female and male) receiving both specific anti-HBV immunoglobulin, fluorometry revealed hyper-Phe in both of them (6,4 and 8,717 mg%). Gas chromatography in one case infirmed PKU, but in the another case raised the suspicion of maple syrup urine disease infirmed later by MS/MS and normal clinical evolution. In another full-term, eutrophic male newborn with hyper-Phe (14,5 mg%) with no possibilities to go to screening center, MS/MS revealed Phe

915  $\mu\text{mol/L}$ , constraining parents to initiate the specific diet with good neurological outcome till now. In a full-term, eutrophic, male newborn (from oligophrenic mother) with TSH 151,59  $\mu\text{mol/L}$  confirmation at Szeged revealed TSH 234  $\mu\text{mol/L}$ . Substitutive treatment was initiated with good neurological outcome till now. As in the above mentioned cases, we excluded other metabolic diseases by MS/MS in a full-term, eutrophic newborn with obstructive jaundice and hypocholic stool, suspected later by Alagille sy, respectively in an eutrophic, female newborn with pseudohermaphroditism caused by 21-hydroxylase deficiency (together with steroidogram), too.

## Conclusions

European Council Recommendation 2009/C151/02 on an action in the field of rare diseases enforced the elaboration of a National Plan on Rare Diseases in Romania. Developing a national expanded NBS for the rare diseases by MS/MS is very useful for the population of Romania. The most often 30-50 rare diseases (of 300 with a debut in the neonatal age) are currently looked for by MS/MS, in most of the European Union countries.

Table

2013.06.19.	Sztteroid profil (nmol/L)						
	Kortizol	17OH-Pro- geszteron	4-Andro- sztendion	21- Deoxi- kortizol	11- Deoxi- kortizol	(17OHP+4AD) /Kortizol	(17OHP+ 21- Deox)/Kortizol
<b>Kiss Nikoletta</b> Vérvétel.:2013.05.12. Szül.: 2013.05.06.	9.26	256	217	65	4.3	51.08	34.67
Normal tartomány (nmol/L)							
<b>Erett ujszülött</b>							
0,01 percentil	2.8	3.3	2.2	2.0	0.2	0.02	0.03
0,1 percentil	3.1	3.3	2.2	2.0	0.2	0.02	0.03
1 percentil	7.8	3.6	2.5	2.4	0.3	0.03	0.04
10 percentil	32.1	5.8	4.3	3.7	1.3	0.06	0.08
50 percentil	127.0	13.1	7.2	7.8	3.5	0.18	0.19
90 percentil	365.0	31.9	14.4	28.6	9.6	0.61	0.53
99 percentil	540.1	63.1	25.2	77.3	21.5	2.63	3.06
99,9 percentil	674.1	72.0	29.2	124.4	34.3	5.29	6.12
99,99 percentil	691.1	72.8	29.6	130.3	36.1	5.57	6.44

## Steroidogram confirming suspected 21-HO-ase deficiency by MS/MS

Az eredmények kongenitális adrenális hiperplázia diagnózisára utalnak.

Picture

Szegedi Tudományegyetem Gyermekgyógyászati Klinika Page 1  
 6720 Szeged Korányi fasor 14-15. : Tel: (62) 54 53 31: File:AAAC\_130326\_012  
 Név:Füzesi Dávid László Szül.idő.:1/14/2013 Azonosító:20130326-01-02  
 TAJ:xxxxxxxxx Vértétel:3/18/2013 Orvos:Dr Szabó József  
 Beküldő:Marghita Városi Kórh.  
 Printed: Tue Mar 26 12:27:51 2013

Sample Report:

1: MRM of 22 Channels ES+

Test Name	Calculated Conc	Units	Test Result
C13-Phe	4.80e+005	Counts	
Val	92.4	µM/L	N
Leu	57.1	µM/L	N
Met	9.66	µM/L	N
Phe	915.	µM/L	Phe high
Tyr	23.0	µM/L	N
Leu/Phe	0.0600	-	N
Met/Phe	0.0100	-	N
Phe/Tyr	39.8	-	N
Gly	93.3	µM/L	N
Ala	106.	µM/L	N
Glu	86.4	µM/L	N
Met/Leu	0.170	-	N

2: MRM of 10 Channels ES+

Test Name	Calculated Conc	Units	Test Result
Cit	10.7	µM/L	N
Arg	2.03	µM/L	N
Orn	15.4	µM/L	N
Orn/Cit	1.44	-	N
Arg/Orn	0.130	-	N
Cit/Arg	5.29	-	N

3: MRM of 8 Channels ES+

Test Name	Calculated Conc	Units	Test Result
C0	14.6	µM/L	N
C2	4.57	µM/L	C2 low
C3	0.240	µM/L	N
C4	0.0700	µM/L	N
C3/C2	0.0500	-	N
C4/C2	0.0100	-	N
C4/C3	0.270	-	N

4: MRM of 31 Channels ES+

Test Name	Calculated Conc	Units	Test Result
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Szegedi Tudományegyetem Gyermekgyógyászati Klinika Page 2  
 6720 Szeged Korányi fasor 14-15. : Tel: (62) 54 53 31: File:AAAC\_130326\_012  
 Név:Füzesi Dávid László Szül.idő.:1/14/2013 Azonosító:20130326-01-02  
 TAJ:xxxxxxxxx Vértétel:3/18/2013 Orvos:Dr Szabó József  
 Beküldő:Marghita Városi Kórh.  
 Printed: Tue Mar 26 12:27:51 2013

Sample Report (continued):

Test Name	Calculated Conc	Units	Test Result
C3DC	0.0100	µM/L	
C4DC	0.0800	µM/L	
C5:1	0.0100	µM/L	N
C5	0.0300	µM/L	N
C5OH	0.0300	µM/L	N
C5DC	0.0100	µM/L	N
C6	0.0200	µM/L	N
C6DC	0.0100	µM/L	N
C8	0.0300	µM/L	N
C10	0.0400	µM/L	N
C10:1	0.0300	µM/L	N
C12	0.0200	µM/L	N
C14	0.0200	µM/L	N
C14:1	0.0200	µM/L	N
C16	0.260	µM/L	C16 low
C16OH	0.0100	µM/L	N
C16:1OH	0.0100	µM/L	N
C18	0.150	µM/L	N
C18:1	0.250	µM/L	C18:1 low
C18:2	0.0800	µM/L	N
C18:1OH	0.0100	µM/L	N
C18OH	0.0100	µM/L	N

**PKU confirmed by MS/MS  
 (high Phe and Phe/Tyr ratio)  
 low C2, C16, C18, C18:1  
 without pathological  
 significance**

A CASE-SERIES OF SYMMETRICAL THALAMIC LESIONS IN NEONATES (883)

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Introduction /Case Report

“Symmetrical thalamic lesions” (STL) were first described in 1962 by Rosales and Riggs. They are sometimes also reported as “symmetrical thalamic calcifications” (STC). STL is a specific neuropathological entity occurring following an acute antenatal insult; it is not the same as a postnatal (mostly unilateral) haemorrhage in the thalamus and should also not be confused with bilateral ischemic injury following hypoxic-ischemic encephalopathy (HIE). On histopathology bilateral lesions of the thalamus will be seen, mostly involving the lateral part of the thalamus, with gliosis, neuronal mineralisation and loss of neurons.

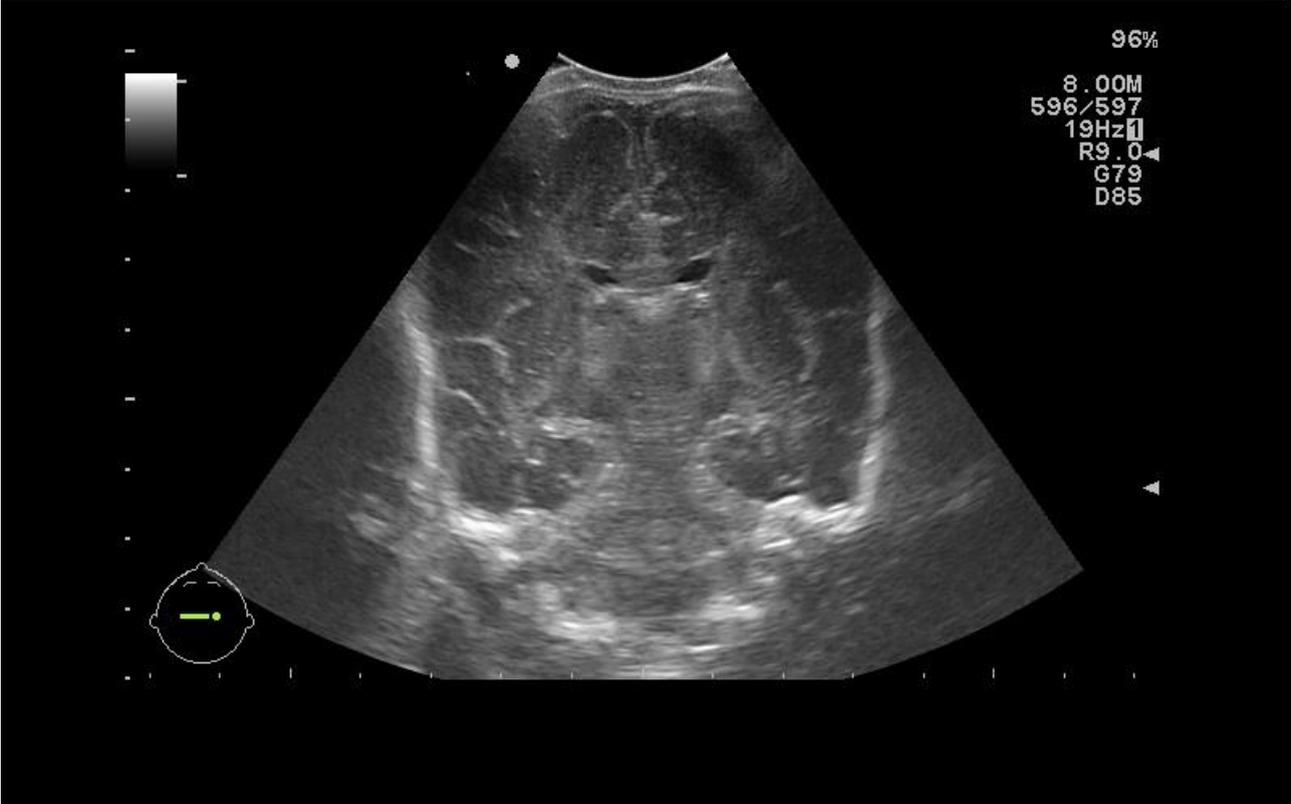
Case Report

Five newborn infants (4 female) with STL are reported. Their gestational age was between 26 and 40 weeks. Low Apgar scores were present in two, with a 1 minute score of 4 and 5 minute score of 6 in both. None of the infants were resuscitated. Clinical presentation included hypotonia, followed by hypertonia, failing on the hearing test in three and swallowing problems in all but one. Three infants died and two showed an abnormal outcome at 6 and 14 months respectively. Cranial ultrasound was performed on admission to the NICU and sequentially until discharge home or death and showed progressive echogenicity in the thalami in all (fig.). MRI- T1 weighted sequence showed an increase in signal intensity in the thalami in all with lack of myelination when assessed at or beyond term equivalent age. Associated abnormalities were seen in the white matter in one, the globus pallidus in another one and small cerebellar haemorrhages in another infant.

Conclusions

In infants without a history of HIE and progressive symmetrical echogenicity in the thalami STL should be considered. There is not always a history of acute antenatal insult. Severe echogenicity may only be present after several weeks. The distinction between haemorrhagic and hypoxic-ischemic injury can be difficult to make with ultrasound. MRI will additionally show absent or delayed myelination and sometimes associated abnormalities.

Picture



## Other / Miscellanea

### RARE TRANSLOCATION t(21q22; 21q22) IN A CHILD WITH LANGDON-DOWN SYNDROME. CASE PRESENTATION (668)

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## Introduction /Case Report

Majority of Langdon-Down syndrome cases are caused by a complete extra copy of chromosome 21. Down sy in 3-4% of cases is caused by Robertsonian translocation (on chromosomes 14; 13; 15; 22) and in rare cases are caused by a t(21;21). A t(21q;21q) with inactivation of the 2nd centromere with/without satellites attached to the long arm is extremely rare described in literature. We present a case with Langdon-Down phenotype with de novo t(21q22;21q22) at the terminal level of the two 21q, preserving 21q22.1-22.3 region (Down Syndrome Critical Region) in all analyzed mitoses.

## Case Report

Proband is belonging to a clinically healthy, young parents with low socio-economical status, 2nd grade cousins in a double manner, having a healthy daughter together. Proband is male, from an unmonitored pregnancy, GA 35/36 wks, G I P I, BW 2300g, Apgar 8/9, with all clinical signs of the Langdon-Down phenotype. Presented a grade II-III/6 holosystolic heart murmur. Initial echocardiography and EKG revealed Complete Atrioventricular Canal Defect (CAVC) Rastelli type A with bidirectional shunt. Till the age of 1½ months (when was accepted by appointment for a complex preoperative evaluation in the Târgu Mureş infant heart surgery center), developed central cyanosis to effort. Complete diagnosis was CAVC, Atrioventricular valve insufficiency (grade II/III with dilated RA and RV, hepatomegaly), Persistent pulmonary hypertension, Ductus Botalli persistens. Suitable age for operation was established between 6-12 months depending on neuro-motor development and adequate weight gain. Child was abandoned by parents. A supportive per os treatment with captopril, hydrochlorothiazide and spironolactone was started. We begun massage and kinethotherapy with good effect, too. Repeated newborn hearing screening revealed deafness. At the age of 4 months a karyotyping was performed (from blood lymphocyte culture) and revealed 46,XY t(21q22;21q22). Karyotyping of parents was normal. At 9 months age child developed a severe pneumonia after otitis with MRSA and presents cardio-respiratory stop finished with death.

Langdon-Down sy is associated in 50% of cases with cyanotic heart malformations of which CAVC represents 60%. In some papers authors revealed the importance of Down Syndrome Critical Region in generating phenotypical characteristics of this condition. Other authors are debating this finding.

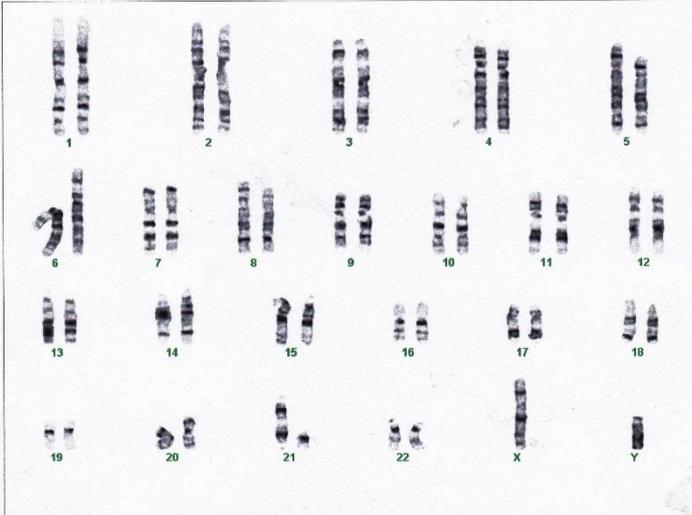
## Conclusions

The Langdon-Down sy case we presented here maybe a unique in Romania due to the extremely rare genetical condition – t(21q22;21q22). Importance of Down Syndrome Critical Region is large debated in the literature. Our case presented all the phenotypical characteristics of Langdon-Down sy (including complex heart malformation and deafness).

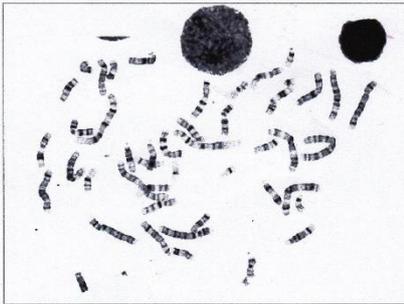
Picture

Referral reason: fenotip Down

Specimen type: limfocite din sange periferic



Case: 27.12 Slide: 1 Cell: 1/142/3 ++

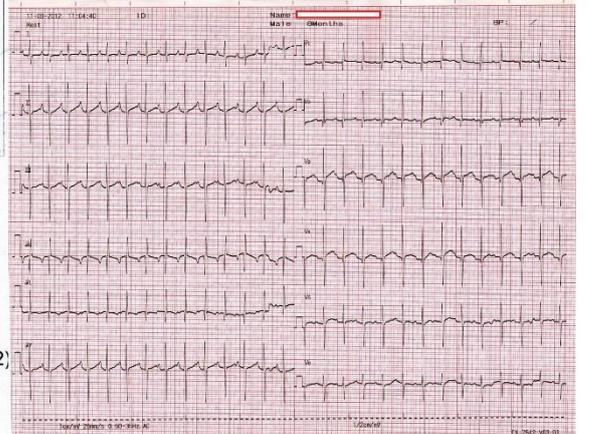
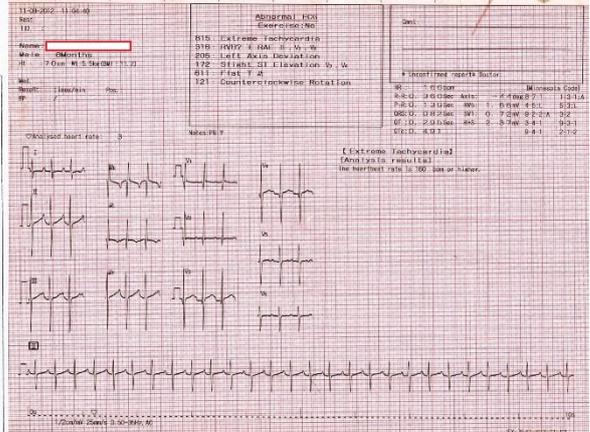


Technologist: As. T. Precup/Dr. O. Iuhas

Case comment:  
marcaj G, 500 de benzi,  
20 metafaze analizate

Result: 46, XY t(21 q22; 21 q22)

Sef Compartiment Genetica  
Prof. Dr. Marius Bembea



**Karyotyping and EKG  
of proband**

PERINATAL STROKE (842)

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Introduction /Case Report

Perinatal stroke is defined as an acute cerebral tissue damage with chronic neurological sequelae occurring between 20 weeks of fetal life and 28 days postnatal life. Classification includes arterial ischaemic stroke (PAIS), haemorrhagic stroke (parenchymal, subarachnoid or intraventricular haemorrhage), cerebral sinovenous thrombosis (CSVT) and thromboembolism. It is an increasingly recognised entity largely due to increased use of MRI. Perinatal stroke is important, because it is 17 times more common in the perinatal period than any other time in childhood and adolescence and it is also thought to account for up to 30% of hemiplegic cerebral palsy in term-born infants.

Patients and Methods

Five term born infants with PAIS and four with CSVT are included in our study. Aetiological background involved placental embolism, infection, clotting abnormalities and injuries of the cervical arteries. Apnoea, irritability and focal seizures were the most common clinical features. Cranial ultrasound scan was not informative in cases of PAIS but MRI imaging was diagnostic in all cases. Management included supportive therapy, anticonvulsive and neuroprotective medication and physiotherapy. Antithrombotic medication was tried in a mother with Leiden mutation with positive result.

Results

Long term follow up was carried out until up to 7 years of age. Complications can include spasticity of one hand, one sided hemiparesis, learning difficulties, epilepsy and speech delay, however most of our patients show little or no neurological sequelae. Multidisciplinary approach, long term follow up and rehabilitation is essential. Recent studies of antithrombotic and antiplatelet medication do not report serious side effects however antithrombotic therapy is still uncommon and large-scale case-control studies are required to understand treatment possibilities better.

Conclusions

Perinatal stroke is associated with considerable lifetime burdens such as cerebral palsy, epilepsy and cognitive impairment. The key to management is a high index of suspicion and prompt and early recognition. Our presentation emphasizes on the importance of long term follow up and rehabilitation to preserve the best neurological outcome.

CEREBELLAR HAEMORRHAGE IN VERY LOW BIRTH WEIGHT INFANTS: A POSTMORTEM STUDY. (890)

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Introduction /Case Report

Cerebellar haemorrhage (CBH) is a more frequently recognised lesion in extremely premature infants thanks to the use of more sophisticated neuroimaging techniques such as MRI and most recent high frequency ultrasound probes utilized also with different acoustic windows (mastoid fontanel). On the contrary recent post-mortem studies are lacking as the haemorrhage was already described in post-mortem studies during the 70's and 80' when the survival rate of most premature babies (at highest risk of developing CBH) was dramatically reduced. The aim of this retrospective survey is to highlight the potential usefulness of postmortem studies in a modern population of very premature babies.

Patients and Methods

26 autopsies of very preterm infants (below 28 wks of gestation) were retrieved from the files of Neonatal Intensive Care Unit at Gaslini Institute since 2012. A complete perinatal autopsy and a systematic neuropathological examination was performed in all cases. The cerebellum was examined using sagittal and transversal sections. The microvasculature of the cerebellum was also assessed with immunohistochemical staining. Moreover, the micro-structure of the vessels was studied.

Results

Intracerebral haemorrhage was present in 6 cases. CBH was found in five cases. In one case it presented as an isolated feature, consisting of microhaemorrhage in the cerebellar white matter.

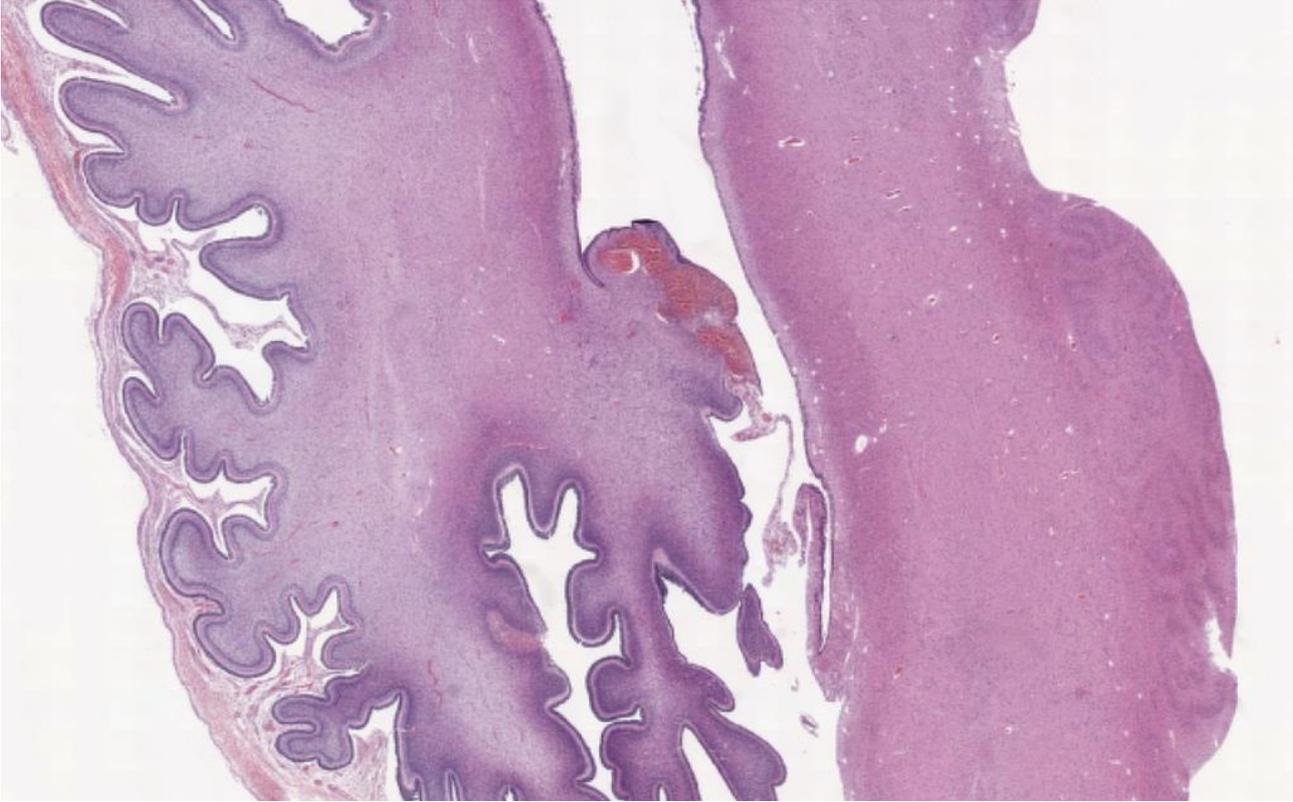
In four cases it occurred together with intraventricular hemorrhage; in one very severe case the amount of blood caused compression and dislocation of all rhombencephalic structures, possibly determining the death of the patient. A more subtle pattern in which the haemorrhage was confined within delicate embryonal structures (germinal matrix in the fourth ventricle) was also found (Figure).

Moreover, a possible 'breaking point' of the delicate cytoarchitecture of the cerebellum could be located immediately beneath the external granular layer. Vascular congestion and subtle signs of vasculopathy were observed in all cases.

Conclusions

A higher incidence of the most severe forms is obvious in this postmortem cases. It remains very difficult to ascertain the origin of the haemorrhage. CBH seems to have a close relationship with germinative structures. Moreover subtle signs of vasculopathy have a potential role in its pathogenesis. Direct and indirect lesions to the proliferative compartments could account for a reduction of progenitor cells jeopardizing cerebellar histogenesis.

Picture



## Other

Immunohistochemical expression of P57 to identify loss of heterozygosity and abnormal imprinting of the 11p15.5 in pediatric adrenocortical neoplasms. (355)

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## Introduction /Case Report

Adrenocortical neoplasms (ACN) are rare in pediatric age. Although ACN in children may manifest in the context of a syndromes, the majority of ACNs rises sporadically. Rearrangements, loss of heterozygosity (LOH), and abnormal imprinting of the 11p15.5 locus, resulting in low p57kip2 have been reported in sporadic ACNs. p57 gene is paternally imprinted and expressed from the maternal allele. It encodes a cyclin-dependent kinase inhibitor that acts to negatively regulate cell proliferation. In normal adrenal gland, cells expressing p57 on immunohistochemistry (IHC) are in the zona reticularis. Aim of the present study is the use of IHC for p57 to identify/predict LOH of 11p15.

## Patients and Methods

Four children, 1 male (1m) and 3 females (12 d, 4m and 22m) presented an adrenal mass. On histology the diagnosis of ACN, 1 clinically benign, 1 uncertain and 2 malignant, was made following the Wieneke classification. In 2 cases the ACN was isolated, while the other were 1 associated with Li-Fraumeni syndrome and 1 with focal hyperinsulinism so the child was analyzed for Beckwith-Wiedemann (BW) syndrome. p57 IHC was made in ACN as well as in normal adrenal formalin-fixed tissue. Genomic DNA was extracted and amplified by polymerase chain reaction (PCR) from ACN and normal adrenal frozen tissue to compared for LOH analysis, using a panel of 12 microsatellite markers linked to 11p15 region. Genetic analysis for BW was made on blood, normal adrenal tissue and ACN.

## Results

A low/absent level of p57 expression was documented in all 4 adrenocortical neoplasia independently if classified as benign/uncertain/malignant on the basis of pathological and clinical criteria, while p57 positive cells were evident in the zona reticularis of normal adrenal cortex. Microsatellite marker analysis confirms the loss of maternal 11p15 region in all 4 ACN. Genetic analysis for BW showed no chromosomal alterations in blood, 11 trisomy in ACN tissue and 11 disomy in normal adrenocortical tissue consistent with a mosaic condition of BW syndrome.

## Conclusions

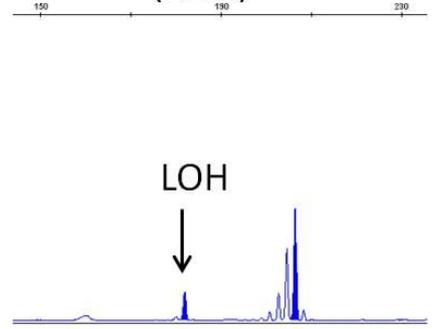
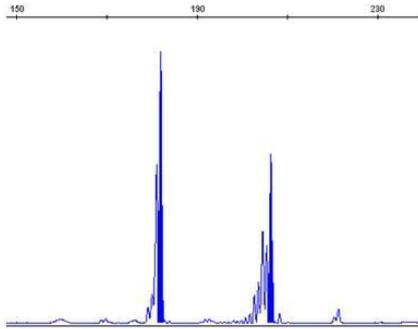
The simple and cheap immunohistologic stain for p57 can be used to recognize in advance ACN associated with LOH of 11p15. 11p15 LOH has a high prognostic value suggesting the p57 gene is an important contributor to ACN pathogenesis. 11p15 alterations could be used as a biological marker for predicting clinical malignancy in ACN after surgical removal.

Picture

Normal tissue  
(Adrenal gland)

Tumor tissue  
(ACN)

D11S4177



Other / Miscellanea

### CAMPOMELYC DYSPLASIA: A CASE REPORT (625)

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### Introduction /Case Report

Introduction: Campomelyc Dysplasia is an inherited disorder with an autosomal dominant pattern, characterized by bowed limbs and tibial dimples. The course could be lethal due to alteration in ventilation performance

### Case Report

Material and Methods: To describe clinical findings and management of a patient with skeleton dysplasia.

Results: An infant born to a 27 year old mother, gravida 3. Born full term by abdominal delivery due to pelvic presentation and nuchal cord. Born in apnea. Apgar score 4-7. Facial malformations are seen in the delivery room, the patient develops respiratory distress and needs to be intubated. Was transferred to a third level hospital for multidisciplinary evaluation. In the evolution four failed extubation attempts were performed. Bronchoscopy: Pulsatile extrinsic compression of the right main bronchus. Angiotomography: Without evidence of vascular ring. Echocardiogram: Structurally healthy heart. Renal Doppler: No malformations. Chest X-Ray cervical and thoracic scoliosis. Limbs x-ray multiple angular deformities in long bones. Karyotype mos 47, XY, + mar [2] /46, XY [28]. Otorhinolaryngology evaluation finds micrognathia, short neck. Tracheostomy was made and mechanical weaning was performed.

### Conclusions

Conclusions: Skeletal campomelic dysplasia, is an inherited disorder with a thoracic deformity accompanied with ventilation impairment. Less severe cases successful ventilation can be achieved by nCPAP, in this case tracheostomy was necessary.

Picture



## Other / Miscellanea

### Glomerular Function in Critically Ill Term Neonates (768)

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## Introduction /Case Report

In most neonatal intensive care units, glomerular filtration rate (GFR) is measured by means of Schwartz formula, which is based on serum creatinine (SCr) level. Several authors found that serum cystatin C (SCysC) is a better marker of GFR than creatinine, even in cases of sub-clinical renal dysfunction.

The objective of this research is to study glomerular function in critically ill term neonates on the basis of measuring levels of SCr and SCysC with calculation of glomerular filtration rate in early neonatal period.

## Patients and Methods

It is a hospital based, prospective case control study. The basic (I) group included 30 critically ill term neonates on their first week of life, the control (II) group - 34 healthy term neonates. GFR was calculated on the basis of G.J.Schwartz's formula:  $GFR (ml/min/1.73 m^2) = k \cdot d (cm) / SCr (\mu mol/l) \cdot 0,0113$ , where  $k = 0,45$  for term neonates; of A.Grubb's formula:  $GFR (ml/min) = 84,69 \times cystatin\ C - 1,680 \times 1,384$ .

## Results

In the infants of the basic group SCr was  $50,0 \mu mol/l$  [43,0; 71,0], in the control group –  $43,0 \mu mol/l$  [41,0; 44,0],  $p < 0,05$ . GFR accordingly to groups of observation was  $42,22 ml/min/1,73m^2$  [29,7; 51,87] and  $49,09 ml/min/1,73m^2$  [47,07; 49,54],  $p < 0,05$ . In the newborns of the first group SCysC was  $1,84 mg/l$  [1,73; 1,93], in the second group –  $1,57 mg/l$  [1,5; 1,79],  $p < 0,05$ . GFR accordingly to groups of observation was  $42,07 ml/min$  [38,83; 45,78] and  $52,3 ml/min$  [44,07; 55,0],  $p < 0,05$ .

## Conclusions

Our study have shown that SCysC levels are superior, or at least equivalent, to SCr levels as an index of renal function of term neonates with disorders of early neonatal period and has been introduced as an alternative to SCr to monitor GFR.

## Brain & Development / Structural and Functional Brain Imaging

### Neurodevelopmental outcome of cerebral infarction in term and preterm population (869)

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### Introduction /Case Report

Neurodevelopmental outcome of newborns with cerebral infarction is a very serious issue which causes anxiety and inconvenience to parents. We studied neurodevelopmental outcome beyond the first year of life in a series of 5 term and preterm neonates with cerebral infarction in relation to topography of brain lesion. All neonates were imaged with serial head scans and brain MRI and had neurodevelopmental and neurocognitive assessment in regular intervals until school age.

### Case Report

Case 1: The first neonate was born at near term by cesarean section and presented with focal seizures on day two of life. Brain MRI with DW revealed an ischemic lesion at the isle of Reil in the area distribution of right middle cerebral artery. Neurocognitive assessment at school age was within the normal limits

Case 2: The second neonate was born at term with cesarean section and presented with focal seizures on day two of life. Brain MRI with DW revealed an ischemic lesion at the left thalamus, lenticular nucleus and isle of Reil at the area distribution of left middle cerebral artery. Neurocognitive assessment at school age was within the normal limits

Case 3: Third neonate was born at term, presented with seizures and brain MRI revealed cortical and subcortical infarct at the area of the left parietal lobe. Neurodevelopmental and behavioral assessment at 18 months of life was normal.

Case 4: Fourth neonate was born at extreme premature twin delivery (Gestational Age 27+1 weeks). Routine head scan on day 7 of life revealed a major hemorrhagic ischemic venous infarction at the right fronto-parietal periventricular area. Neurodevelopmental evaluation at 2 years of age she has normal cognitive and behavioral assessment with left sided hemiplegia. She is walking independently and she is using both hands with a right side preference. She has regular physiotherapy intervention.

Case 5: Fifth case was born at the borders of viability (Gestational Age 23 weeks) and routine head scan and brain MRI revealed a right sided periventricular venous infarction. Neurodevelopmental assessment at 2 years of age revealed mild immaturity in all areas of development with independent walking. Upper limbs muscle tone was normal with a left side preference.

### Conclusions

In our series children born at term and presented with an infarct in the distribution area of middle cerebral artery had no neurodevelopmental impairment. Preterm children with periventricular venous infarction had mild hemiplegia and neurodevelopmental immaturity. Conclusively not all cerebral infarcts have

adverse effects on brain development and therefore counseling of the parents should be based on the exact involved anatomic area of the brain and not on the insult itself.

## Other / Neonatal Transportation

### ACUTE BRONCHIOLITIS, IS IT A SERIOUS ILLNESS? (407)

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## Introduction /Case Report

Acute bronchiolitis (AB) is a common disease during two first years of life, especially during winter season. Recovery occurs without any treatment in most of cases. However in few patients respiratory support is needed for a short period and usually it is provided as non invasive ventilation (NIV). Our mobile PICU (dedicated team) transfers these newborns and infants from pediatric or emergency departments to PICU when they require intensive care. The aim of this study was to evaluate if the diagnosis of AB in the first 28 days of life is a risk factor for a poorest short time outcome and to try to highlight some severity predictive factors.

## Patients and Methods

All infants less than 1 year transported for AB from 10/31/2014 to 1/31/2015 were eligible. We only considered infants transferred to the PICU for AB and excluded all infants with congenital heart disease, chromosomal abnormalities or chronic lung diseases.

Age, birth weight, gestational age, sex, type of ventilatory support and length of it, blood gases at the mobile PICU admission and Wang Respiratory Score (composite clinical score with respiratory rate, retraction, wheezing and general condition) were recorded. Main outcome was the PICU stay.

## Results

126 patients were enrolled. 21 had an exclusion factor, therefore study cohort consisted of 105 patients. Population was subdivided between neonates and infants and univariate analysis did not show any significant difference except for the birth weight ( $p=0.007$ ) and the  $pCO_2$  at the admission ( $p=0.04$ ). There is a modest but significant correlation between age and  $pCO_2$  (Spearman  $\rho=0.271$   $p=0.01$ ).

Neonatal age seems to do not be a risk factor of severe short outcome. Study presents some shortfalls such as retrospective design and small population size.

## Conclusions

In our cohort, the age at diagnosis is not a risk factor for a poor outcome in infants with AB. Clinical signs (Wang score) does not discriminate the risk of long PICU stay.

Table

Table 1:

	Total (n = 105)	≤ d28 (n = 35)	> d28 (n = 70)	p
GA (weeks)	39 [37-40]	39 [38-40]	38 [35-39]	0.058
BW (g)	3032 (±763)	3314 (±573)	2892 (±810)	0.007
pCO <sub>2</sub> (mm Hg)	56 [48-67]	63 [53-68]	51 [44-65]	0.044
pH	7.30 (±0.08)	7.30 (±0.08)	7.30 (±0.08)	0.518
NIV duration (d)	2 [1-4]	3 [2-5]	2 [1-4]	0.238
PICU stay (d)	4 [3-6]	4 [3-6]	4 [2-5]	0.755
Wang score	6.56 (±2.28)	6.71 (±1.79)	6.49 (±2.50)	0.691

## Other / Medical Education and Training

### CURRENT STATE OF THE APPROACH TO DESORDERS OF SEXUAL DEVELOPMENT (DSDs) IN NEONATAL PERIOD. A CASE REPORT OF AN INFANT WITH GENITAL AMBIGUITY (242)

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## Introduction /Case Report

The diagnostic approach to a newborn with ambiguous genitalia involves a multidisciplinary team.

Physical examination is important to rule out a malformation syndrome in a patient with intersex disorder. Karyotyping and palpation for gonads should be performed to all patients. If patient has no palpable gonads a CAH screen should be done. If this is positive, an ultrasound and voiding cystourethrogram should be ordered to confirm the diagnosis. If there are palpable gonads present, or CAH screen is negative, a biochemical profile, ultrasound and gonadal inspection should be done.

## Case Report

We present a case of a newborn, delivered with a birth weight 2000 grams following a 34-weeks uncomplicated pregnancy, a premature labor, and delivery with Apgar scores 5 and 7 at 1 and 5 minutes respectively. The physical examination revealed dysmorphic facial features, limbs' deformities and genital ambiguity: clitoromegaly, hypoplastic major labia and hypertrophic small labia. There were no palpable gonads. The CAH screening was negative (17-OHP was 9,8 mmol/l). The 11-deoxycortizol and 11-deoxycorticosterone were normal, too. The serum electrolytes were unremarkable.

Genomic DNA was extracted from peripheral blood leukocytes using salt-extraction standard protocol. DNA analysis was performed to determine the sex chromosomes of the newborn. QF-PCR (Quantitative Fluorescent Polymerase Chain Reaction) analysis was performed by Aneufast commercial and a total of 9 markers located on chromosome X and Y were tested on ABI3130xl genetic analyzer. Two X chromosomes were detected; the absence of Y-chromosome was indicated by non amplification of SRY region. The genetic sex of the newborn was determined to be female.

## Conclusions

The social sex was assigned to the baby after the evaluation was completed and the family was encouraged to name it

Other / Miscellanea

A RAPIDLY INVOLUTING CONGENITAL HAEMANGIOMA PRESENTING WITH LIFE THREATENING CARDIAC FAILURE. (149)

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### Introduction /Case Report

Introduction: Although 5% of all infants have infantile haemangiomas (IH), and these are generally benign with complications rare, rapidly involuting congenital haematomas (RICH) are clinically distinct and much less common. They may not be recognised by neonatal teams. The maximum proliferative potential is in utero, with rapid postnatal involution. Babies are born with full sized lesions, most requiring no treatment. I highlight a serious and life threatening complication.

### Case Report

Case Report: I present a term baby girl, with a birth weight of 3.555Kgs who required increasing respiratory support, intubation, ventilation and inotropic support due to high output cardiac failure secondary to a RICH diagnosed postnatally. At birth she was noted to have a prominent 8x8x5cm parieto-temporal vascular lesion (image 1). Ultrasound scan confirmed the presence of a large soft tissue mass with an intact skull vault containing extensive vascular spaces with feeding vessels and prominent blood flow. This increased in size over the first day of life. She rapidly developed signs of high output cardiac failure and was referred to a tertiary centre for insertion of 18 platinum coils. However the lesion continued to grow and she was referred to a specialist centre for percutaneous embolization. After this her cardiac function improved. The patient was treated with diuretics for 4 months and cardiac function returned to normal. Multidisciplinary, multicentre care was provided to optimise her development and skin integrity and the lesion regressed over the first year of her life. (image 2). She had a normal outcome after significant intervention.

### Conclusions

Conclusions: RICHs are clinically distinct from infantile haemangiomas and kaposiform haemangioendotheliomas. They can be confused with lymphatic abnormalities and encephaloceles, particularly if noted on antenatal scans. They particularly occur on the limbs, head and neck. RICHs are rare and usually involute by 1 year of age, and require observation only. However they can have life threatening complications, as in this case.

Table



Picture



Other / Miscellanea

## RECOGNITION OF THE COAT-HANGER SIGN LEADS TO A PROMPT DIAGNOSIS OF KAGAMI-OGATA SYNDROME (PATERNAL UNIPARENTAL DISOMY 14 AND RELATED CONDITIONS) (702)

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### Introduction /Case Report

It is challenging to choose an effective diagnostic approach in order to identify genetic disorders. Here we report a patient whose diagnosis depended on the recognition of a pathognomonic radiological sign: the coat-hanger appearance of the ribs. The diagnosis Kagami-Ogata syndrome refers to paternal uniparental disomy 14 (patUPD14) and related conditions. PatUPD14 is a rare disease caused by inheritance of both chromosomes 14 of the father. PatUPD14 results in a unique constellation of features with a small bell-shaped thorax with coat-hanger appearance of the ribs, facial abnormalities, abdominal wall defects and polyhydramnios. Little more than 40 cases have been reported.

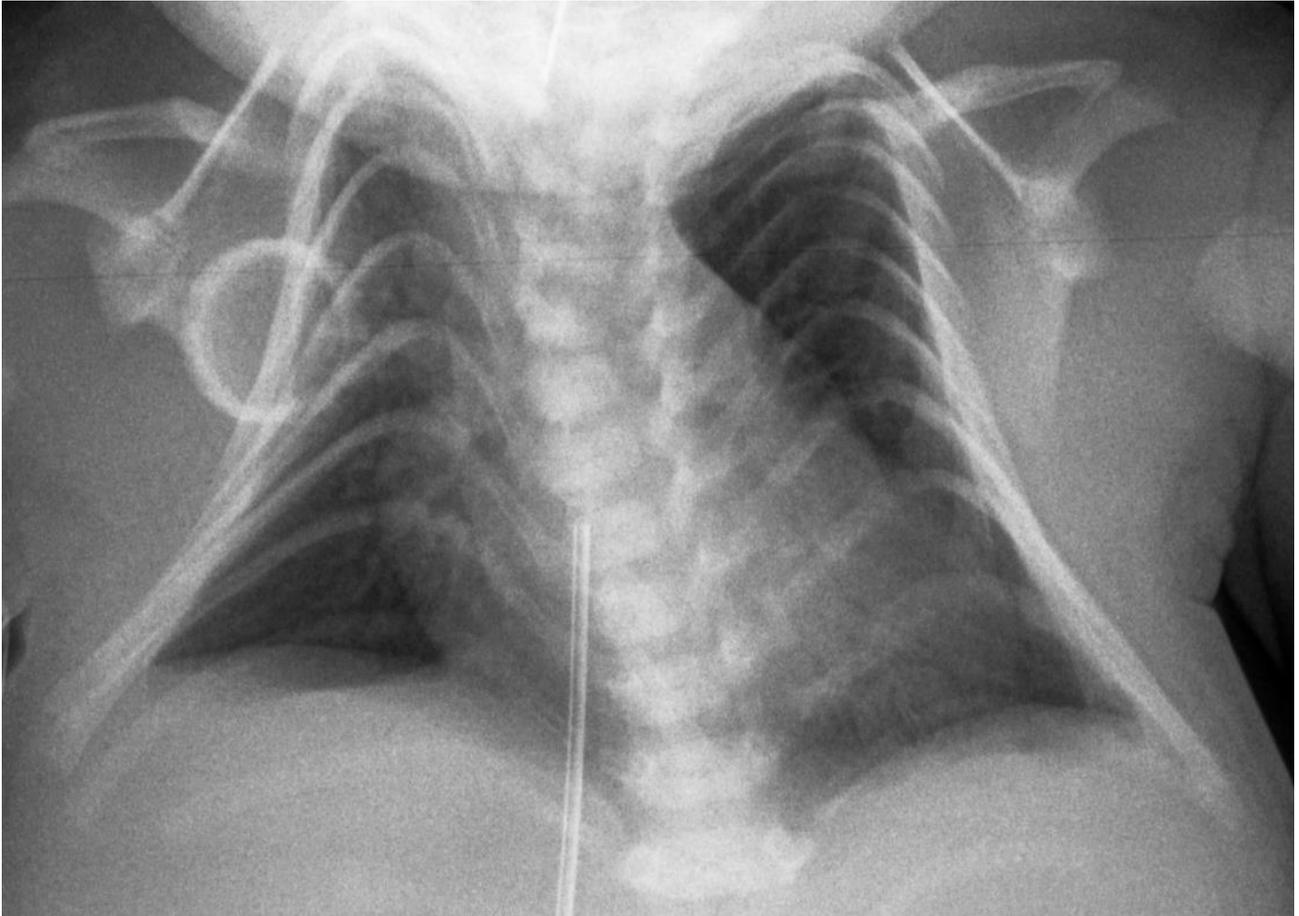
### Case Report

We report a male newborn of 37 weeks of gestation, delivered by emergency cesarean section due to partial placental abruption. He was born to a healthy 29-year-old gravida 2, para 2, after a pregnancy complicated by polyhydramnios from the 3rd trimester. By amniocentesis a normal karyotype (46, XY) had been found. He presented asphyctic at birth and required intubation in the delivery room for lack of respiratory effort. On physical examination, significant findings included a bell-shaped small thorax, diastasis recti, facial dysmorphic features (broad nasal bridge, frontal bossing, hairy forehead, prominent philtrum, puckered lips, micrognathia, retrognathia, short neck, H-shaped vertical skin creases of the chin, creased ear lobe), joint contractures of feet, fingers and hands with ulnar deviation, kyphoscoliosis, single transverse palmar creases, undescended testes and bilateral inguinal hernias. He showed marked muscular hypotonia. Echocardiography revealed a small muscular ventricular defect. The chest X-ray showed a narrow bell-shaped thorax with coat-hanger appearance of the ribs. Several experts were involved. Only one of 4 experts, who evaluated the eye-catching X-ray of the chest, suspected patUPD14. Genetic diagnostic confirmed patUPD14. In view of various case reports suggesting improvement of respiratory symptoms and muscular hypotonia over time we continued the intensive care for several months. The patient could be weaned to binasal continuous positive airway pressure for 2 short periods: 14 days and 7 days, respectively. There was no improvement of the respiratory situation. In contrast, the patient suffered from massive endotracheal secretions and required repeated extensive endotracheal suctioning more than 40 times daily. This clinical problem had not been reported previously. He required nasogastric tube feeding. Joint contractures and muscular hypotonia improved only slightly. A hypertrophic cardiomyopathy was diagnosed at the age of 3 ½ months and anticongestive therapy with bisoprolol was started. So far, only 2 more patients with hypertrophic cardiomyopathy have been reported. After counseling the local clinical ethical committee and in shared decision making with the parents, the patient was extubated and deceased at the age of 4 months.

## Conclusions

The recognition of the coat-hanger sign is crucial for proper diagnosis of this rare disease. This sign may not be known well enough, as 3 experts had evaluated the patient without suspecting patUPD14. Distinct characteristics of our individual patient were respiratory failure, massive endotracheal hypersecretion and hypertrophic cardiomyopathy.

## Picture



MORBIDITY AND MORTALITY IN TRIPLE CHILDBIRTH VS SINGLETON BIRTHS, OUR CASUISTRY (843)

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Introduction /Case Report

Assisted reproduction techniques produce an increase in multiple pregnancies. Triplet pregnancies have an increased risk of morbidity and mortality compared with singleton pregnancies due to the higher incidence of prematurity

Patients and Methods

Retrospective observational study; a group of triple birth in hospital materno-infantil de Málaga between January 1, 2010 and December 31, 2014, and a second group of single births correlated with the first group in the period of birth and gestational age. In both groups prenatal data (gestational age, birth weigh, gender), postnatal data(respiratory distress, PDA,necrotizing enterocolitis ,intraventricular hemorrhage III/IV(IVH) ,retinopathy of prematurity > III (ROP) ) and discharge data (survival, severe consequences ROP >III, HIV III/IV) is collected.

Results

In the group of triplets the mean age was 31 with a range of 20-34 years. In 65,1% of cases pregnancy was due to assisted reproduction techniques. Prenatal maturation with corticosteroids was performed in 94,2% of cases.

In the group of single births the mean age was 30,6 with a range of 15-41 years. In 9,8% of cases pregnancy was due to assisted reproduction techniques. Prenatal maturation with corticosteroids was performed in 22,6% of cases.

Table 1 shows the rest of postnatal data and data in the moment of discharge of both groups.

Conclusions

Rate of prematurity in triplets was 100% with mean gestational age of 32 weeks . Comparing morbidity, mortality between both groups no significant differences were found. The percentage of assisted reproduction techniques in the group of triplets is higher. 94,2% of prenatal maturation with corticosteroids in triplets compared to 22,6% in single pregnancies which tells of a better monitoring and obstetrical control of triple pregnancies.

Table

	ma	ART	ac	ga	c	m/f	w	cpap	PDA	s	ECN	HIV	ROP	M
Triplets n 86	31(20-34)	65	94.2	31.96 (27-34)	100	51/35	1592 (570-2310)	60.7	19.7	19.7	1.16	3.5	1.1	3.5
Single n 172	30.6(15-41)	9.8	22.6	31.96 (27-34)	60.7	92/76	1740 (670-2670)	57.3	17.8	20.23	4.16	4	1.16	4.16

Results in %. Maternal age (ma), Assisted reproduction techniques(ART), antenatal corticosteroids (ac), gestational age(ga),caesarean (c), male/female (m/f), weigh(w), respiratory distress/CPAP (cpap), PDA, sepsis(s), necrotizing enterocolitis (ECN), intraventricular hemorrhage (HIV), retinopathy of prematurity > III (ROP), Mortality (M).

#### Other / Quality improvement and Safety and Error Preventio

A multicentre survey on current practice across Neonatal units in UK regarding methods to confirm central lines position (PICC and UVC) (017)

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#### Introduction /Case Report

The use of central catheters through a peripheral vein and Umbilical venous catheters for administering TPN and other drugs reduces significantly the complications compared with the use of peripheral venous catheters and improves the quality of life of the premature neonate.1,2.Long lines and umbilical catheters insertions are also associated with serious and sometimes fatal complications including cardiac tamponade ,thrombosis and extravasations.This can lead to morality and significant morbidity.There has been recent alert regarding fatal complications of central lines.We aimed to identify current practice at Neonatal units across uk regarding methods to verify PICC and UVC position.

#### Patients and Methods

We identified 150 neonatal level 2 and level 3 units all across uk. We achieved response from 84 neonatal units all across uk. Study was conducted over two months period from 01/10/14 till 30/11/2014. We had response of 51 level 3 units and 33 level 2 units. We conducted a telephone survey based on our questionnaires. Our questionnaire focused on use of contrast for peripherally inserted central venous

catheters and Umbilical venous catheters. Type of contrast and volume of contrast used. Use of Echocardiograms and Lateral X-rays to confirm UVC position.

## Results

Out of 84 units, 46(54%) said they don't use contrast to confirm PIIC tip position. But 38(45 %) said they use contrast to confirm PIIC tip position.

Some of those were using contrast only when there was doubt in tip position on plain x-ray film.

Majority of them were using omnipaque as contrast medicine. Volume used was variable from 0.2ml to 2ml depending on the size of catheter and type of catheter.

Regarding UVC catheter, 83(97%) units said they don't use contrast and only 2 units used contrast to confirm UVC tip. Only 4 units said they use ECHO to confirm UVC Position but this was not routine. Only 3 units (4%) said they use lateral x-rays to confirm long UVC position.

## Conclusions

This study suggests variable practice to confirm PIIC line position. Majority of responders rely mainly on plain AP x-rays to confirm UVC position. This study identifies lack of unified approach to confirm central line position and lack of evidence about use of contrast. We feel that there is a need of evidence-based practice to avoid serious complications. We hope that this study will highlight the need for larger studies regarding best possible method to identify central line position.

## Other / Quality improvement and Safety and Error Preventio

Unrecognized Gap in Providing Adequate Neonatal Resuscitation in Birthing Hospitals with Level 1 & 2 Nurseries. (815)

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### Introduction /Case Report

The Regional Intensive Care Nursery at Memorial in Johnstown, Pennsylvania serves 5 outlying birthing hospitals. As part of our efforts to improve care delivery in the region and to help improve the condition of the sick infants prior to transfer, we provide outreach education and training for the staff of these hospitals. 4 are Level 1 Care Nurseries and 1 is a Level 2, total about 2500 births yearly. Statistically 10% or 250 may need some assistance initiating breathing at birth, 1% or 25 may need more extensive resuscitation. The best outcome for a neonate requiring resuscitation at birth depends on an effective immediate appropriate response along the guidelines provided by the NRP.

### Patients and Methods

We were able to scheduled NRP brush up sessions in 4/5 of our referring hospitals. We first met with the nursing staff at the delivery area and performed an “unscheduled” mock code walk through of an unplanned full neonatal resuscitation breaking it down in steps noting all the issues they had in their response as well as their suggestions for improvement. Technical help was given to improve skills. We also paid close attention to the overall layout of their unit, equipment available, work flow, communication protocols and provider availability. We analyzed the observations. In a separate meeting with the physicians and nurse manager we presented our findings, identified weaknesses and formulated responses tailored specifically to their hospital.

### Results

#### All 4 Hospitals

1-2 Nurses present at any delivery, NRP trained, start PPV & Chest compression. Not allowed to intubate, place UVC, IO, or give epinephrine because outside their scope of licensed practice.

Call for help means interrupting resuscitation to call pediatrician.

“Advanced” Resuscitation Pediatrician dependent. Not normally in hospital. Fastest response from office was 10 minutes in day, more at off hours.

Not all OB NRP trained. Not readily available because attending to maternal issues.

Fix: Develop Neonatal “Code blue” system similar to adults. One call activation. Response team to include at least Emergency room or resident physician (always in hospital). Have laminated NRP algorithm card and Intraosseus Needles for vascular access to resuscitation equipment list.

## Conclusions

Resuscitation can be initiated by nurses but does not progress beyond BVM & Chest compression until pediatrician called arrives 10 minutes later!

Ready Fix available by developing Neonatal Code Blue system.

Vulnerability identified may be inherent in the basic set-up of most Level 1&2 birthing hospitals.

Possible Magnitude of problem: 62 other similar institutions in Pennsylvania, about 1500 in US, >20,000 neonates vulnerable? Need statewide and possible nationwide review!

Other / Quality improvement and Safety and Error Preventio

PERINATAL AND NEONATAL OUTCOMES OF BABIES BORN TO MOTHERS WITH HISTORY OF POLYHYDRAMNIOS IN PREGNANCY (009)

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### Introduction /Case Report

Polyhydramnios carries a higher incidence of adverse perinatal outcome. There are various aetiological factors for polyhydramnios and this may contribute to various morbidities in infants born to mothers with a history of polyhydramnios. These include their mode of delivery, rate of neonatal admission and postnatal morbidity.

### Patients and Methods

Retrospective case notes and Xrays review of 110 infants born between January 2012 and December 2014, who had chest X-ray following Nasogastric tube (NGT) insertion for polyhydramnios/ +/- small stomach during the antenatal period (Local Institutional Policy) , to exclude Oesophageal atresia (OA) postnatally. Aim was to find the mode of delivery, neonatal admission rate and if they had any other diagnosis made and to evaluate the clinical relevance of postnatal NGT insertion followed by chest xray in this cohort.

Time taken for CXR to be taken was used as a proxy to time to first feed

### Results

Total number of deliveries for the period- 15,600

110 infants were born to mothers with polyhydramnios

All had NGT inserted followed by a chest xray post-delivery before their first feed

Mean time for NGT+Xray (away from mothers and before their first feed) was 2hrs 40 mins (range 55 mins – 6hrs 53 mins)

Total OA cases – 5 out of which 2 had history of polyhydramnios (Local incidence of 0.03%; occurs in 1:3120 live births)

All cases with OA presented immediately after delivery with features that required immediate Neonatal ICU admission

6 of the 110 (5.5%) were born <37 weeks gestation.

67/110 (61%) were born by Cesarean section (C/S) of which 26 of the 61 (43%) were Emergency C/S; compared to local C/S rate of 28%

19 of the 110 (17%) required Neonatal ICU admission.

2/110 (1.8%) both from the OA group had other anomalies (Goldenhar and Trisomy 18)

## Conclusions

There was increase Cesarean Section rate in the mothers.

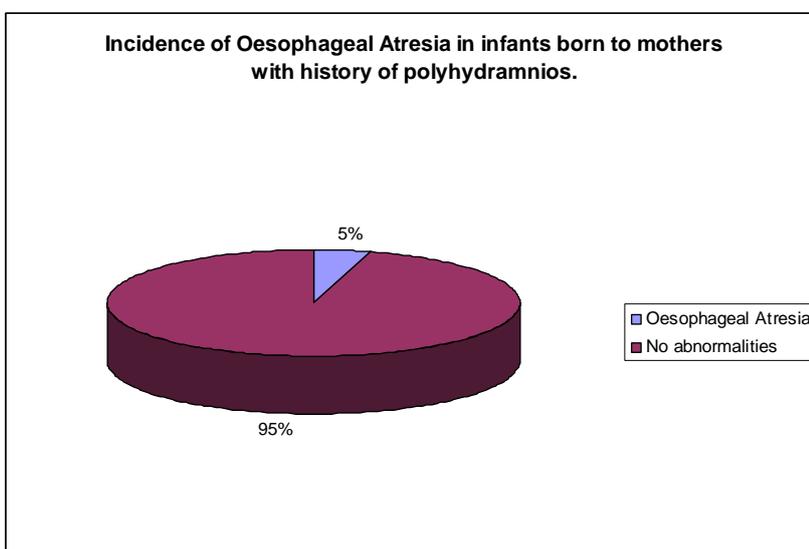
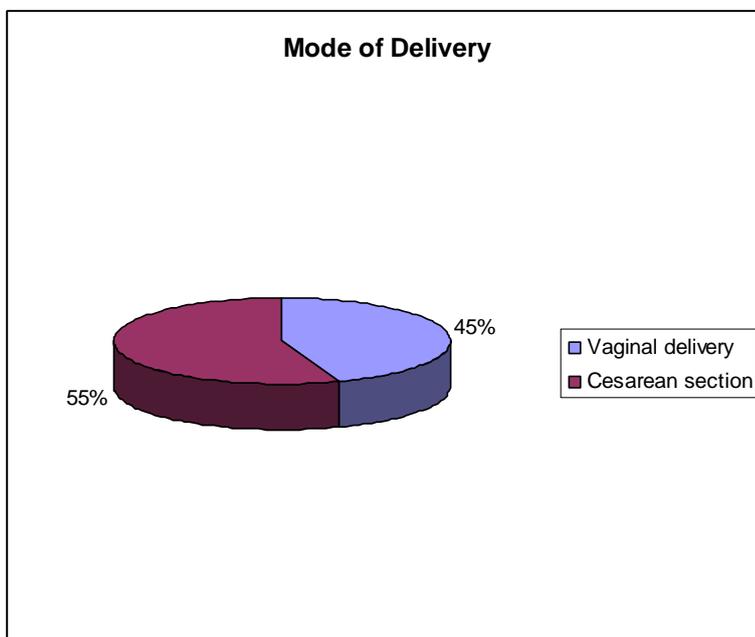
Isolated polyhydramnios+/-absent/small stomach is very poor at predicting the diagnosis of OA

Postnatal NGT+Xray are not indicated in isolated polyhydramnios+/-small/absent stomach with cost saving implications

Separating these babies from their mothers after birth is not warranted and goes against The Baby Friendly Initiative and may lead to Hypoglycaemic episodes

Exposure to ionising radiation can be avoided in these babies

## Table



## Other / Miscellanea

### THREE-YEARS FOLLOW-UP OF CHILDREN, WHO REQUIRED MECHANICAL VENTILATION IN THE NEONATAL PERIOD (512)

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#### Introduction /Case Report

Traditional mechanical ventilation (MV) is the most common method to treat infants with respiratory failure. Despite improved modes of ventilation, which reduced the mortality of newborns, in some cases infants, who require MV, have serious complications. The frequency of miscarriage and birth of preterm infants with extremely low birth weight is increasing. In this situation survive children, who demand MV. That determines the necessity of study, analysis and forecasting of long-term effects in children, who needed MV in the neonatal period.

The aim of this work was to value physical, psychomotor development, morbidity in early-aged children after neonatal MV.

#### Patients and Methods

80 children, requiring respiratory support at the neonatal intensive care unit of Lviv City Children's Clinical Hospital (2010-2012), were under observation until 3 years of age. Children were divided into 2 groups: 1st - 55 children, on SIMV/PS, 2nd - 25 neonates on nCPAP. The average duration of ventilation in the 1st group -  $5.7 \pm 0.49$  days, 2nd -  $3.6 \pm 0.29$  days. The average gestational age of children in the 1st group -  $35.9 \pm 0.56$  weeks, mean birth weight -  $2588.2 \pm 128.57$  g, in 2nd group -  $36.1 \pm 0.68$  weeks and  $2748.0 \pm 177.4$  g respectively. Control group included 25 healthy children. Physical development of children was evaluated using method of sigmal tables and computer program Eurogrowth (2000), psychomotor development - Munich functional diagnostics of child development (1994).

#### Results

At the end of the 1st year of life delayed physical development was found in 42 % of children, 2nd - in 47.6 %, 3rd - in 39% of children from 1st group; delayed psychomotor development by all criteria in 22%, 23.8% and 26.1% of children respectively. The risk of delayed physical development in infants increased after prolonged MV ( $\beta=11,353$ ), the risk of delayed psychomotor development - after asphyxia at birth ( $\beta=9,915$ ), prolonged MV ( $\beta=0,492$ ) with pulmonary complications ( $\beta=1,106$ ). Bronchopulmonary pathology prevailed in the structure of morbidity, its risk increased after prolonged MV ( $\beta=0,754$ ). 32% of children from 1st group had neurological disorders, their risk increased after asphyxia at birth and detected changes on neurosonography in the neonatal period: intraventricular hemorrhage, periventricular leukomalacia, cysts ( $\beta=2,901$ ).

## Conclusions

In order to generate risk groups of delayed physical, psychomotor development, development of neurological and bronchopulmonary pathology in children after neonatal MV, it is advisable to consider the most informative risk factors: asphyxia at birth, changes on neurosonography, duration and pulmonary complications of MV. Children after neonatal MV require rehabilitation according to the "Early intervention" program.

## Other / Involvement of parents in care

### KANGAROO CARE (KC) IN LEVEL 3 NICUS – WHAT CAN CHANGE FOR PROFESSIONALS AND PARENTS (795)

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## Introduction /Case Report

The use of KC hasn't been a priority in countries with resources and access to modern technology, nevertheless nowadays the practice of skin to skin contact has been adopted in many NICUS with good outcomes. A project supported by a European grant and a parental association (XXS) was developed in 3 level 3 NICUS in Portugal (one in Porto, two in Lisbon). NICU 1 has 26 nicubeds, NICU 2 with 14 and NICU 3 has 42 nicubeds. The project used the KC as a transversal strategy regarding development centralized care, a model developed by Mary Coughlin and all. Our aim was to evaluate impact of a systematic use of KC on staff and parental knowledge and skills and confidence to use it.

## Patients and Methods

To evaluate the knowledge on KC a survey (survey 1) was applied to staff and parents with babies in the NICU before the project started. The project included designing a guideline for systematic application of KC in NICU, evaluation of tolerance of the method, staff and parental educational and training sessions. After 4 months period of KC use in the NICUS the same survey (survey 2) was applied. The questions generally concerned the method itself, the experience of it, advantages, disadvantages and concerns. Combined analysis of staff survey was done, comparing answers of both surveys in the 3 Units. Concerning parents the published data is from NICU3.

## Results

Staff survey 1 was answered by 71% and survey 2 by 78%. The main results are published in table 1.

Concerning parental knowledge on benefits of KC the large majority had significant difference between survey 1 and 2.

## Conclusions

We concluded that a systematic introduction of KC supported by a clear guideline, parental educational sessions and staff training, as well as defined evaluation of tolerance seems to be an effective strategy to improve knowledge, parent empowering and staff skills on this method, being an important milestone to successfully apply a centralized development care policy.

Table

		<b>Survey 1</b>	<b>Survey 2</b>	
<b>Staff</b>		n=133	n=126	
	Transfer confidence			
	Sitting transfer	92%	42%	
	Standing transfer	7%	57%	p 0,0001
	Grading obstacles to use KC*			
	Elegibility criteria not clearly defined	5,1	4,1	p 0,0390
	Lack of a guideline	5,1	4,6	p 0,0304
<b>Parents</b>		n=19	n=34	
	Knowledge of KC	76,23%	91,43%	
	Frequency of opportunities to use KC			
	Never	36,8%	14%	
	Every day	26%	29%	
	Evaluation of the KC experience			
	Very good	85%	100%	p 0,0361

\*Grades 1 to 7, being 1 the most considerable barrier and 7 the lowest barrier.

Table 1 – Summary of results: KC survey 1 and 2.

Other / Quality improvement and Safety and Error Preventio

## CONSERVATIVE APPROACH TO NEWBORNS WITH INFECTIOUS RISK BASED ON CORD BLOOD PROCALCITONIN (185)

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### Introduction /Case Report

Early diagnosis of neonatal sepsis remains a clinical problem in neonatal units. The unspecificity of clinical signs and the absence of sensitive early markers of infection, means an unnecessary interventional approach in many newborns with infectious risk. Procalcitonin (PCT), an early marker of bacterial infection difficult to interpret in newborns due to physiological changes in the first days of life, determined in cord blood has shown to be useful to identify newborns with increased risk of sepsis. We have developed a protocol of clinical approach to newborns with infectious risk based on the determination of PCT in cord blood, and have evaluated its usefulness and safety.

### Patients and Methods

PCT was determined in cord blood of newborns with the following risk factors: spontaneous delivery less than 34 weeks, clinical chorioamnionitis, or at least two risk factors (maternal fever, prematurity less than 37 weeks, amniorrhexis more than 18 hours or untreated SGB). Newborns with PCT  $\geq 0.6$  ng/ml were evaluated according to clinical signs and analytical assessment at 6 hours of life. Newborns with PCT  $< 0.6$  underwent surveillance for six hours until discharge (algorithym). Patients were classified finally as confirmed infection, probable infection or no infection, according to a score of clinical and analytical data. Receiver operator characteristics curves (ROC) of PCT versus infection (confirmed or probable) were determined by MedCalc.

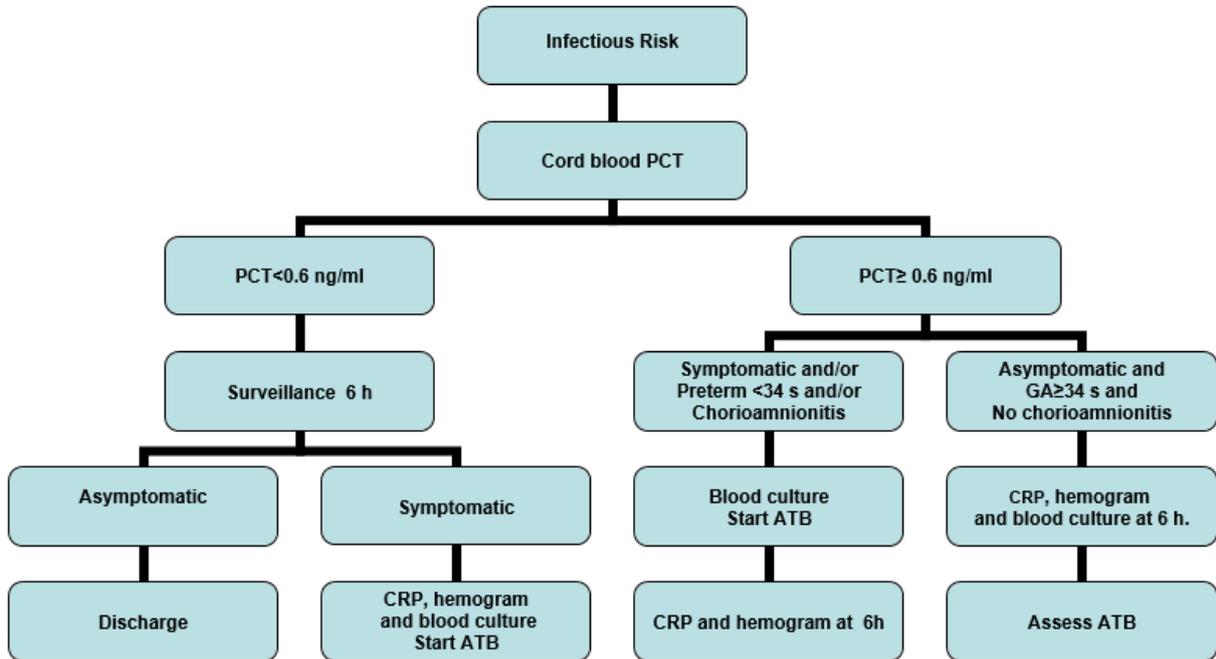
### Results

Among 2811 live newborns, 148 (5.2%) met criteria of infectious risk, and nine (0.32%) of them sepsis criteria. Fourteen had cord blood PCT  $\geq 0.6$  and nine of them were considered infected: positive predictive value 64.3% (95% CI: 35.1-87.2). The remaining 134 had cord blood PCT  $< 0.6$  and none of them resulted infected: negative predictive value 100% (97.3-100). The sensitivity and specificity of PCT versus infection with a cutoff  $\geq 0.6$ , were 100% (66.4-100) and 96.4% (91.8-98.8) respectively, with an area under curve of 0.982 (0.945-0.997) and a significance level ( $p < 0.0001$ ). The incidence of infection in the whole group (pre-test probability) was 6%, with the highest value in chorioamnionitis group (26%), which had also the highest post-test probability: 90.7% (77.8-97.4).

### Conclusions

Determination of cord blood PCT in newborns with infectious risk might allow a safe and conservative approach to these patients, reducing unnecessary blood extractions and antibiotic therapies. It might also discriminate cases that would need an early therapy. Newborns of mothers with chorioamnionitis could be those in which this approach might be more profitable.

Table



## Other

### The Systems Biology of Neonatal Immune System Development (718)

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## Introduction /Case Report

Newborns, particularly if preterm, are susceptible to infections, and the basis for this is not well understood. Also, inflammatory conditions like BPD are major causes of morbidity and mortality in neonates. A better understanding of immune regulation in newborn children is now needed. The complexity of the system has hampered a definition of metrics of immunological health and prevented us from identifying children most at risk. We have developed a systems-immunology approach measuring all blood cell populations and many serum proteins. We recently used this approach to show that human immune systems are shaped by environmental, rather than heritable influences (Brodin et al, Cell 2015).

## Patients and Methods

To massively profile blood cell populations, Mass cytometry (CyTOF, Fluidigm Inc) was recently developed (Bendall et al, Science 2011). We optimized this technology for blood samples as small as 100 microliters available from newborns. We are now able to profile phenotypes and functional states across millions of individual blood cells using a 45-antibody panel targeting both surface proteins and intracellular signaling molecules. Combined with novel computational tools (Brodin, et al, PNAS 2014), we define and follow previously unknown immune cell populations in newborns. Preterm infants born before w30 and full-term babies born at Karolinska University Hospital were included. Cord blood and blood samples obtained at 1, 3 and 12 weeks of life was used. Also, parental samples were used.

## Results

We have identified over 400 different immune cell populations within the principal cell lineages; granulocytes, monocytes, dendritic cells, NK-, T- and B-cells. Phenotypes of all these cell populations in newborns are distinct from the cells present in their parents. We see developmental progressions towards parental-like cells during early life, although the timing varies between cell lineages. Also, inter-individual differences are seen in the kinetics of immune cell development after birth, suggesting that this could explain some of the differences in infectious disease susceptibility seen between patients. Signaling and activation states across cell populations change dramatically at specific time-point, without any clinical signs of infectious disease or immune activation; possibly suggestive of normal developmental patterns only visible using this high-dimensional profiling.

## Conclusions

Here we present a unique experimental approach for systems-level profiling of neonatal immune systems. We are describing the process of immune system development in neonates at an unprecedented level of

detail with important implications, both for our understanding of normal immune system development, and the increased susceptibility seen in specific neonates.

Other / Miscellanea

Lemierre's syndrome (018)

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### Introduction /Case Report

Lemierre's syndrome is also called forgotten disease. Incidence of 3.6 cases per 1 million per year . We present a very rare case that explains the challenges and initial uncertainty in making a unifying diagnosis and bringing together symptoms and signs.

### Case Report

A 15 years old girl , with history of sore throat and high fever. She had been feeling unwell, febrile and lethargic for 6 days. She had generalized abdominal pain /chest pain and left leg pain . She was febrile, and tachycardia with hypotension. She had abdominal tenderness and left ankle swelling. Clinically and biochemically she had severe sepsis . She had very high urea and creatinine suggesting acute kidney injury.. After stabilization she was taken to theatre for laprotomy . She had multiple pelvic abscesses and pus in fallopian tube so surgeons/obstetricians and paediatrics team felt the diagnosis probably was severe pelvic inflammatory disease leading to sepsis . She was transferred to gynaecology ward. On day 5 She was moved to adult HDU due to respiratory distress. Her CT chest suggested multiple lung abscesses and ultrasound neck suggested thrombosis of internal jugular vein. Lemierre's syndrome was thought t be the explanation for clinical signs and transferred to local tertiary hospital where diagnosis was confirmed . She was given anticoagulant and antibiotics. She has fully recovered from her illness.

### Conclusions

This case demonstrates the process of multidisciplinary team involvement to reach a single rare diagnosis and initial minor mistakes made in an attempt to reach to an answer for a rare medical condition.

Other / Miscellanea

NON-IMMUNE HYDROPS FOETALIS: CASE STUDIES AND EVIDENCE (396)

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### Introduction /Case Report

Hydrops foetalis is an accumulation of fluid in two or more compartments of the developing foetus. There are two distinct forms of HF: immune and non-immune. Since the widespread use of "Anti-D" the incidence of immune hydrops foetalis has fallen significantly. In developed health systems NIHF accounts for >90% of cases of HF, for this reason we will focus on NIHF.

The incidence of NIHF is thought to be between 1 in 1500 to 1 in 3800 births . The mortality is approximately 81% .

Here we present 4 case studies of babies with NIHF who were managed at our tertiary centre over a 6 month period.

### Case Report

Baby A was delivered by elective Caesarean section, at 32 weeks gestation, due to persistent foetal SVT and ultrasound findings consistent with hydrops foetalis.

Maternal medical cardioversion was attempted with digoxin, flecanide and amiodarone, but failed.

At the delivery Baby A's heart rate was 230 bpm and he was markedly oedematous. He was transferred to neonatal intensive care and placed on a ventilator. 0.3mg/kg of adenosine was given via UVC, after which the heart rate was 130-140bpm. An amiodarone infusion was commenced initially at 7.5mg/kg/day after checking TFTs and LFTs. A diagnosis of Wolf-Parkinson-White syndrome was made.

Despite the a gradual improvement in cardiac function, the patient was extremely difficult to manage. There were significant difficulties with oxygenation, due to pulmonary hypertension and hypoplasia. On the 6th day of life the decision was made to re-orientate care, and later that day he passed away.

Baby H was delivered at 35 weeks by emergency Caesarean section following unsuccessful trial of forceps. A diagnosis of HF had been made the week prior to his delivery. Bilateral chest drains were inserted on delivery suite; approximately 1500ml of fluid were drained in the 1st 24hours. This gradually reduced. He remained ventilated for the entire stay, but required low pressures, suggesting this was not a primary lung pathology.

He was noted to have a relative immunodeficiency and required further treatment with second line antibiotics (ceftazidime and vancomycin) and later was treated with fluconazole and amphotericin B due to growth of *Candida lusitanae* from blood cultures and ET secretions.

It proved very difficult to fluid restrict Baby H whilst maintaining adequate blood pressure and renal perfusion. He gradually deteriorated and went into multiorgan failure. The decision was made with family to re-orientate care.

Post mortem examination revealed a normal spleen, thymus and lymph nodes, with no evidence of immunodeficiency. It was concluded that it was likely that the low immunoglobulins and T-cells were a consequence of the HF, not the cause.

Baby R was delivered by emergency Caesarean section, due to suspicious CTG, at a district general hospital at 35 weeks gestation following prolonged membrane rupture.

The pregnancy was known to have been complicated by polyhydramnios, but HF had not been diagnosed antenatally. Baby R required full resuscitation at birth.

She was oedematous with dysmorphic features including low set ears, and 5th finger clinodactyly.

She was transferred to our tertiary centre for on-going care and for cardiology opinion.

Cardiac echo showed :

“aortic valve regurgitation, tricuspid regurgitation, mitral regurgitation. Tricuspid stenosis. Patent ductus arteriosus, patent foramen ovale”

Surgical treatment was concluded to be impossible. Therefore the decision was made to re-orientate care . She died on her 10th day of life.

Baby M was born by spontaneous vaginal delivery at 32 weeks. Delivery had been planned in a nearby tertiary unit, but her mother presented in advanced labour to her local district general hospital.

Baby M required prolonged resuscitation at birth. She was commenced on nitric oxide with a good response, and dopamine, dobutamine and hydrocortisone . She was transferred to our tertiary centre.

A trial of HFOV did not improve her ventilation. Gases gradually improved on conventional ventilation. The nitric oxide was weaned quickly and stopped successfully.

Cardiac echo showed:

“normal systemic venous return, PFO with right to left shunt. Moderate tricuspid regurgitation. No VSD. No LVOTO/RVOTO. Large PDA with right to left shunt. Small pericardial effusion.”

Her early course was complicated by coagulopathy, jaundice and a corneal exposure secondary to sedation. In addition, it was found incidentally on ultrasound that the UVC had migrated through the hepatic vein into the liver parenchyma. A collection had formed. The infusions were stopped, a peripheral long line was inserted and the UVC removed.

After a failed extubation attempt, one episode of sepsis where *Pseudomonas aeruginosa* was grown in blood cultures (which required inotropes to be recommenced), and then a further episode of culture negative sepsis, she was eventually successfully extubated onto high flow therapy on day 29.

On her 38th day of life she was transferred back to her local hospital for on-going care. She was continuing on diuretics (spironolactone and chlorothiazide) and a weaning dose of oral morphine.

She was noted on examination to have an unusual patch with covering hair on her back, but we were unable to link that to the diagnosis of HF. The cause of the HF remains idiopathic.

After completing the preceding case reports, we carried out a literature review, and have formed some guidelines.

## Conclusions

Establishing a diagnosis of NIHF can be straight forward, and is based upon the clinical features of the neonate.

However, as demonstrated by the case reports, it can be extremely difficult, or impossible, to find the underlying cause of the NIHF. The investigations required may be complex and diverse.

As with all neonatal medicine, clear communication with the obstetric team is vital and the parents must be well supported, as the case reports demonstrate the associated high mortality .

Other / Miscellanea

EYES, LUNGS AND HEART; WHAT'S THE CONNECTION? (770)

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Introduction /Case Report

We would like to report a child born with Anophthalmia and significant respiratory distress and cardiac problems.

The baby was initially treated with nCPAP for 16 hours.

On stopping nCPAP, she continued to have persistent oxygen requirement.

Subsequent X-rays and ultrasound raised suspicion of a Pulmonary Hypoplasia and Diaphragmatic hernia which required surgery.

Echocardiography demonstrated a Ventricular Septal defect.

Results

The association of Pulmonary Hypoplasia, Diaphragmatic Hernia, Anophthalmia and anatomic Cardiac defects has been reported in literature as PDAC Syndrome, Matthew-Wood Syndrome, Spear syndrome, or MCOPS9 syndrome/Microphthalmic syndrome 9.

Recessive mutations in STRA6, encoding a membrane receptor for the retinol-binding protein have been reported in literature in relation to PDAC syndrome. A genetic screen on the baby demonstrated a normal female Karyotype with no mosaicism.

Subsequent gene analysis demonstrated a heterozygous de novo mutation in RARB gene with c.1159C>T mutation.

Conclusions

From a literature review it appears this is third ever reported case of such mutation.

As this is a heterozygous de novo mutation, recurrence risk is postulated to be less than 1%.

Other / Miscellanea

## THE RISK OF SEVERE HYPERBILIRUBINEMIA IN INFANTS (035)

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### Introduction /Case Report

In recent years, the increased prevalence of breastfeeding in conjunction with early discharge practices has increased the risk for marked hyperbilirubinemia in term infants. The aim of this study was to investigate the risk factors for significant hyperbilirubinemia in Taiwanese infants.

### Patients and Methods

A prospective cohort study was conducted to investigate the effects of birth weight, gestational age, sex, mode of delivery and feeding, glucose-6-phosphate dehydrogenase deficiency, variant UDP-glucuronosyltransferase 1A1 (UGT1A1) gene, and solute carrier organic anion transporter 1B1 (SLCO1B1) gene on hyperbilirubinemia. Those term infants with a positive Coombs test or with severe neonatal illness care were excluded. The PCR- restriction fragment length polymorphism (RFLP) method was applied to detect the known variant sites in the UGT1A1 and SLCO1B1 gene in Taiwanese. Phototherapy was started if the bilirubin level exceeded the hour-specific phototherapy treatment threshold. We analyzed the risk factors for significant hyperbilirubinemia using univariate logistic regression models.

### Results

A total of 289 full term infants were enrolled in this study. Of these, 58 (20.0%) infants received phototherapy with significant hyperbilirubinemia. Birth weight, maternal age, Apgar score, sex, and cephalohematoma were not significantly different between the hyperbilirubinemia and control groups. The significant risk factors were a variant nucleotide 211 in UGT1A1 (1.90; 95% CI, 1.10 to 3.26;  $P=0.021$ ), G6PD deficiency (13.96; 95% CI, 2.03 to 95.81;  $P=0.045$ ), vaginal delivery (3.04; 95% CI, 1.43 to 6.48;  $P=0.004$ ), gestational age (0.73; 95% CI, 0.53 to 0.99;  $P=0.045$ ) and breast feeding (5.99; 95% CI, 1.05 to 34.37;  $P=0.044$ ).

### Conclusions

The infants who are G6PD deficiency, carry the 211 variants in the UGT1A1, vaginal delivery, low gestational age and breast feeding are at high risk to develop severe hyperbilirubinemia.

Other / Organization of perinatal care

Neonatal thyroid function in infant born to mother with thyroid disease over 12 years in a tertiary institution in Singapore (302)

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### Introduction /Case Report

The infant of a mother with thyroid disease may be at risk of abnormal thyroid function. Universally infants born to thyroid disease are routinely screened with cord TSH (Thyroid stimulating hormone) screening like all other newborns. We hypothesize; infants born to mother with thyroid disorders, particularly autoimmune thyroid disorders are high risk for thyroid dysfunction and should be screen with repeat thyroid function tests (TFT) on day 5-7, irrespective of unremarkable Cord TSH and even when they are clinically asymptomatic.

### Patients and Methods

The aim of study is to determine which infants are at-risk and need for repeat thyroid function monitoring besides a universal cord TSH newborn screening test and to suggest guideline for management of this particular cohort of infants born to mother with different aetiologies of thyroid diseases. This is a retrospective analysis of infant born to mothers with all aetiologies of thyroid diseases between 2001 and 2012, at Singapore General hospital (SGH). Maternal and neonatal demographics data and antenatal TFT, thyroid receptor antibody (TRAB) levels, Thyroid peroxidase antibody levels (TPOAB) and antithyroid medications during pregnancy (for patients with known Graves' disease) and neonatal cord TSH at birth and repeat (D5-7) newborn TFT were also analysed.

### Results

Cord TSH was abnormal in 35/529(6.6%) of infants, but only one baby with low cord TSH had abnormal day 5-7 TFT requiring treatment with thyroxine. There were 407/529(77%) infants born to mother with thyroid disorder, were screened for routine repeat freeT4/TSH done on day 5-7, 273/407(51.6%) had higher free T4 and 7/407(1.7%) had low free T4 on day 5-7TFT. There were 404/529(76.3%) had repeat TSH done on day 5-7. In this group, 40/404(7.5%) had low day 5-7 TSH and 51 /404(9.6%) had high cord TSH on day 5-7TFT. Total 4 babies were treated after abnormal day 5-7 TFT. Incidentally all 4 babies requiring treatments were born to mother with autoimmune thyroid disease like Grave's disease or Hashimoto thyroiditis.

### Conclusions

We recommend, appropriate management of maternal autoimmune thyroid disease throughout pregnancy is essential and infant born to mother with autoimmune thyroid disease, must be screened with repeat day 5-7 thyroid function test, in spite of normal cord TSH and even if they are asymptomatic, to pick up subclinical hypo/hyperthyroidism and to prevent undesirable neonatal outcomes by early treatment for hypo/Hyperthyroidism in infant.

## Brain & Development / Neurodevelopmental Outcome

Prediction of cerebral palsy and motor impairment in children born very preterm: Two decades of research – what do we know? (138)

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### Introduction /Case Report

Surviving children born very preterm (VPT;  $\leq 32$  weeks gestation) or with very low birth weight (VLBW;  $\leq 1250$ g) are at high risk of neurodevelopmental problems, including cerebral palsy (CP) and motor impairment. There is a large literature reporting risk factor analyses for poor long term outcome in this population, which to date has not been formally summarised.

### Patients and Methods

We performed a systematic review of multivariable risk prediction models for CP and motor impairment in children born VPT or with VLBW after 1990 using the Medline, Embase and Pyscinfo databases. We extracted key information on study design, outcome definition, risk factor selection, model development and reporting, and conducted a risk of bias assessment. The strength of evidence for the prognostic value of risk factors identified was summarised graphically. The methods have previously been published in a review protocol (<http://www.crd.york.ac.uk/PROSPERO/>), registration number CRD42014006943. Results were reported according to the PRISMA guidelines.

### Results

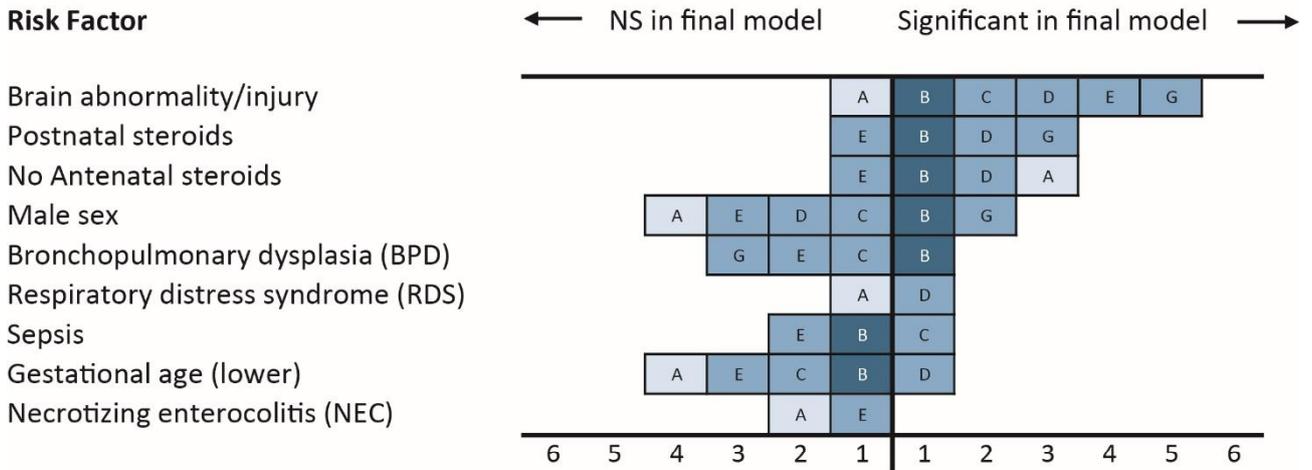
28 studies comprising 44 risk factor models were included. There was strong evidence that intraventricular haemorrhage and/or periventricular leukomalacia are prognostic factors for CP. There was some evidence that the use of postnatal steroids increased the risk of CP and that the use of antenatal steroids was a protective factor. Male sex was of limited use as prognostic factor for CP, however in children over 5 years with no major disability, there was evidence that it was a predictive factor for motor impairment. Gestational age was found to be of limited use as a prognostic factor in this population with a limited gestational age range of  $\leq 32$  weeks.

### Conclusions

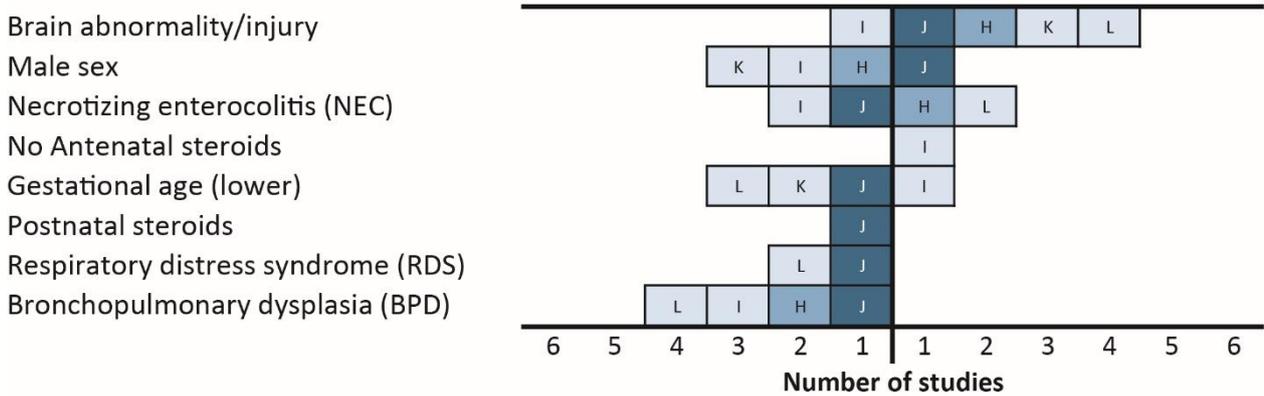
This review has identified factors which may be of prognostic value for CP and motor impairment and will help to form the basis of future prognostic research.

Picture

**Age at assessment <5 years (n=7 studies)**



**Age at assessment ≥5 years (n=5 studies)**



## Other / Miscellanea

### Acute myocarditis in newborn (172)

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## Introduction /Case Report

Disseminated neonatal herpes, with mortality rate of 85%, is the rarest presentation of neonatal herpes (10-25%) and its prevalence is increasing (2-33/100000 births, 50 cases/year in France). 80% of neonatal contamination is during labour or delivery, rarely in utero or in post-partum (due to contaminated staff). HSV2 is involved in 2/3 cases, with a transmission rate from 1% to 25- 50 % for mother infection in late pregnancy. Symptoms are non-specific in children (less than 40% of cutaneous lesions, which is one explanation to delete diagnosis and high mortality) and mother (asymptomatic in 80%, prolonged fever).

## Case Report

J, a 31GA preterm infant, degraded on 4 days of life with acute respiratory distress syndrome, hypotonia, macular lesion on torso, pericardic effusion but initial infectious tests negative. Deterioration is very prompt despite large antibiotherapy and antifungal with death of the patient due to refractory cardiac hypocontractility 18 hours after beginning of symptoms. Final medical evaluation highlights 1 million of HSVE copies in cerebro spinal fluid,  $\alpha$ interferon $>$ 200 and positive HSV2 PCR in mother, who was asymptomatic during and after pregnancy.

## Conclusions

HSV in an uncommon case of acute myocarditis (2/38 cases) with symptoms as failures, shock, pericardial effusion, rhythm trouble or calcifications. There are 3 steps in disease progression: cells destruction by HSV virus (innate immunity), autoimmunes lesions by cardiac antibodies and at last myocardial remodeling with evolution towards dilated chronic myocarditis. High level acyclovir can improve prognostic partially, as new therapeutic as losartan.

## Brain & Development / Structural and Functional Brain Imaging

### INFLUENCE OF SEVERE ILLNESS AND BRAIN INJURY ON GROWTH OF THE MOTOR PATHWAY STRUCTURES IN EXTREMELY PRETERM INFANTS (317)

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#### Introduction /Case Report

Many infants and their parents have to face the implications of neurodevelopmental deficits following extreme preterm birth. A better understanding of brain development in these infants may elucidate explanations for these impairments. This study evaluates the effect of severe illness and brain injury on the extra-uterine growth of different components of the motor pathway in extremely preterms. It examined the central sulcus (with the start of about 30% of the motor tracts) and different underlying structures.

#### Patients and Methods

71 infants born < 28 weeks of gestation (mean 26.5 weeks) underwent brain MRI around 30 weeks postmenstrual age and term equivalent age. A 3D reconstruction of the central sulcus (CS) in Brainvisa® was created using T2-weighted brain tissue segmentations (Chita, 2013). This allowed calculation of the surface (mm<sup>2</sup>). With an applied method (Makropoulos, 2014) volumes of different motor pathway regions were obtained. Clinical parameters were extracted from the infants records. Mechanical ventilation longer than 7 days was used as measure for severe illness, a grade 3 or 4 IVH as measure for severe brain injury. Multivariable regression analysis, with correction for age at scan, was carried out to determine the influence of gestation, sex, birth weight z-score and multiple pregnancy.

#### Results

A strong positive correlation between the surface of the central sulcus and volumes of underlying components (parietal white matter, thalamus, caudate nucleus, brain stem) appeared, as shown in table 1. Also a strong synchronicity in growth of all structures was found. Volumes of motor tract structures were significantly reduced in infants with prolonged mechanical ventilation (35% of cases), the surface of the CS only at early age. Prolonged ventilation influenced the relation between the structures, but no significant differences between infants with and without existed. Severe brain injury (14% of cases) did not significantly influence the simultaneousness of growth between the different components, but the relation seemed to appear stronger in those infants who suffered a severe IVH. Influences of other clinical parameters can be found in table 1.

## Conclusions

This study shows the synchronicity in growth of the motor cortex and underlying components. Severe brain injury shows a more general effect on the structures, where severe illness seems to disturb the synchronicity of growth. Possibly in these cases the cortex catches up before other volumes overtake, leading to unequal growth. These different patterns, with other underlying etiologies, might relate differently to alterations in neurodevelopment.

Table

		Parietal lobe		Thalamus		Caudate Nucleus		Brainstem	
		r <sup>2</sup>	p-value	r <sup>2</sup>	p-value	r <sup>2</sup>	p-value	r <sup>2</sup>	p-value
Central sulcus	30 weeks left	0.507	0.000	0.540 <sup>#0</sup>	0.000	0.442 <sup>#</sup>	0.000	0.533 <sup>#0</sup>	0.000
	30 weeks right	0.395	0.000	0.463	0.000	0.434	0.000	0.388	0.000
	40 weeks left	0.413 <sup>*</sup>	0.000	0.374 <sup>*</sup>	0.000	0.343	0.000	0.432	0.000
	40 weeks right	0.301 <sup>*</sup>	0.001	0.284	0.002	0.264	0.004	0.284	0.002
	Growth left	0.452 <sup>*</sup>	0.000	0.505 <sup>*</sup>	0.000	0.346 <sup>*</sup>	0.000	0.534	0.000
	Growth right	0.394 <sup>#</sup>	0.000	0.373	0.000	0.308	0.000	0.419 <sup>#</sup>	0.000

Influence of <sup>\*</sup>Birth weight z-score, <sup>#</sup>Multiple pregnancy, <sup>0</sup>Gestational age

## Other / Miscellanea

Longitudinal impact of music therapy on premature infants and their caregivers: Study protocol for a feasibility randomized controlled trial (028)

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## Introduction /Case Report

Preterm birth and prematurity is a major medical, psychological and socio-economical problem worldwide. More than 1 in 10 of the world's newborns are born prematurely corresponding to 14.9 million premature infants each year. Previous research suggests positive effects of music therapy for premature infants and their parents/caregivers, though methodologically rigorous studies with emphasis on long-term follow-up and child/parental psychological outcomes are needed. In order to carry out more generalizable, rigorously designed, and adequately powered trials investigating music therapy in prematurity, the feasibility and acceptability of study procedures must first be determined.

## Patients and Methods

This paper presents a feasibility study protocol of the first randomized controlled trial of music therapy for Norwegian premature infants and their caregivers in the NICU and after discharge to home. A single-blind randomized controlled feasibility trial will be conducted to evaluate the effectiveness of music therapy intervention on premature infants and their parents/caregivers across a 6-month time period. Trained music therapists will deliver the treatment intervention in collaboration with each neonate's parents, using a variety of live, interactive music therapy approaches tailored to infant developmental level. This feasibility study protocol reports study design, objectives, treatment, study schedule, recruitment and retention, adverse effects, personnel, facilities and equipment.

## Results

This study will evaluate the feasibility and acceptability of intervention, measurement and trial procedures for a randomized controlled trial. This study will also determine the characteristics of the population recruited, and explore recruitment and retention patterns. Responding to the need for more rigorously designed trials examining the effectiveness of music therapy in the field of prematurity, this pragmatic trial will generate findings that inform the design and implementation of a multi-site randomized controlled trial. Information gleaned from the feasibility and multi-site trials will in turn contribute to the emerging development of music therapy clinical practice for premature infants and their families within Northern Europe.

## Conclusions

Assessment of protocol feasibility is an important initial step in the conduction of a quality, multi-site research study. The use of music therapy for premature infants and their families is currently in inception within Nordic countries. Through discussion of our feasibility study protocol, we aim to stimulate dialogue

among European researchers interested in this area of practice, in order to increase the level of rigor of future studies.

## Other / Neonatal Transportation

### EMERGENCY TRANSPORT OF INFANTS AND CHILDREN - TOGETHER WE STAND, DIVIDED WE FALL (330)

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#### Introduction /Case Report

The provision of emergency transports for newborn infants is a high-risk medical procedure with a significantly increased risk of mortality, adverse event and near-misses. With the increasing regionalisation of secondary and tertiary health care centers, the need for complex inter-facility transport is as high as ever. However, the provision of this service differs a lot from one country to another. There is therefore an urgent need for an international cooperation of transport service providers.

#### Patients and Methods

Based on the experience from the Neonatal and Paediatric Emergency Transport Service (NEO-PETS) in Copenhagen with > 2000 acute high risk infants being transported since 1993, we describe the per protocol and real-life target groups, our results (no deaths occurring during transport, 40% intubated, 15% PICU), the transport flow-chart, the transport team composition, educational background and primary obligations, the provided services, the transport means, the equipment, and advanced treatment options (incl. NO and HFO).

#### Results

Our opportunity is to deliver a 24/7 service with a very short response time within a fairly large geographical area. Our transport team always consists of a neonatologist and/or a physician with paediatric expertise together with a neonatal intensive care nurse. Our equipment has been down-sized and optimised for transport, and we provide diagnostics, stabilisation, and treatment options as at a Level III/IV NICU at the referring hospital. However, we do have challenges, in terms of f.ex. telemedicine, fixation of the infant, active cooling, and quality control measures.

#### Conclusions

Our opportunities and challenges are probably very much alike when comparing with other countries. The patients and their disease entities are the same. There is a need for the establishment of an international society of transport team services, to enhance transparency, exchange of information and research cooperation, to decide on universal quality and outcome indicators, and to build a database of emergency neonatal transports, including a registry of adverse events and near-misses.

Other / Quality improvement and Safety and Error Preventio

Hypothermia, an enigma: three year comparative review in a tertiary neonatal unit (439)

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### Introduction /Case Report

Hypothermia is well recognised as a factor influencing new born health and one of the major factors contributing to neonatal morbidity. Despite various interventions and increased awareness, maintenance of normothermia in the newborn particularly in the first few hours can be challenging. We noted a rise in the incidence of babies admitted to our neonatal unit with hypothermia in the first quarter of 2013 as compared to two other tertiary units within the regional network. This observation prompted immediate attention and formation of a working group to formulate a multidisciplinary plan.

### Patients and Methods

Our aim was to determine the incidence of neonatal hypothermia at the time of admission to our neonatal unit prior to and after the institution of sustained programme of awareness and room temperature modifications (commenced in April 2013). Retrospective data of all babies admitted to our neonatal unit with a temperature of 37 weeks, 34-36+6 weeks, 29-33+6 weeks and <29 weeks) and severity of hypothermia ( babies with temperature < 36.5°C and those with mild hypothermia >36°C and < 36.5°C)

### Results

Number of overall admissions with hypothermia fell from 40.7% in 2012-2013 to 34% in year 2013-14 and subsequently to 24% in 2014-15. There was a drop from 8% to 5% in incidence of hypothermia in babies 36.0°C (65.4% 70.5%, 72.5%). Results within varying gestations have been tabulated in Table 1.

### Conclusions

Achieving normothermia and maintaining a warm chain, facilitated by health professionals and immediate care providing staff at the time of birth can prevent associated complications. Formulating an action plan and maintaining awareness needs consistent commitment and sustainable plans and goals that are realistic with key involvement from all stake holders.

Table

Table 1: Infants with hypothermia according to gestational age

Year, n (%)	2012- 2013 N = 399 (40%)	2013-2014 N = 391(34%)	2014-2015 N = 306 (24%)
<29, n (%)	31(8)	29 (7.5)	16 (5)
29-33+6, n (%)	55 (14)	56 (14)	40 (13)
34 - 36+6, n (%)	134 (33)	135 (34.5)	94 (30)
>37, n (%)	179 (45)	171 (44)	156 (50)

## Other / Neonatal Transportation

### BED-SIDE ROP SCREENING IMPLEMENTED ON NEONATAL EMERGENCY SYSTEM – HEALTH ECONOMIC ASPECTS (636)

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## Introduction /Case Report

Most of consequences of ROP deteriorate patients' quality of life and imply significant societal costs. Recognizing ROP in time is essential to ensure the best possible outcome. DRI combined with remote interpretation has advantages over BIO, one of the most important being that potentially instable premature newborns do not have to be transported. PCA launched its Premature Eye Rescue Program (PERP) in 2009 to perform bed-site ROP screening with remote interpretation in order to decrease the need for transportation of premature babies. The aim of this analysis has been to demonstrate cost savings achieved by PERP

## Patients and Methods

As several studies demonstrated that DRI has high diagnostic performance, only the cost of traditional screening and digital retinal imaging were compared, assuming their diagnostic performance to be equal. The total costs of investment and maintenance of bed-site screening were compared to the costs of a hypothetical situation in which all the cases were transported and screened traditionally with no bed-site investigations. The analysis time-horizon was 10 years and was performed from the service provider's perspective.. The costs used for calculation were actual costs incurred between 2009-2013 and projected costs assumed for 2014-2018. All costs before 2013 were inflated and all costs after 2013 were discounted to 2013, and non-specific PCA's overhead costs were not included.

## Results

Since the launch of PERP up to the end of 2013, 2934 examination were performed and the RetCam was installed on sites in 606 occasions (4.8 examinations per installation). PERP covered 25 NICUs. Performing the screening examination at bed-site and consequently avoiding several transports of premature babies saved 64,507 km from 2009 to 2013. The saved working load of the staff was 2765 hour. The yearly saved nominal costs were 17,435 Euro, 24,608 Euro, 21,819 Euro and 33,609 Euro from 2009 to 2013, respectively. Taking account of the initial investments (assets and human capital), inflating the costs before 2013 with cumulative consumer price index and discounting the costs after 2013 (with 3.7% recommended in Hungary), at the end of 2013, the net present value of PERP was 104,205 Euro, with a payback period of 59 months and an internal rate of return of 18.22%.

## Conclusions

PERP was established to ensure bed-site ROP screening of premature infants to avoid the need to transport them. In addition to avoiding transports, it was demonstrated that bed-site screening with DRI and remote interpretation, compared to transport-based screening with BIO, was cost-saving from the perspective of

the service provider and there was a return on initial investment and maintenance costs within five years after the project initiation

## Other / Quality improvement and Safety and Error Preventio

Outcome of Babies born by Caesarean Section under General Anaesthesia over a 19 month period in a General Hospital with a Level 3 NICU (777)

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### Introduction /Case Report

Various Neonatal outcomes have been described for caesarean section under general anaesthesia due to influences from indication for the urgent section and the general anaesthetic.

Our objectives was to find the

- number of deliveries by Cesarean section under GA
- the indications
- time of birth (out-of-hours [1700-0800 hrs] or in-hours [0800-1700 hrs])
- the neonatal outcomes of the babies

### Patients and Methods

- Jan 2012- July 2013 (19 months period)
- Babies who were born by cesarean section under General Anaesthesia (GA), the indications and time of birth (out-of-hours [1700-0800 hrs] or in-hours [0800-1700 hrs])
- Demographics of the babies

### Results

- Total born under GA = 121 (total deliveries over the same period = 7,800)
- Indication for C/section – 91 not documented; Fetal distress 6; Cord prolapse 7; Failure to progress 1; Uterine rupture 3; Abruption 4; APH 1; Pathological CTG 7; Failed induction 1
- Born in-hours = 47; out-of hours = 68
- M:F = 67:54
- Gestation: 7 (37wks)
- Resuscitation after birth- 80 required no resuscitation; 30 required Airway and Breathing (AB) support; 8 needed AB with intubation (I); 2 required ABI + CPR (C); and only 1 required ABIC with drugs
- Mean Apgar: at 1 minute: 7.2 and at 5 minutes 9.3
- 23 were admitted. Indications: Prematurity: 12, RDS 3, Sepsis 4, IUGR 6, Poor perinatal adaption 2, CVS disease 1, Maternal drug use 2, Mother admitted to HDU 1
- Art cord gas pH done 107: 7.2 = 69

- Mortality: 6 (were all 48hrs old)

#### Conclusions

- Under 2% deliveries were by C/section under GA
- More of such babies were born out-of-hours
- Less than a tenth had suboptimal cord pH
- Majority of the babies did not require resuscitation
- Later mortality (>48hrs) were only in the extreme preterm (<28 week gestational age) group

## Other / Miscellanea

Experiences with insulin therapy in extremely low birthweight prematures (343)

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### Introduction /Case Report

In Extremely Low Birthweight (ELBW) prematures, especially, if they are also small for gestational age, high blood glucose levels are frequently observed. Since hyperglycaemia is generally associated with metabolic acidosis and critical intracellular metabolism, insulin infusion may reverse the condition without lowering glucose intake. We aimed to examine the efficacy of insulin therapy in the case of our ELBW patients.

### Patients and Methods

We retrospectively analysed the data of our ELBW patients born between 01/01/2012 and 31/12/2014 (n=31), regarding blood glucose levels, standard bicarbonate levels, as well as gestational age, birthweight, clinical parameters and insulin doses and daily total insulin intakes during the first week of life. Survival rate of our ELBW population was compared with the identical Hungarian and European population known from the literature.

### Results

During the examined period 31 ELBW patients were cared (birthweight:  $739\pm 169$  g; gestational age:  $26.0\pm 1.9$  weeks, percentile:  $30.3\pm 28.5$ , mean $\pm$ SD). Insulin therapy was necessary in 24/31 patients. The therapy lasted for  $4.6\pm 10.3$  days, the average highest dose was  $0,081\pm 0,060$  IU/kg/h. We exceeded the recommended dose ( $0,1$  IU/kg/h) in 4 cases, the maximum dose was  $0,3$  IU/kg/h. Compared our SGA patients with non-SGA patients (ELBW prematures with percentiles 0.1 percentile, n=16) there was a significant difference ( $p<0.01$ ) between the birthweight of the two groups, however, there was no difference between the maximal dose of insulin and the duration of insulin therapy. The maximum recommended dose was exceeded in 4 neonates of the SGA group. There was no insulin supplementation in 3/17 prematures of the SGA group and 4/14 patients of the non-SGA group.

### Conclusions

In our practice in ELBW prematures, especially in SGA ELBW prematures insulin therapy was frequently necessary. Perfusion rates higher, than in the recommendations were also applied in selected cases with low insulin sensitivity. This policy may have contributed to higher survival rates in this vulnerable subgroup of neonates

Other / Miscellanea

#### A SEVERE CASE OF MATERNAL-FETAL INCOMPATIBILITY (790)

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#### Introduction /Case Report

Maternal-fetal incompatibility is caused by placental transfer of Immunoglobulin G alloantibodies directed against erythrocyte antigens present on fetal red blood cells (RBC) developed in the course of a previous pregnancy, blood transfusion or transplantation.

These antigens, adsorbed by red blood cells, can lead to abrupt hemolysis in the fetus and the newborn.

We hereby report a case of severe maternal-fetal incompatibility due to anti-c immunization that resulted in severe haemolytic anemia and hyperbilirubinemia requiring 5 exchange transfusion.

#### Case Report

The baby, third child of non-consanguineous parents, was born at 39 weeks gestation by urgent cesarean section because of abnormal cardiotography tracing. The mother was a 38 years old woman with negative history for diseases or blood transfusion, negative antibody profile and A Rh positive blood group.

Immediately after birth, the baby presented respiratory distress, hence we performed withdrawal cord that showed severe anemia and hyperbilirubinemia (Hb 5 g / dl, Bil 8 mg%). Consequently he was ventilated with nasal continuous positive airway pressure (NCPAP). Laboratory evaluation revealed A Rh positive blood group and positive Direct Antiglobulin Test. We repeated maternal antibody screening which showed presence of high titer Rh anti-c antibody and she was typed A Rh D +, C +, E-, c-, and e+.

General medical treatment was administered immediately, including rehydration therapy, high-doses intravenous immunoglobulin, continuous multiple phototherapy and exchange transfusion. Despite these efforts, the infant's condition worsened and the bilirubine level increased (18.08 mg% at 9 hours of life). Therefore we had to perform 4 additional isovolumetric double volume exchange transfusion of irradiated, packed red blood cells reconstituted in fresh frozen plasma. Only after 36 hours, the bilirubin gradually decreased to the normal range, the haemoglobin reached its normal value and DAT became negative.

At 48 hours of life we stopped the non-invasive ventilation and 11 days after birth he was discharged in good conditions.

The child undertook a close clinical and instrumental follow-up (including cerebral ultrasound and MRI) and currently he is in good health with no signs of relapse anemia or neurological impairment.

#### Conclusions

Anti-c is, after anti-D, the most important RBC antibody to cause severe haemolytic disease of fetus and newborn.

Several cohort studies have shown similar postnatal outcome in neonates with severe Rh c and Rh D haemolytic disease and have justified a similar postnatal management<sup>2,3</sup>.

However a single exchange transfusion may not be sufficient to solve these forms, even though timely treatment avoids hematological and neurological sequelae.

Other / Quality improvement and Safety and Error Preventio

## NATIONAL SURVEY OF THE USAGE OF PERCUTANEOUS FEMORAL ARTERIAL AND VENOUS CATHETERISATION IN LEVEL 3 NICU UNITS IN UNITED KINGDOM (180)

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### Introduction /Case Report

Cannulation of the femoral vessels to establish central venous access and invasive arterial access is widely used in Paediatric intensive care units (PICU) but less so in Neonatal intensive care units (NICU). Femoral vessel cannulation in neonates is more difficult and is normally only performed when other forms of access have failed or exhausted. This may in part be because clinicians have concerns about line infection and thromboembolic complications of femoral vessel cannulation.

### Patients and Methods

We performed a questionnaire survey to study the current usage pattern of percutaneous femoral arterial and venous catheterisation in neonates in UK Level-3 NICUs.

### Results

Forty level-3 NICU units responded to the survey. They were completed by 32 consultant neonatologist and 8 Neonatal grid trainees. 16 units are inserting the femoral lines. In 10 units they are inserted by neonatal consultants with specific training or experience in the procedure, in 8 units by the paediatric anaesthetist, in 5 units by PICU consultants and in 1 unit by the paediatric surgeon. 8 units insert the line under ultrasound guidance. 2 units stated that they have minimum weight restriction of 1200g and 1000g When asked the reason for not using the lines, 20 units stated that they have no expertise in performing this procedure, 18 units stated about concerns of ischaemic injury to the leg and 12 units has concerns about risk of infection.

### Conclusions

The main clinical concerns that prevent the more widespread use of this technique are concerns about risk of ischemic injury to the legs and infection. The single main factor that prevents the use of these lines is the absence of expertise in performing the procedure in neonates. Further information about the utility and safety of this procedure in babies would be helpful in allowing neonatologists to make use of this potentially useful means of establishing vascular access.

Other / Miscellanea

## COAGULASE NEGATIVE STAPHYLOCCAL MENINGITIS IN A PRETERM INFANR WITHOUT AN INTRA-VENTRICULAR DEVICE (251)

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### Introduction /Case Report

Coagulase-Negative Staphylococcus (CoNS) is the main cause of late onset neonatal sepsis in very low birth weight (VLBW) infants and accounts for 48% of all gram positive infections (1).It contributes significantly to morbidity and mortality in VLBW neonates.Prolonged NICU stay and use of invasive medical procedures are predisposing factors.CoNS meningitis is uncommon and mainly reported in patients with intra-ventricular devices.When isolated in the central nervous system of a patient without an intra-ventricular device,it is often thought to be a contaminant (2).We present a case of a VLBW neonate with CoNS sepsis and meningitis in the absence of an intra-ventricular device.

### Case Report

AA, a baby girl and first of twins was born in a District General Hospital at 25+3 weeks gestation by emergency caesarian section following cord prolapse. Birth weight was 697 grams and she was born in a relatively stable condition. Following intubation, a dose of surfactant, and intravenous (IV) antibiotics (Benzyl Penicillin and Gentamicin), she was transferred to our tertiary neonatal unit. Within few hours of arrival, she was extubated to Bi-level Positive Airway Pressure (BiPAP). Initial blood cultures were negative. On Day 2, following a rise in C Reactive Protein (CRP) to 27, a second blood culture was sent. IV Cefotaxime was added and IV Gentamicin discontinued. Over the next few days, inflammatory markers improved, second blood culture was reported negative and antibiotics were stopped after 5 days. On Day 6, CRP increased again to 14 and a third blood culture sample was sent. This time, IV Vancomycin and Gentamicin was commenced, umbilical lines removed (and tips sent for culture) and a percutaneous long line inserted. The following day (Day 7), she became clinically unwell with worsening respiratory acidosis and feed intolerance requiring intubation and ventilation. Feeds were discontinued. The third blood culture and the umbilical line tips grew CoNS. It was sensitive to Vancomycin; a seven-day course of Vancomycin was planned and Gentamicin stopped.

However, she continued to deteriorate clinically with worsening respiratory status and features of septic ileus on abdominal x ray. On Day 11, CRP increased further to 36 and platelets dropped to 38. Consequently, a fourth blood culture was sent which also grew CoNS. Vancomycin was now administered through the long line and in view of her clinical deterioration, IV Cefotaxime was restarted.

A lumbar puncture was done on Day 12. Microscopy showed 90 white cells; 95% lymphocytes, 5% polymorphs, 1700 red cells. Cerebro spinal fluid culture showed a pure growth of Staphylococcus Capitis (on two separate plates) that was sensitive to Vancomycin and Rifampicin. Cefotaxime was subsequently discontinued after 5 days.

Following discussion with Microbiologist, Rifampicin was added on Day 16; both antibiotics were given for a total of 21 days. A 5th blood culture sample taken after commencing Rifampicin was reported negative.

Subsequently, her clinical condition improved. Feeds were restarted and a new long line was inserted for ongoing parenteral nutrition. She completed 21 days of antibiotics and repeated blood cultures remained

negative. She established full feeds and was eventually transferred back to the District General Hospital for continuing care.

### Conclusions

CoNS infection is commonly attributed to the presence of central venous catheters and ventriculo-peritoneal shunts. Although commonly isolated from blood, it is rarely grown from cerebrospinal fluid. It is treated with Vancomycin, a glycopeptide antibiotic with good bactericidal activity. However, some infants remain unwell as in the case of our patient. Rifampicin as an adjunctive therapy has proved to be successful (7). It certainly did in our patient!

Other / Organization of perinatal care

USING NORMALIZATION PROCESS THEORY TO IMPROVE THE TRANSLATION OF EVIDENCE BASED PRACTICE INTO ROUTINE NEONATAL NUTRITIONAL CARE (698)

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### Introduction /Case Report

Many evidence-based practices fail to become part of routine care due to a failure of translation from published research or guidance into practice. Normalization Process Theory (NPT), a novel sociological framework which focusses on how people work to make a new practice become embedded in routine care, offers a way better understand this process. NPT has four constructs; coherence, cognitive participation, collective action and reflexive monitoring. As part of a larger study, we used NPT to develop, measure, and guide the implementation of complex intervention to improve the nutritional care of preterm infants in neonatal intensive care.

### Patients and Methods

We developed and implemented a practice-based, evidence based complex intervention for the nutritional care of preterm infants (<1500g or <30 weeks gestation at birth), including nutrition guidelines, a screening tool for nutritional risk, and multidisciplinary ward round. The intervention was implemented during 2012, with the implementation process informed by staff focus groups and application of NPT. Serial audits of guideline compliance carried out to measure the extent to which the new practice were being carried out. In parallel, the extent to which the new practices were being embedded into routine care was assessed with a bimonthly staff questionnaire based on NPT. The relationship between NPT and audit scores was analysed using linear regression modelling (Stata 12.1).

### Results

During the intervention period, NPT scores were used to identify areas where staff felt the implementation of intervention was lacking, allowing these to be addressed in a dynamic way during the study. In particular, the NPT construct of reflexive monitoring scored poorly, suggesting that initially staff failed to see the benefit of the new practices in their daily work. This was addressed by displaying preliminary results around the neonatal unit, resulting in improved guideline compliance and NPT scores. Mean audit guideline compliance and NPT scores both increased in a linear fashion over time, ( $r=0.86$  and  $0.15$ ,  $p=0.028$  and  $0.023$  respectively). There was also a significant linear association between the mean audit scores and the mean NPT scores during the implementation period ( $r=0.22$ ,  $p<0.002$ ).

## Conclusions

Using NPT to guide the implementation process appears to have led to improved guideline compliance and better embedding of the new practices into routine care over time. These findings demonstrate that measures of practice change using NPT can be related to real measures of clinical practice, suggesting that NPT offers an effective way of implementing and monitoring the introduction of new practices.

COOLING PRETERM INFANTS: IS RDS A SIGNIFICANT RISK? (839)

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Introduction /Case Report

Recently an increasing number of asphyxiated newborn infants have been cooled outside the standard criteria. Many centres offer therapeutic hypothermia for late preterm infants based on case by case consideration. The effect of hypothermia on the clinical severity of RDS in this population remains uncertain. Our aim was to present observational data regarding ventilatory support requirements in our preterm cooled patients.

Patients and Methods

We have retrospectively reviewed patients' records at the level III NICU of the 1st Department of Paediatrics at Semmelweis University, Budapest, Hungary. 23 preterm infants were identified who received therapeutic hypothermia (33-34 °C) for severe birth asphyxia based on the attending neonatologist's decision and verbal parental consent. In our cohort all cooled infants were intubated and managed on mechanical ventilation irrespective of lung pathology as per local protocol, therefore surfactant administration was based on oxygen requirements. 3 preterm infants had multi-organ failure and died within 36 hours of age, their further data were excluded from analysis. Descriptive statistical methods were used and non-normally distributed data were presented as median (min-max) values.

Results

9 cooled babies were moderately preterm (32-33 weeks, birth weight 1990 [1240-2500] g) and 14 late preterm (34-35 weeks, birth weight 2365 [1750-2730] g). All 23 were ex utero transfers, only 3 received antenatal steroids. Cooling was started at 2 (1-7) hours following a severe hypoxic-ischemic insult (initial pH 6.85 [<6.5-7.16]). 8/23 (6/9 moderately and 2/14 late) preterm infants received surfactant for RDS (138 [66-270] mg/kg Curosurf) and 1 underwent surfactant lavage for MAS. 1/8 received surfactant prophylactically on FiO<sub>2</sub> 21%, 7/8 however required rescue surfactant on 90 (65-100) % FiO<sub>2</sub>. 6 surviving babies with RDS reached and remained on FiO<sub>2</sub> 21% 1.5 (1-8) hours after surfactant administration, only one required a repeated dose of surfactant. 18/23 preterm infants survived, they were extubated on day 5 (3-25) of life and needed 7.5 (4-28) days of overall ventilatory support.

Conclusions

In our cohort RDS was common amongst asphyxiated preterm infants (32-35 weeks of gestation), however responded well to surfactant treatment. The clinical improvement observed after surfactant administration lasted throughout the entire cooling. Further studies are needed to evaluate the safety and effectiveness of therapeutic hypothermia in asphyxiated preterm infants.

Other / Quality improvement and Safety and Error Preventio

## EFFECT OF THERAPEUTIC TOUCH ON MORTALITY RATE AND VENOUS BLOOD GASES IN PREMATURE INFANTS WITH RESPIRATORY DISTRESS SYNDROME (123)

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### Introduction /Case Report

Therapeutic touch (TT) was developed recently by nurses is an attempt to bring a more humane and also a holistic approach to their practice. TT continues to be practiced in neonatal intensive care units

### Patients and Methods

Design of this study was a randomized clinical trial with intervention and control groups. There were 22 subjects in intervention group and 28 subjects in control group. Data collection approaches were: questionnaires and biological measures (VBG). Two questionnaires were used: subject selected questionnaire and demographic data questionnaire. VBG were obtained at baseline immediately at birth and first, second and third day after birth. Subjects in the intervention group received TT by a trained TT practitioner when they were in incubator with oxygen therapy. Duration and frequency of TT intervention were determined by this practitioner while assessing the quality of energy flow by scanning during second phase of TT.

### Results

There were no significant differences between two in extraneous variables. Chi square showed Mortality rate of subjects in intervention group decreased significantly in compared to control group ( $p=0.006$ ). Repeated measurements showed  $po_2$ , PH and  $pco_2$  increased in intervention group compared to control group but they were not significant ( $p>0.05$ ).  $Pso_2$  was increased significantly in intervention group. Compared to control group ( $p=0.002$ ).

### Conclusions

Therapeutic Touch attempts to bring a more humane and holistic approach to nursing practice and other medical services.

Keywords: Therapeutic touch- RDS- Prematurity

Other

## MALIGN INFANTIL OSTEOPETROSIS: A RARE CASE OF NEWBORN (784)

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### Introduction /Case Report

Osteopetrosis is a rare (1/100.000 – 1/250.000), inherited disease which causes pervasive osteosclerosis due to disruption of osteoclastic activity. Autosomal recessive form is known as malignant infantile osteopetrosis and it presents with signs of impaction on optic, oculomotor and auditory nerve depending on restriction of bone foramina in the first months of life, hydrocephalus, insufficiency and extramedullary hematopoiesis depending on sclerosis in bone marrow. Here, a preterm newborn with malignant infantile osteopetrosis, is presented.

### Case Report

A female infant, who has been born by vaginal birth at 35 weeks of gestation, was hospitalized at neonatal unit due to lack of ingestion. It was learned that mother and father are relatives and the mother's sibling had lost two infants. One of them was at 45 days of life and the other was at 3 months of life. On physical examination, coarse face, large forehead, periorbital ecchymosis, 1/6 systolic murmur on mesocardiac area, hepatomegaly (5 cm), splenomegaly (3 cm), weakness of newborn reflexes, and normal fundoscopic examination were detected. Laboratory findings were as follows: bicytopenia (Hb 7,6 g/dL, trombocyte 47.000 K/uL), direct hyperbilirubinemia (5.07 mg/dL). Secundum atrial septal defect on echocardiography and pervasive increased density were detected all over the costae, vertebrae and periorbital area. Electrolytes, liver, kidney functions' tests, bleeding profile, the levels of vitamin B12, folic acid, and ferritin, chromosome analysis (46 XX), bilateral hearing test were normal. Direct Coombs, TORCH serology were negative. Bone marrow was hypocellular and homogenous. 76% myeloid, 22% lymphoid, 2% erythroid series cells were detected; blast, storage cell, megakaryocyte, leucoerythroblastosis were not found. The patient was diagnosed osteopetrosis Hypocalcemia, hypophosphatemia, hypomagnesemia were developed at 12 days of life and serum level of 25-OH D vitamin was 18 ng/mL (35–55 ng/mL), parathormon was 162 pg/mL (15–65 pg/mL). Oral calcium, vitamin D, intravenous potassium phosphate, magnesium and calcitriol (0.04mcg/kg/day) was applied; the patient was supported with erythrocyte and trombocyte suspensions. No convulsion was observed during her clinical follow-up. However, left humerus and radius proximal shaft fractures were developed. Adequate donor (10/10 tissue match) was found and the patient was referred for bone marrow transplantation to Department of Pediatric Hematology of Hacettepe University. Homozygous single nucleotide mutation on gene of CLCN7 (g.21558C>T) and neurological involvement in cranial MRI were detected and it was thought that the patient diagnosed with neuropathic form of osteopetrosis will not have been benefited from bone marrow transplantation.

## Conclusions

Osteopetrosis should be considered to differential diagnosis of newborns that have bicytopenia, hepatosplenomegaly, direct hyperbilirubinemia, hypocalcemia and increased density in the bone radiographs and these patients should be early guided to centers to performed bone marrow transplantation.

Brain & Development / Placenta and prenatal factors

## RELATIONSHIP OF PERINATAL FACTORS AND PVL IN PRETERM INFANTS (637)

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### Introduction /Case Report

Periventricular leukomalacia (PVL) is one of the most severe complications in very low birth weight infants (VLBW). The aim of this study is to evaluate the relationship of maternal factors and PVL in preterm infants.

### Patients and Methods

We retrospectively reviewed the medical records of 162 preterm infants (<1,500g or < 32 weeks gestational age) admitted to the neonatal intensive care unit at our hospital from January 2009 to December 2014. We excluded IUGR, congenital anomaly and patients were transferred from another hospital after birth. They were divided into PVL group (18) and non-PVL group (144). PVL was diagnosed by brain MRI.

### Results

Mean gestational age of PVL group and non-PVL group were 28.2 and 28.4 weeks GA and mean birth weight of both groups were 1091.1g and 1136.7g. According to analysis of maternal factors, preterm labor and PROM in causes of preterm birth were similar incidences in both groups. But incompetent internal os of cervix was significantly lower incidences and fetal distress was significantly more in PVL group. Magnesium sulfate known as having effect for neuroprotection was not different in both groups. The operation cases were more in PVL group but not significant.

### Conclusions

In this study, we knew that fetal distress of causes of preterm birth was relation to PVL in preterm infants.

## Brain & Development / Neurodevelopmental Outcome

NEURODEVELOPMENTAL OUTCOMES FOR EXTREMELY-LOW-BIRTH WEIGHT INFANTS WITH SURGICAL NECROTISING ENTEROCOLITIS OR SPONTANEOUS INTESTINAL PERFORATION COMPARING PRIMARY INTERVENTION WITH PERITONEAL DRAIN OR LAPAROTOMY: A SYSTEMATIC REVIEW. (880)

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## Introduction /Case Report

Necrotising enterocolitis (NEC) and spontaneous intestinal perforation (SIP) are associated with significant morbidity and mortality in extremely-low-birth weight (ELBW) infants. Primary surgical interventions for NEC and SIP include peritoneal drainage (PD) or laparotomy (Lap) with excision of necrotic bowel. PD and Lap have a similar risk of mortality in the short-term, however it is unknown whether these interventions impact the high risk of long-term neurodevelopmental impairment (NDI) observed in ELBW survivors of NEC and SIP. The aim of this systematic review was to assess the risk of NDI for ELBW infants with NEC and SIP comparing primary intervention with PD or Lap.

## Patients and Methods

Databases (EMBASE, PubMed, CENTRAL and Cochrane Reviews) were independently searched by the two authors. No language restriction was applied. Studies were assessed for eligibility based on pre-defined selection criteria. Primary outcomes of interest were NDI or death at  $\geq 12$  months' corrected age (CA) and NDI at  $\geq 12$  months' CA, where NDI was defined as  $\geq 1$  of developmental delay, cerebral palsy, cognitive impairment, deafness or blindness. The Cochrane Handbook for Systematic Reviews of Interventions guided this review.

## Results

Search returned 74 citations. Abstracts of 43 studies assessed for eligibility. Article and reference list reviewed for 9 studies. One study (a multi-centre, prospective cohort study of 156 infants) met inclusion criteria. Primary outcomes reported. At 18-22 months' CA, 48 (68%) infants who received primary treatment with Lap had NDI or died compared to 64 (84%) infants treated with PD (unadjusted OR 0.39; 95% CI 0.18–0.86;  $p=0.02$ ). Although favouring Lap, this result was not significant after adjusting for potential confounders (adjusted OR 0.44; 95% CI 0.16–1.2) or in a restricted cohort that excluded infants considered by their treating physicians to be too unwell to undergo Lap (restricted cohort OR 0.56; 95% CI 0.19–1.69). At 18-22 months' CA, 14 (40%) surviving infants who received primary treatment with Lap had NDI compared to 20 (56%) infants treated with PD (OR not reported).

## Conclusions

This systematic review demonstrates a paucity of evidence with respect to long-term neurodevelopmental outcomes to recommend primary intervention for ELBW infants with NEC or SIP. Further research that addresses this important question is needed.

Other

Respiratory Alkalosis in a Lethargic Newborn: Measure Ammonia! (455)

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### Introduction /Case Report

Urea cycle disorders (UCD's) are caused by genetic mutations resulting in a deficiency of one of the six enzymes involved in the cycle. This deficiency may result in hyperammonaemia which is toxic to the brain and can result in significant morbidity and mortality. Early recognition and treatment is essential to prevent devastating neurological sequelae. We present a case of neonatal hyperammonaemia that was promptly recognised and treated, with a good clinical outcome to date.

### Case Report

A 4 day old full-term breastfed female infant, born to non-consanguineous parents, presented with lethargy, poor feeding and abnormal cyclical movement of the limbs. There was a maternal history of 3 spontaneous abortions and one neonatal death, due to sepsis. The presenting infant had a full evaluation for sepsis and was commenced on triple antibiotics. She was self-ventilating in room air and initial venous blood gas revealed a respiratory alkalosis with pH of 7.515 and PCO<sub>2</sub> of 3.42 kPa. Urea was 1.6 mmol/L. Preliminary results from cerebrospinal fluid and blood cultures were negative for infection. The clinical condition of the infant failed to improve. A second venous blood gas in room air revealed worsening respiratory alkalosis with a pH of 7.64 and pCO<sub>2</sub> 1.69 kPa. Hyperammonaemia as a cause of the worsening respiratory alkalosis and clinical condition was suspected. Serum Ammonia was 281 µmol/L. The infant was transferred to a paediatric intensive care unit for further management and was commenced on intravenous Arginine and ammonia scavenging drugs. Serum amino acids confirmed a diagnosis of Argininosuccinic acid Lyase deficiency, a urea cycle disorder. Serum ammonia normalised within 4 hours of commencing treatment, less than twenty four hours after her initial presentation. Her clinical condition improved rapidly. Protein was slowly reintroduced under the guidance of the metabolic team. The infant is now established on a feeding regime with three breast feeds daily, essential amino acids and a protein free infant formula to appetite. She remains clinically well with normal development at eight weeks of age.

### Conclusions

Respiratory alkalosis in a self-ventilating neonate presenting with lethargy and poor feeding is an indicator of a likely urea cycle disorder, as it is an uncommon finding due to other causes. Low urea in a poorly feeding infant, and a family history of neonatal death following a similar presentation with lethargy, are further clues to the diagnosis in this case. Ammonia should be checked in all neonates presenting with lethargy and poor feeding.

## Other / Medical Education and Training

### ENSURING QUALITY IN NEONATAL NURSING (362)

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#### Introduction /Case Report

The need for expert competence in neonatal nursing is profound. The purpose of the post graduate education in Neonatal nursing is to contribute to a higher quality health care service and patient safety.

The postgraduate program has a total of 60 ECTS, and has a clinical profile, which is reflected in the student learning outcomes, teaching methods and assessments. Lovisenberg Diaconal University Collage collaborates with clinicians and researcher in university hospitals. Students acquire knowledge about premature, neonates and newborns requiring medical attention and care and acute critically ill children in the age group 0-3 months as well as their parents, siblings and close relatives.

#### Patients and Methods

Through theoretical and clinical training the students develop clinical skills for observation and assessment, as well as advanced performance in neonatal nursing for premature and ill newborns and their families. Students also develop the ability to recognize pathophysiological processes, identify effects and side effects of various types of drugs and fluids, and use advanced medical equipment, while the child's basic physical and psychological needs for growth and development are safeguarded. In addition, the ethical and legal principles for neonatal nurse's role and responsibilities are emphasized.

Students develop skills in collaboration, organization and professional management and competencies in promoting evidence-based practice.

#### Results

##### Learning outcomes:

##### Knowledge

Demonstrate advanced knowledge in nursing and disease processes and reactions due to different conditions and diagnoses and additional

basic physical and psychological needs for the growth and development of neonates and infants.

Demonstrate advanced understanding of the needs, reactions and coping strategies of parents, siblings and close relatives.

##### Professional skills

Perform comprehensive neonatal nursing and delegated medical treatment for premature newborns and newborns requiring medical attention and care and acute critically ill children in an independent, responsible and caring manner.

##### Proficiency

Practice neonatal nursing in accordance with ethical guidelines. Lead, coordinate and ensure patient care both in their own unit, and with affiliated health care services. Contribute to research and participate in innovative processes.

#### Conclusions

Preterm and sick newborn have a need for competent neonatal nurses to ensure their needs. This post-graduate education meet the important needs of the premature and sick newborn and their families.

The students undergo theoretical and clinical training to achieve in depth knowledge, professional skills and high proficiency.

## Brain & Development / Neurodevelopmental Outcome

### AMINOACYLASE 1 DEFICIENCY - CASE REPORT OF A NEWBORN WITH REFRACTORY SEIZURES (821)

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#### Introduction /Case Report

Aminoacylase 1 (ACY1) enzyme is involved in the cytoplasmic degradation of N-acetylated proteins by hydrolyzing N-acetyl amino acids into the free amino acid and acetic acid. Deficiency of ACY1 is a rare autosomal recessive disease diagnosed by accumulation of N-acetylated amino acids in urine. It has been recently discovered in children, presenting with heterogeneous neurological symptoms such as psychomotor delay, seizures and intellectual disability.

#### Case Report

Our patient was the second child of non-consanguineous parents. A spontaneous rupture of membranes complicated pregnancy at 24 weeks of gestation. He was born at 26 weeks of gestation by elective caesarian section due to oligohydramnios and suspected chorioamnionitis. His physical examination was unremarkable except for a microcephaly (PT (p.R353C) in exon 14 and a novel mutation c.689G>A (p.R230Q) in exon 10.

After clinical stabilization he was gradually weaned off of midazolam and clonazepam. He was discharged home with 3 months and 22 days under maintenance dose of phenobarbital, exhibiting a mild global hypertonia. On follow-up he remained without seizures, with normal EEG and was weaned of Phenobarbital, keeping clinically stable.

The patient has currently nineteen months and his growth in weight, length and his head circumference are appropriate. He has no development delay and has a normal neurologic examination.

#### Conclusions

We report the first Portuguese case of ACY1 deficiency, presented in an extremely premature newborn. The diagnosis was not straightforward, as his MRI could have explained his initial symptoms. ACY1 deficiency is a rare condition, nevertheless, it should be considered in a newborn with epileptic encephalopathy. Genotype-phenotype correlation remains uncertain, which might explain our patient's good prognosis. More cases should be published.

Other / Involvement of parents in care

Ginkgo extract improved vasospasm and gangrene change of digits after arterial intervention (484)

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### Introduction /Case Report

Vasospasm and gangrene change of digits was an uncommon but severe complication at neonatal intensive care unit (NICU). Arterial line placement and inotropic agent infusion is the major risk factor for the gangrene change and vasospasm of digits in extremely low birth weight (ELBW) neonates. Ginkgo, a ancient herbs, was indicated in treatment for dementia, circulatory disorders and tinnitus which improve blood flow and reduces red blood cell aggregation and blood viscosity in humans. We expect to use Ginkgo to improve the outcome after vasospasm and gangrene change of digits occur from our case series and review of the literature

### Case Report

This is a observational case series study from 2006 to 2007. We collected 4 premature infants with vasospasm or gangrene change of digits after arterial puncture or arterial line placement or inotropic agent infusion and use topical gauze packing with Ginkgo extract solution. Case 1 showed a premature infants born with gestational age 29+5 weeks and birth body weight 865 gm received Dopamine for hypotension after birth. Vasospasm with pale change of left forearm was noted on day 2. We used Ginkgo extract solution with gauze packing (concentration: 0.08 mg/ml) on left forearm. Vasospasm and pale change of left forearm improved after 3 hours of Ginkgo extract gauze packing. Case 2 showed a premature infants born with gestational age 26+3 weeks and birth body weight 990 gm received Dopamine for hypotension after birth. Vasospasm with pale change of left forearm was noted on day 2 like case 1. After 3 hours and 10 minutes of Ginkgo extract gauze packing (concentration: 0.08 mg/ml), the vasospasm improved and pale change of left forearm recovered. Case 3 showed a premature infants born with gestational age 24 weeks and birth body weight 785 gm received arterial line placement after birth. Acro-cyanosis occurred on 2nd-4th fingers of right hand and 2nd-3rd fingers of left hand on day 12. We used Ginkgo extract solution with gauze packing (concentration: 1.1 mg/ml), however, gangrene change occurred on day 19. The case expired due to renal failure on day 31. Case 4 showed a premature infants born with gestational age 26+4 weeks and birth body weight 930 gm received arterial line placement after birth. Acro-cyanosis occurred on 2nd-5th fingers of right hand on day 1. Ginkgo extract solution with gauze packing was used and concentration was titrated according to the recovery status of right hand. Initial concentration was 0.5 mg/ml and titrated gradually to maximal concentration of 2 mg/ml. After Ginkgo extract gauze packing for 24 days, the acro-cyanosis of right hand improved.

### Conclusions

Our case series indicates that Ginkgo extract solution with gauze packing exerts its effect to improve the outcome of the gangrene change of digits. The mechanism needs to be clarified and its influence on

prostaglandin metabolism, antagonism of platelet aggregating factor, and free radical scavenging might play a role. The optimal concentration of Gingko extract solution is unknown. Further clinical studies should be encouraged

Table

**Table 1. Demographic data & results of Gingko Tx**

No.	Sex	GA (Wks)	BW (gm)	Onset (day)	Risk #	Signs	Gingko conc. (mg/ml; duration) / Results
1*	M	29+5	865	2	D	Pale, left forearm	0.08(3h) / Recovery
2	F	26+3	990	2	D	Pale, left forearm	0.08(3h10m) / Recovery
3 <sup>†</sup>	M	24	785	12	A	Acro-cyanosis R/L hand(2-4th/ 2-3rd fingers)	1.1(19d) / Gangrene
4	M	26+4	930	1	A	Acro-cyanosis R Hand (2nd- 5th fingers)	0.5(D0-2)→1 (D2-4) →1.5(D4-5)→2 (D5- 16)→1(D16-24) / Recovery

\*46,XY,del(9)(p24); expired at 14d/o; <sup>†</sup> Renal failure, expired at 31d/o

# D: Dopamine, A: A-line

Picture



**960730 (Day1)**

**960803 (Day5)**

**960813 (Day15)**

Circulation, O<sub>2</sub> Transport and Haematology / Placenta and prenatal factors

The risk factors for the extreme prematurity (642)

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### Introduction /Case Report

The incidence of the prematurity is 8-10% and can reach up to 25%, in developing countries.

The risk factors involved in the etiology of the premature births are general maternal factors, local factors and socioeconomical and environmental.

### Patients and Methods

The group study consists of 42 infants weighing less than 1000 g (representing 8.6% of all premature babies) treated in Maternity Bega, during 01.01.2012-31.12.2013.

### Results

The prematurity risk factors identified in the study are: HTAI (19%), HELLP syndrome (19%), placenta praevia (11.9%), premature detachment of normally inserted placenta (11.9%), transverse presentation (15.5%), gemelarity (9.5%), premature ruptured membranes and early (4.7%), personal history of abortions (52%), age over 35 years (9.5%), pregnancy with twins (2.3%), metrorrhagia (11.9%), anemia pregnant (40%), chronic viral hepatitis (2.2%), cervical cerclage (9.5%), maternal heart malformation with pulmonary embolism (2.2%), stroke, cerebral aneurysm substance and coma (2.2%), short interval between pregnancies (14.2%), circular umbilical cord (16.6%), umbilical cord prolapsing (4.7%), intraamniotically infections (54.7%), isoimmunization in Rh system (16.6%), origin (rural 54, 7%; urban, 45.3%), socio-economical situation (38%), smoking (21.4%).

### Conclusions

The intraamniotically infections are a fundamental risk factor for the extreme prematurity. Birth by cesarean births represent 42.8% of the total, while natural birth is found in 57.2%.

### Introduction /Case Report

Therapeutic hypothermia is the standard treatment after hypoxic-ischemic (HI) brain injury. However, pre-clinical studies testing hypothermia (HT) demonstrate inconsistent effects which might be due to different treatment regimes and species differences. Only few studies were performed in mice thereby revealing rather low efficacy. Another important potential pitfall is that HT is supposed to delay pathological processes without inhibiting the progression of injury and thereby not providing long term neuroprotection. Therefore, we tested different modes of HT and evaluated sub-acute brain injury as well as long lasting functional outcome.

### Patients and Methods

9-days-old C57BL/6 mice were subjected to either sham surgery or underwent ligation of the right common carotid artery followed by hypoxia (10%) for one hour. HI mice were randomly assigned to normothermia (Rectal 35.5°C) and hypothermia (Rectal 32.5°C) for 4 hours starting either immediately or 2 hours after HI. Body temperature was controlled with a rectal probe connected to a digital thermometer. 7 days post HI brains were analysed for regional tissue injury. Three weeks after HI motor coordination and spontaneous anxiety / exploration behaviour were evaluated using the Rota Rod and the Elevated Plus Maze.

### Results

Neuropathological assessment of brain tissue sections revealed that delayed hypothermia does not modulate sub-acute brain injury whereas immediate hypothermia leads to a significant reduction of brain tissue injury in the hippocampus. However, other brain regions were not protected by both treatment regimes. In agreement with unaltered histological signs of brain injury delayed hypothermia failed to induce long-lasting protection from the development of HI-induced functional deficits whereas immediate hypothermia resulted in a reduction of motoric deficits. Nonetheless, exploratory activity of HI mice was modulated neither by delayed nor by immediate HT.

### Conclusions

Our data provide evidence that hypothermia mediates only moderate neuroprotection when started immediately after HI whereas neither brain tissue injury nor functional outcome could be improved by a delayed onset of cooling. Further evaluation of therapeutic approaches combining other potential neuroprotective or neuroregenerative therapies with therapeutic cooling after neonatal HI brain injury is urgently needed.

Nutrition and gastroenterology / Nutrition of the Very Preterm

IMMATURE SYSTEMIC IMMUNITY DURING THE FIRST TWO WEEKS OF LIFE IN PRETERM PIGS (146)

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### Introduction /Case Report

Immature systemic and mucosal immunity predispose preterm infants and preterm pigs to infections and necrotizing enterocolitis (NEC) during the first weeks of life. Correspondingly, antibiotics are commonly used to prevent or treat these conditions. By many clinical variables, preterm pigs delivered at 90% gestation can be considered similar to infants born at 70-75% gestation. We used this clinically-relevant pig model to better characterize how and when key components of the systemic immune system develop postnatally.

### Patients and Methods

Preterm pigs were delivered by caesarean section (n = 34, 90% gestation) and gradually transitioned from parenteral nutrition to enteral nutrition with bovine milk. Maternal plasma (20 mL/kg) was provided at birth as passive immunity, and antibiotics (intramuscular enrofloxacin and oral gentamicin) were given if required according to clinical symptoms of infections, sepsis or severe diarrhea. Venous blood was collected at birth and during week 1, 2, 3 and 4 for cell counting, analysis of plasma C-reactive protein (CRP), and various blood assays including analyses of NK cells (CD172a- CD16+ lymphocytes), progenitor cells, immature (CD172a+ 6D10+ 2B2-) and mature neutrophils (CD172a+ 6D10+ 2B2+), phagocytosis capacity against E.coli, and cytokine responses to TLR and NOD agonists.

### Results

Preterm pigs showed poor growth and some diarrhea throughout the experiment. Antibiotics were used for 5-7 days but no pigs developed NEC. Newborn preterm pigs had low leukocytes vs. term and adult pigs (0.5 vs. 3.0-5.0×10<sup>9</sup> neutrophils/L, P<0.001), and marginal cytokine responses to TLR1/2/5/7, and NOD1/2 agonists. The postnatal systemic immunity gradually matured by increasing number (5-10 fold) and phagocytic capacity (2 fold) of neutrophils and monocytes, and numbers of NK cells, immature and mature neutrophils at week 2-4 (P<0.05). At week 3-4, the ratio of immature to total neutrophils was greater than 0.2, the cut-off value for suspected sepsis although CRP levels remained low (<10 mg/L). TLR2/4 agonist-induced IL-6 and TNF-α secretion elevated at week 2 with no increase thereafter. Neutrophil counts at week 2 (7×10<sup>9</sup>/L) were close to those obtained from term pigs at birth.

### Conclusions

Systemic immunity is immature in newborn preterm pigs but reaches a degree of maturity that is similar to that in newborn term pigs within 2 weeks. This immune immaturity may result in a pro-inflammatory state,

slow growth and need for antibiotics, reflecting short term postnatal conditions in preterm infants. The results underline the importance of optimal hygiene and protective milk diets (e.g. mother's milk) to avoid excessive antibiotics use during the first postnatal weeks.

Nutrition and gastroenterology / Nutrition of the Very Preterm

POSTNATAL GROWTH RATE IN PRETERM INFANTS HOSPITALIZED IN NICU (398)

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#### Introduction /Case Report

The aim of this study was to interpret postnatal growth rate of preterm infants, in dependency of gestational age, condition at the birth, initiation of enteral feeding, respiratory support, duration of parenteral nutrition and types of enteral feeding (mother milk with fortification or preterm formula).

#### Patients and Methods

Postnatal growth was analyzed in 100 preterm infants hospitalized in NICU: GW7 days (168 hours) and were free of major congenital anomalies. Standard statistical methods were used.

#### Results

Average time of achieving full enteral feeding in infants <28GW was 25,0 days; in infants 29-32 weeks 12,0 days; and in infants 33-36 GW 11,0 days. At time of discharge 26,7% infants with GA <28 weeks had body weight <10p. APGAR score and duration of respiratory support are shown to be statistically associated with postnatal growth rate at 14. and 28. day after birth. In infants with initiation of enteral feeding within first 3 days, body weight was statistically higher at 14. day, 28. day and at discharge comparing with infants with initiation of enteral feeding after 3 days. In infants with less tolerance of enteral feeding, including NEC, body weight at 14. day was significantly lower ( $p<0,05$ ) at 28. day ( $p<0,05$ ) and at discharge ( $p<0,01$ ). Infants fed with mother milk with fortification had higher body weight at time of discharge ( $p<0,01$ ) comparing with formula fed infants.

#### Conclusions

Postnatal growth rate of preterm infants depends not only of conditions affecting growth but also nutritional management practice. Achieving optimal postnatal growth rate is very important, since it improves long term outcome of preterm infants.

## Nutrition and gastroenterology / Nutrition of the Very Preterm

Influence of global and nutritional care on head growth at 36 weeks postconceptional age in extremely low birth weight infants (422)

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### Introduction /Case Report

Postnatal nutritional and growth deficit is a concern in extremely low birth weight (ELBW) infants. Extra-uterine growth restriction has been associated with later morbidities, and suboptimal head size is an independent risk factor of impaired neurodevelopmental outcome. Growth deficit can be reduced depending on practices in each neonatal unit. Postnatal growth of ELBW infants was compared in two European neonatal intensive care units to assess the influence of neonatal care and nutritional protocols on growth.

### Patients and Methods

Infants born before 28 weeks with a birth weight below 1000g, staying more than 7 weeks in neonatal unit were included in a retrospective study comparing postnatal growth in ELBW infants admitted in centers A or B. There were differences in care (more individualized developmental care, less weight monitoring, higher energy and protein targets in center B). Weight, crown-to-heel length and head circumference were collected from birth to discharge. We calculated standard deviation z-score and delta z-scores from birth to 36 weeks, using Olsen's reference values. Major morbidities were documented and we calculated a composite index of severe morbidity. Data was collected by the same person (EB). We used non parametric tests (Wilcoxon or Fisher) to compare growth parameters in the 2 centers.

### Results

Between January and December 2012, 71 infants were included. More infants in center A received insulin (89% vs. 8%,  $p < 0.001$ ) and postnatal steroids (35% vs. 8%,  $p = 0.028$ ). Severe morbidity index did not differ. The prevalence of necrotizing enterocolitis was similar, but less infants needed abdominal surgery (8.7% vs. 28%,  $p = 0.043$ ) in center A. Median hospital stay was similar in both groups (87 vs. 85 days,  $p = 0.389$ ). At discharge, median body weight (2.99 vs. 2.39 kg,  $p = 0.011$ ), and head circumference (34.7 vs. 34.2 cm,  $p = 0.001$ ), but not crown-to-heel length (46.5 vs. 44.0 cm,  $p = 0.104$ ) were higher in center A than in center B. Median loss in z-score from birth to 36 weeks was significantly lower in center A for body weight (delta z-score: -0.3 vs -1.0,  $p = 0.002$ ), and for head circumference (delta z-score: -0.3 vs -1.1,  $p = 0.002$ ). There was no difference for length ( $p = 0.891$ ).

### Conclusions

Careful assessment of postnatal evolution and growth in ELBW infants showed that in-hospital growth restriction was reduced in center A, despite an increased use of postnatal steroids. These differences could

be related to differences in nutritional care and daily growth monitoring. It suggests that the nutritional care could help to compensate for difference in neonatal practices to support efficient postnatal growth.

## Nutrition and gastroenterology / Necrotising Enterocolitis

Necrotising enterocolitis in term and near-term infants – risk factors, radiologic features and outcome (657)

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### Introduction /Case Report

Necrotising enterocolitis (NEC) is the most common gastrointestinal emergency in very preterm neonates. Nonetheless, NEC occasionally affects more mature or even term infants. The pathophysiology of NEC in these babies is unclear, although several risk factors have been described. We have retrospectively analysed a cohort of 45 neonates born at 35 weeks gestation or later who were treated for NEC in a single centre over five year period and reviewed risk factors, clinical and radiological findings, and surgical outcome.

### Patients and Methods

The median gestational age of our cohort was 38.14 weeks (range 35 – 41.43 weeks). Maternal risk factors included diabetes during pregnancy, pre-eclampsia, clinical chorioamnionitis and vasoactive drug abuse. Fetal and neonatal risk factors were small for gestational age (defined by a birth weight <5th centile), birth depression (5 minute APGAR score <7), sepsis and congenital anomalies of the heart and the intestine. In terms of disease development and management, we considered clinical signs and symptoms, radiological findings and surgical management.

### Results

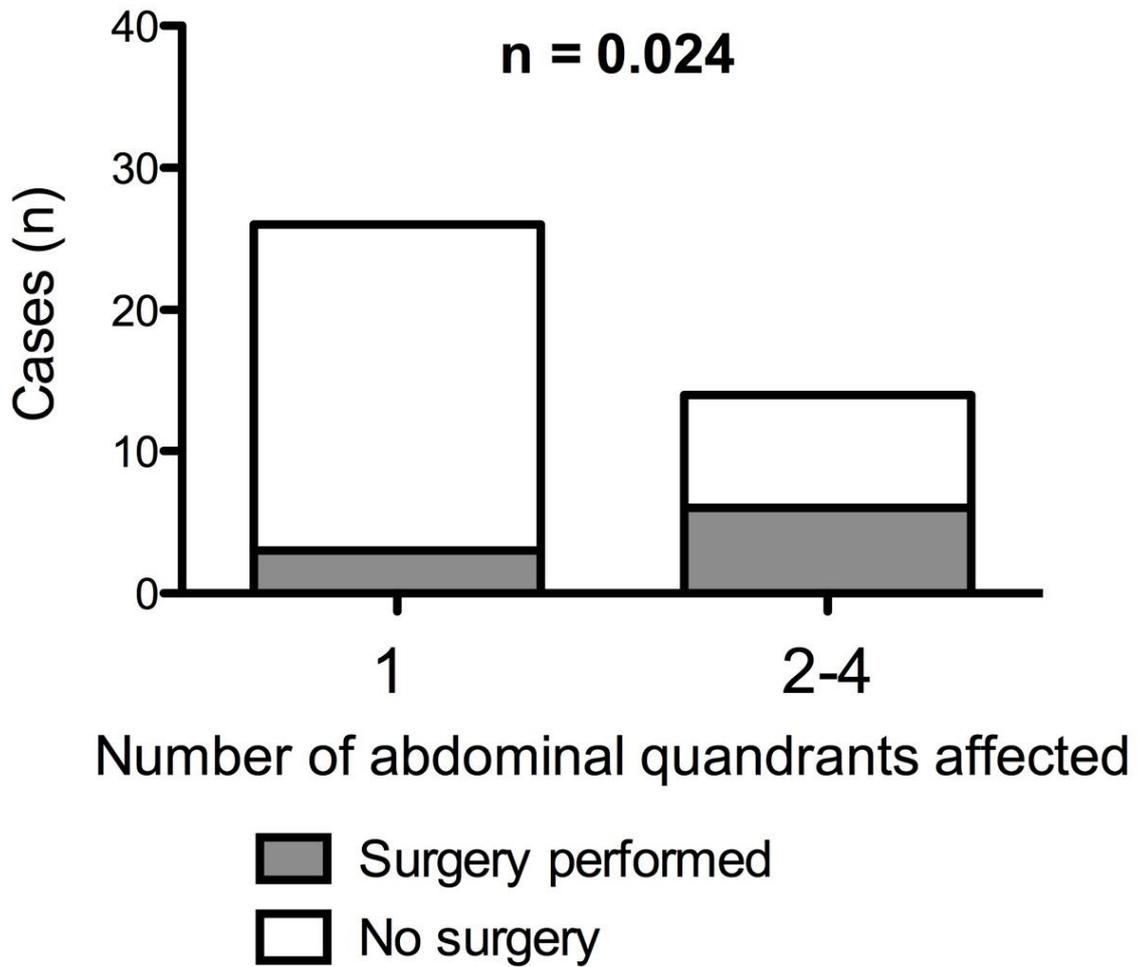
Most babies had at least one risk factor for NEC. 14 infants (31.1%) had maternal risk factors, 9 (20%) were small for gestational age, and 18 (40%) had congenital anomalies. Only 2 (4.4%) of the infants had no risk factors. 33 children (75%) were on some feeds and developed the disease at a median age of 4 days, after a median of 2.5 days nutrition, while 25% developed the disease while nil by mouth. Abdominal distension occurred in 60%, bilious vomiting in 60% and bloody stool in 11% of the infants. Pneumatosis intestinalis was found in 61% of neonates, bowel loop separation in 22.2%, ascites or perforation in 11.1%. 24% (n=11) of our cohort required surgery, and the extent of the radiological anomalies (defined as number of abdominal quadrants affected) was predictive of the necessity of surgery ( $p < 0.05$ , Figure 1). Only 1 neonate of our cohort did not survive to discharge.

### Conclusions

We could identify a risk factor for NEC development in almost all cases. The disease developed at an earlier postnatal age than the classic presentation in preterm neonates. There was no clear association between radiological and clinical findings, but the extent of radiological anomalies was predictive of the need for surgical intervention. Finally, the mortality of NEC in our cohort was lower than previously shown for preterm or term babies.

Picture

## Surgical NEC in term infants



## Epidemiology

The incidence of retinopathy of prematurity in a LEVEL III Centre from Romania (224)

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## Introduction /Case Report

Retinopathy of prematurity remains one of the most severe disability for the preterm newborns and the incidence is unchanged over the years

## Patients and Methods

The study was retrospective and we included 1709 ROP screening newborns in five years in a III level Romanian NICU.

Laser incidence was 8.54% at a mean of GA 28.53 weeks and a mean of BW 1204 grams. Of these, 91 (62.32% had stage 3 (4.79%) stage 4 and 48 (32.87%) AP.

## Results

32.17% of the infants with laser was from Level III Center having a mean of GA 26.5 weeks and mean of BW 989 grams GA (48% BW <1000gr, 48% 1001-1499 gr, 3,3% 1500-1999 gr and 0% over 2000 gr). ROP incidence is similar for the preterm newborns who are born in Level III but is four times higher from the preterm newborns that are transfers from level II centres. 99% of infants from level III have GA less than 34 weeks compared to 88% from level II. Distribution groups of newborns with laser from transfer was 48% under 30 wks, 40% GA under 32 wks and 12% with GA under 34 wks. There is a downward trend in the incidence of ROP laser therapy although the number of preterm with BW below 1000 grams doubled.

## Conclusions

ROP remains the leading cause of blindness in premature infants and the incidence increases with decreasing GA. The incidence is higher in preterm newborns where respiratory therapy, oxygen therapy, sepsis, increase the risk of disease even the GA is over 32 weeks.

Brain & Development / Early developmental care

## CEREBRAL FUNCTION MONITORING IN YOUNG INFANTS PRESENTING TO THE GENERAL PAEDIATRIC WARD WITH ABNORMAL MOVEMENTS (542)

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### Introduction /Case Report

Cerebral function monitoring (CFM) has proved a very useful tool in the neonatal intensive care unit, where it is extensively used in neonates admitted with encephalopathy and for diagnosis and monitoring of seizures. However, reports of its use in older children are limited and it is unclear if CFM is used in the general paediatric setting at present. We aimed to: i) evaluate our recent clinical use of CFM in young infants <6 months referred to our general paediatric ward with abnormal movements or suspected seizures; ii) survey general paediatric wards in our region to ask whether they use CFM and regarding their local availability of conventional electroencephalography (cEEG).

### Patients and Methods

Infants aged <6 months referred acutely with a history suggesting possible seizures underwent routine clinical monitoring with CFM for up to 36 h following admission to the paediatric ward. A dual-channel cerebral function monitor was used (Brainz BRM3, Natus Medical Inc, USA). Digital amplitude-integrated EEG (aEEG) recordings obtained by CFM were reviewed offline by an independent clinician to assess background voltage and the presence of any electrographic seizure activity. Clinical diagnoses at discharge were obtained by review of the clinical case notes. In May 2015 we telephone surveyed the general paediatric wards in 16 other hospitals in the Eastern region of the UK. We asked if they used CFM in infants admitted with possible seizures and about local cEEG availability.

### Results

Results: Over a 6-month period, six infants of postnatal ages 5 days to 5 months underwent CFM on the paediatric ward. Duration of aEEG recorded ranged from 9.5-34.1h. Background voltage was normal in four cases, but one showed burst-suppression. Of four with seizure activity on initial aEEG, three also had seizures on a subsequent cEEG done 14.5-65 h after admission. Eventual clinical diagnoses were: epileptic encephalopathy; left thalamic infarct; tuberous sclerosis; and deletion of 16p13.3 and 16p11.2; one infant was normal. Early confirmation of seizures by CFM allowed prompt anticonvulsant treatment in one infant whose cEEG 2.7 days later was normal.

Our telephone survey found that no other general paediatric ward in our region (0/16; 0%) was presently using CFM in young infants admitted with suspected seizures, while only 2/17 (11%) had on-call weekend cEEG availability.

## Conclusions

Conclusions: CFM presently appears to be a very underused tool in the general paediatric setting. Yet, in the absence of round-the clock conventional EEG availability, CFM may have a useful role within the general paediatric ward. Routine bedside monitoring by digital CFM can potentially facilitate timely diagnosis and treatment of seizures in young infants on the general paediatric ward also.

Epidemiology / Nosocomial infection and colonization

The incidence and risk factors of candidiasis among very low birth weight infants (233)

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### Introduction /Case Report

Candidiasis is an important morbidity among very low birth weight infants (VLBWI) and is associated with up to 32% mortality. Risk factors for neonatal candidiasis include prematurity, VLBWI, use of central venous line, intubation, parenteral nutrition, and broad-spectrum antibiotics administration. This study was documented to describe the incidence and risk factors of candidiasis in VLBWI.

### Patients and Methods

From September 2008 to December 2014, medical records of 171 infants with birth weight less than 1,500 grams in Inje University Ilsan Paik hospital NICU were reviewed retrospectively. Patients were divided into the candidiasis group (CAN, n=11) and the non-candidiasis group (Non-CAN, n=160). Demographic findings and factors associated with candidiasis were compared between these groups.

### Results

Eleven infants were diagnosed with candidiasis and treated with antifungal agent. The mean GA and BW were no significant difference between the two groups. The maternal demographic findings such as chorioamnionitis and prenatal steroid therapy were significantly low in the CAN group. There were no significant differences in the incidence of RDS and PDA. The durations of intubation, central venous catheter use, and hospital day were significantly longer in the CAN group. There were no significant differences in the mortality and complication such as IVH (Gr $\geq$ 3) and PVL. However, the incidence of BPD was higher in the CAN group compared to the Non-CAN group. In the logistic regression analysis, the duration of central venous catheter use ( $p=0.027$ , OR: 0.67, 95% CI:0.96-0.90) and intubation ( $p=0.030$ , OR:0.14, 95% CI:1.05-0.99) were the significant factors for neonatal candidiasis.

### Conclusions

Risk factors for candidiasis in VLBWI were longer duration of central venous catheter use and intubation in our study. Preventive strategies to decrease the incidence of candidiasis and aforementioned risk factors should be investigated in the future.

Pulmonology / Delivery room management

Small manometers improve bag and mask ventilation: a manikin study (352)

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### Introduction /Case Report

Self-inflating bags (SIB) remain widely used for neonatal resuscitation. Insufflation pressures from SIB are difficult to assess and can be inadequate. Ventilation monitoring improves pressure control, but is not accessible to most resuscitators. Small spring manometer or a pressure line to a needle and dial manometer can be connected through a side port on the SIB. Those devices are cheap and easily available, but their efficacy needs to be assessed. Observation of the manometer could also be considered as a distraction, with increased risk of leak or inadequate insufflation rate. We therefore aimed to evaluate the effect of mechanical manometers on the quality of insufflations with a SIB.

### Patients and Methods

Participants to the Belgian Pediatric Society meeting were invited to ventilate a manikin with a 300 ml SIB. The leak-free manikin was modified with a flow-meter at tracheal level connected to a neonatal test lung. Participants had to aim for a 25 mbar pressure and a rate of 40-60 during 3 sequences of 45 seconds. A spring (S), a dial (D) manometer or nothing (N) was added to the SIB in random sequence. Pressure data from the SIB and flow data from the manikin were obtained through a ventilation monitor. Peak pressure (PIP), tidal volume (VTi), and insufflations rate (RR) were calculated for each breath. Theoretical leak was evaluated by subtracting real from theoretical volumes derived from a leak free calibration (taped facemask). Data were analyzed with ANOVA and posthoc Bonferroni.

### Results

Five neonatologists (Neo), 15 pediatricians (Ped) and 11 residents ventilated the manikin for a total of 5279 insufflations. Manometer use was associated with an increase in PIP (N: 17+-6 mbar; S:18+-4 mbar\*; D: 19+-4 mbar\*#)[\*p<.05 vs N; #:p<.05 vs S]. Changes in VTi (N:3+-1 ml; S:3.1+-1 ml\*; D:3.2+-1 ml\*) and RR (77-82 bpm) were small. Leak did not increase. The effect of manometer use on PIP, VTi and leak was more important with Neo (PIP-N:16+-7 mbar; S and D:20+-4 mbar\*) and Ped. With residents, no change occurred in PIP (~17 mbar), Vti (2.9 ml) or leak (31-35%). However, for first sequences of ventilation, manometer use was associated with higher PIP (N: 12+-4 mbar; S: 16+-3 mbar\*; D: 20+-4 mbar\*#), VTi (N:2+-1 ml; S:3+-0.8 ml\*; D:3.3+-1 ml\*#) and lower leaks (N: 38+-16%; S: 27+-12%\*; D: 34+-13%\*#) and this observation for first sequences was found in all 3 categories of providers.

### Conclusions

Bag and mask ventilation remains difficult. In this model, the addition of a manometer is associated with improved pressures and VTi, and with decreased theoretical leak. This effect is predominant for initial ("naïve") ventilation, with a dial manometer, and is also related to operator experience. Small, inexpensive manometers have the potential to improve SIB ventilation of newborn infants.

Nutrition and gastroenterology / Perinatal growth

EVALUATION OF GROWING OF PRETERM INFANTS (23-34 GA) BORN AND HOSPITALISED IN INSTITUTE OF MOTHER AND CHILD IN WARSAW. (153)

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## Introduction /Case Report

Nutrition of preterm infants should result in growth similar to that of normally growing fetuses of the same gestational age. Unfortunately, some group of preterm infants do not achieve this objective and it results in extra uterine growth restriction, which is especially common in very preterm infants and is associated with an increased risk of poor neurodevelopmental outcome.

## Patients and Methods

Retrospective study, 250 AGA and/or SGA preterm infants (23-34GA) born in 2013-2014 were included. 102 cases (40.4%) were excluded (death, cong. malformations, hospitalization less than 2 weeks). Remaining population of 148 infants (59.6%) which completed the study was divided into 2 groups:

Group I: born 23+0/7 to 29+6/7 GA(n=54)

Group II: born 30+0/7 to 34+6/7 GA(n=94)

At the start and at the discharge weight, length and head circumferences were measured and they were calculated according to Fenton 2013 Growth Calculator for Preterm Infants.

Extra-uterine growth restriction was defined as body weight<10th perc. of the predicted value at discharge. Another indicators of malnutrition were length and head circumferences being<10th perc. of the predicted value.

## Results

### Group I

The growth restriction was: 4 infants(7.4%) at birth and 7(12.9%) at discharge.

3 infants(5.5%) were born with head circumferences < 10th perc. of the predicted value.

At discharge 5 (9.3%) demonstrated C/A deficit. 2 newborns (3.7%) had L/A deficit

and at discharge we couldn't closely evaluate this indicator because of 2 methods

of measurement of the length. Most of infants with growth restriction had serious medical complications.

### Group II

The proportion of growth restriction was: 11 infants (11.7%) at birth to 22 (23,4%)

at discharge. 10 infants (10.6%) were born with head circumferences < 10th perc.

of the predicted value. At discharge 11 (17.7%) demonstrated C/A deficit. 4 newborns (4.2%) had L/A deficit and at discharge we couldn't closely evaluate this indicator because of 2 methods of measurement of the length. Only a few infants had serious medical complications.

## Conclusions

1. The deterioration of anthropometrical evaluation during hospitalization of preterm infants, especially AGA and without medical complications, would imply a failure to assure an adequate energy and nutrient supply not only for catch up growth from the intrauterine growth restriction but also for maintaining the extra uterine growth velocity.
2. We should duly evaluate nutrient intake in AGA and SGA preterm infants after birth.

Circulation, O<sub>2</sub> Transport and Haematology / Systemic circulation and cardiac output

## RETROSPECTIVE INVESTIGATION OF PATENT DUCTUS ARTERIOSUS SURGERY FOR EXTREMELY LOW BIRTH WEIGHT INFANTS IN OUR INSTITUTION. (370)

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### Introduction /Case Report

In Japan, prophylactic indomethacin for the prevention of intraventricular hemorrhage is recommended. In our institution, despite the increased use of prophylactic indomethacin, patent ductus arteriosus (PDA) surgery has also increased. The aim of this study is to clarify the causes of this increase in surgery.

### Patients and Methods

We conducted a retrospective study of 30 inborn extremely low birth weight (ELBW) infants who underwent PDA surgery in our institution from 2004 to 2014. Patients were divided into two groups, 7 infants who were admitted from 2004 to 2009, and 23 from 2009 to 2014.

### Results

In the former and later groups, the gestational age was  $24.4 \pm 1.7$  weeks vs.  $24.7 \pm 2.2$  weeks, birth body weight  $653 \pm 174$  grams vs.  $674 \pm 156$  grams, apgar score (1 minute)  $3.1 \pm 2.0$  vs.  $2.9 \pm 1.7$ , apgar score (5 minute)  $5.3 \pm 3.0$  vs.  $5.3 \pm 2.3$  and age of PDA operation  $38 \pm 21$  days vs.  $33 \pm 16$  days, respectively. Prophylactic indomethacin usage rate was 0% vs. 30% and vasopressor usage rate was 100% vs. 100%. There was no significant difference between the two groups.

The total water intake on the day of PDA surgery was  $93 \pm 11$  ml/kg/day vs.  $115 \pm 15$  ml/kg/day (median), and total hydrocortisone amount (from birth to PDA operation day)  $0.064 \pm 0.094$  mg/kg/day vs.  $0.64 \pm 0.88$  mg/kg/day. The steroid usage rate for bronchopulmonary dysplasia (BPD) was 33% vs. 81%. In the latter group, there was a higher water intake and level of steroid administration ( $p < 0.05$ ).

### Conclusions

Our results suggest that an increased water intake and steroid administration might be a cause of the increase in PDA surgery.

## Pulmonology / Lung injury

### THE 5-YEAR PREVALENCE AND OUTCOMES OF BABIES WITH CHRONIC LUNG DISEASE IN A UK NEONATAL INTENSIVE CARE UNIT (441)

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#### Introduction /Case Report

Chronic lung disease (CLD) is a major cause of morbidity and mortality in preterm infants. It is relevant in the current health care climate due to the costs it may generate, owing to long term respiratory and neurodevelopmental complications.

#### Patients and Methods

We looked at the prevalence and outcomes in babies with CLD admitted to our neonatal intensive care unit (NICU) in Birmingham, United Kingdom over a 5 year period.

We utilised the Badger database to retrospectively analyse the outcomes of preterm babies with oxygen requirement at a corrected gestational age of 36 weeks. The time period looked at was April 2009 to March 2014.

#### Results

There were 6818 neonatal unit admissions during the study period, with 228 babies diagnosed with CLD. Their gestations ranged from 23 to 34 weeks, with the outborn babies of lower mean gestation compared to the inborn babies (25 weeks versus 27 weeks). The average length of stay in hospital was around 100 days and 44% of babies with CLD went home on oxygen. Patent ductus arteriosus was the commonest co-existing morbidity, affecting 71% of the cohort. Other complications including retinopathy of prematurity requiring laser surgery, necrotising enterocolitis requiring surgery and significant intraventricular haemorrhage were slightly more common in outborn babies.

#### Conclusions

Chronic lung disease is a significant morbidity in preterm babies, whose survival is improving. This data aims to show demographics and concurrent short term health problems which may help to inform future service planning, research considerations and counselling of parents.

## Pulmonology / Delivery room management

Management of Respiratory Distress Syndrome in preterm infants – Survey of practice across a large neonatal network in United Kingdom (563)

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## Introduction /Case Report

Management of preterm neonates in the first hour after birth has far reaching consequences beyond the immediate neonatal period. These babies are exposed to various stresses during this transitional period that may predispose to lung and brain injury. In recent years evidence has accumulated to support an approach that promotes gentle transition rather than aggressive interventional management. Aim of this study was to survey and scope practices across a large neonatal network in UK and compare against 2013 update of European consensus guidelines on management of respiratory distress syndrome in preterm infants.

## Patients and Methods

A web based survey questionnaire was emailed to all Neonatal unit leads within the East of England neonatal network. The questionnaire was designed to identify the level of care and availability of written guidelines on first hour care of premature infants. Further questions targeted towards prenatal care, delivery room stabilisation, initial respiratory management and practices around oxygen saturation targeting. Units were also asked to provide information on appropriate equipment availability to deliver required interventions as per current standards. Results were analyzed using Excel 2013 software.

## Results

16/17 (94 %) units (3 NICUs, 10 LNUs & 3 SCBUs) responded to the survey. Only 3 units (19 %) had a written guideline on early care of preterm neonate with RDS. All units offered antenatal steroids (100 %), however, only 11 units (68 %) offered antenatal magnesium sulfate for gestation less than 30 weeks. Only 4 units (25 %) used an admission checklist to document various interventions done in the first hour. Thermoregulation standards were followed consistently except for monitoring of delivery room temperature. Early CPAP at birth was started in 15 units (94%) while only 5 units (35%) practiced INSURE and 4 units (28%) used lower than the recommended dose of surfactant. Up-to-date recommendations on oxygen saturation targeting were followed in 10 units (66%) and 8 units (58%) used early caffeine. Results summarized in table 1.

## Conclusions

Our survey identified wide variation in practice even within a single neonatal network when compared to recommendations listed in European Consensus Guidelines 2013 update. Our survey results prompted a network wide initiative to standardize care in line with current evidence thereby reducing the risk of adverse outcomes. A network wide standardized first hour care pathway is the next step in this quality improvement initiative.

Table

**Table 1: Summary of survey findings**  
(16 out of 17 units responded to survey questionnaire)

<b>Unit level responses (n =16)</b>	
NICU (Level 3)	3 (100 %)
LNU (Level 2)	10 (100 %)
SCBU (Level 1)	3 (75 %)
<b>Policy available (n =16)</b>	
Yes	3 (19 %)
No	13 (81 %)
<b>Admission Checklist (n =16)</b>	
Yes	4 (25 %)
No	12 (75 %)
<b>Guidance available (n =16)</b>	
Antenatal steroids	16 (100 %)
Magnesium Sulfate	11 (68 %)
<b>Thermoregulation (n =16)</b>	
Delivery room temperature 25 C	0 (0 %)
Plastic wrap/bag < 28 weeks	16 (100 %)
Hats	16 (100 %)
<b>Delivery room management (n =16)</b>	
Delayed cord clamping	11 (68 %)
Room air resuscitation	12 (75 %)
Pulse oximetry	13 (81 %)
<b>Early respiratory management</b>	
CPAP/PEEP (n =16)	15 (93 %)
Surfactant (n=14)	
Prophylactic	4 (28.5 %)
Prophylactic if risk factors	5 (35.7 %)
InSurE	5 (35.7 %)
Surfactant dose (n =14)	
200 mg/kg	10 (72 %)
100 mg/kg	4 (28 %)
<b>Oxygen saturations ( n =15)</b>	
90 – 95 %	10 (66 %)
85 – 89 %	2 (14 %)
No guideline	3 (20 %)
<b>Early Caffeine (n =14)</b>	
Yes	8 (58 %)
No	6 (42 %)

## Pulmonology / Delivery room management

The Good, the Bad, the Marginal: respiratory management of <29 weeks infants according to subjective assessment of perinatal adaptation. (580)

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## Introduction /Case Report

Even if a primary CPAP strategy gives benefits in extremely preterm infants, many still require intubation at birth. Half of those initially managed with primary CPAP will require further support: surfactant administration or mechanical ventilation. Those infants have increased risks of death and neonatal morbidities, and will require longer duration of respiratory support. Identifying them early, during the birth stabilization process, might lead to improvements in respiratory care. A subjective classification of perinatal adaptation as Good, Bad or Marginal has been suggested but requires further evaluation. We aimed to evaluate respiratory management according to perinatal adaptation.

## Patients and Methods

Premature infants of less than 29 weeks and admitted between 01/2013 and 07/2014 were retrospectively studied. Neonatal database and discharge summaries provided neonatal care and outcome data. Good perinatal adaptation (GPA) was considered for infants with good respiratory drive, tone and low oxygen requirement in the delivery room. Infants with marginal (M) PA had intermittent respiratory drive, normocardia with ventilation, and decreasing FiO<sub>2</sub>. Bad (B) PA is considered with hypotonia, bradycardia, apnea and high FiO<sub>2</sub>. Data are presented as mean +/- SD, median (interquartile range) or incidence and analyzed with ANOVA, Kuskal-Wallis test or Chi<sup>2</sup>.

## Results

Sixteen infants had GPA, 19 MPA and 23 BPA. Their GA was 26 4/7 wk (24-28) and BW was 885 +/-187g.

Risk factors for bad PA are (NS) male gender, lower GA, and no complete antenatal steroid exposure. Apgar at 1 min increases with better PA [B3 (2-5); M6 (3-7) and G8 (7-8)\*] (\*p<.05 vs B & M), and improves at 5 min: [B7 (6-7); M7 (6-8); G 9 (8-9)\*]. Risk of intubation at birth is associated with poorer adaptation (B 87%; M 47%; G 12%, p<.01).

Primary CPAP success was not different according to group (B 3/3; M66%; G56%). Surfactant while on CPAP (LISA method) was given to 11/16 patients, including 7 delivery room administrations. If intubated by day 3, duration of first invasive ventilation was shorter (NS) for GPA (9h) [MPA (15h), BPA (29h)].

Early neonatal death tended to decrease with better PA: 26%, 16% and 0% (p=.08). There is no difference in BPD at 36 weeks (B 19%, M13%, G 12%).

## Conclusions

Infants with better perinatal adaptation have increased chances of being initially managed with CPAP. Primary CPAP success may be improved with less invasive surfactant therapy. Outside of the delivery room,

perinatal adaptation assessment tends to identify risk of early neonatal death, but is not predictive of respiratory outcomes.

NEONATAL APNEA – HOW OFTEN DO WE RECALL PERINATAL STROKE? (291)

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Introduction /Case Report

Perinatal stroke is an under-recognized condition and, despite relatively low mortality, is a major cause of long-term neurodisability. Seizures are the most common clinical presentation. However, not all neonates present with seizures – subtle difficulties that initially go unnoticed, may gradually develop into significant problems, delaying the diagnosis until 6 months of age or later when motor asymmetries prompt neuroimaging. Apnea in the neonatal period can result from multiple causes, including airway obstruction, sepsis, gastroesophageal reflux, cardiac arrhythmias or the sole manifestation of a seizure.

Case Report

We present the case of a term female newborn with no relevant family history. Her mother had gestational diabetes treated with insulin. Delivery by caesarean section was incident-free, without meconium stained amniotic fluid. Apgar score was 9/10 at 1 and 5 minutes, respectively. Physical examination was normal.

At 14 hours after birth, sudden cyanosis was observed, requiring admission to the Neonatal Intensive Care Unit. After admission, countless episodes of cyanosis were recorded, accompanied by apnea and bradycardia, which required intermittent positive pressure ventilation, with full recovery.

Complementary examination findings, including echocardiography, basic biochemistry, metabolic studies, C-reactive protein, blood culture and neurosonography were normal.

On day 4 neurosonography showed slit left ventricle, left fronto-parietal parenchymal hyperechogenicity and hyperechoic left sylvian fissure. Electroencephalography (EEG) demonstrated the presence of electrographic seizures in the left fronto-parieto-temporal region and Cranial Magnetic Resonance Imaging revealed ischemic infarction in the distribution of the left middle cerebral artery.

EEG improved with Phenobarbital administration.

Family history of thrombophilia was ruled out and no coagulation abnormalities were found in the newborn.

Conclusions

The etiology of perinatal stroke is multifactorial and no obvious cause is identified in up to 50% of cases. Neurocognitive outcome depend on the site of brain damage and the stage of neurodevelopment at the time of the insult, but perinatal stroke remains as the leading cause of hemiplegic cerebral palsy. This report emphasizes the need to consider stroke in term neonates with unexplained apnea, even in the absence of an abnormal neurosonography.

## Pulmonology

### EVALUATION OF MORBIDITIES AND COMPLICATIONS OF NEONATAL INTENSIVE CARE UNIT PATIENTS WITH RESPIRATORY DISORDERS (715)

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#### Introduction /Case Report

Respiratory failure due to acute pulmonary diseases is common and life-threatening in the neonatal period. The aim of this study is to evaluate the incidence of acute neonatal respiratory disorders and the main related complications. The results are described of a 1-year single centre study, which focused on the following points: the incidence of respiratory diseases in newborns and related mortality; the relationship between acute neonatal respiratory disorders rates and gestational age, birth weight, gender, Apgar score, maternal age, mode of delivery ; and the incidence of complications associated with respiratory disturbances.

#### Patients and Methods

16 494 live births was born in Zekai Tahir Burak Hospital, of these patients 2546 (15.4%) were hospitalized in the Neonatal Intensive Care Unit between January 2013- December 31, 2013. Respiratory disorders were respiratory distress syndrome(RDS), transient tachypnea of newborn(TT), meconium aspiration syndrome(MAS), pneumonia, congenital diaphragmatic hernia(CDH), pulmonary maladaptation and other respiratory disorders. Other disorders were sepsis, congenital airway and cardiac malformations, chromosomal disorders, perinatal asphyxia, pulmonary hypoplasia and hydrops fetalis. The complications studied were for necrotising enterocolitis(NEC), patent ductus arteriosus(PDA), intraventricular haemorrhage(IVH), bronchopulmonary dysplasia(BPD) and air leak.

#### Results

In our study the male / female ratio was found to be 279/207. The prematurity rate (gestational age <37 weeks) was %75, while the extremely low birthweight(ELBW; <1000g), very low birthweight(VLBW; <1500g) and low birthweight (LBW; <2500g) rates were 56(11.5%), 124(25.5%) and 317(65.2%) respectively. 45 (9,2%) of the 486 hospitalized patients with respiratory distress died during the follow-up. The incidence of RDS was 28.8%(140). The occurrence of TT, MAS, pneumonia, CDH, pulmonary maladaptation and other respiratory disorders were 31.7%(154), 1.6%(8), 7%(34), 0.6%(3), 21%(102) and 9.3(45) respectively. Complications of respiratory disorders was found to be 8%(39), 21.5%(104), 25.1(122), 3.9%(19) and 5.3%(26) for NEC, PDA, IVH, BPD and air leak respectively. Frequency of complications according to birth weight was shown in Table 1.

#### Conclusions

In the literature, there is limited data on this issue. Our study has a different epidemiological point of view in terms of evaluating the etiology of respiratory distress and complications in the neonatal period. With the completion of our study we are expecting to reach more reliable and updated results.

## Table

**Table 1.** Frequency of complications in relation to birth weight

Birth weight (g)	Complication				
	NEC	PDA	IVH	BPD	Air leak
ELBW (<1000)	39,3 (22/56)	76,8 (43/56)	73,2 (41/56)	30,4 (17/56)	7,1 (4/56)
VLBW (1000-1499)	20,6 (14/68)	64,7 (44/68)	55,9 (38/68)	2,9 (2/68)	4,4 (3/68)
LBW (1500-2499)	1,6 (3/193)	8,3 (16/193)	19,2 (37/193)	0 (0/193)	3,6 (7/193)
Normal weight (2500-4000)	0 (0/160)	0,6 (1/160)	1,9 (3/160)	0 (0/160)	7,5 (12/160)
>4000	0 (0/9)	0 (0/9)	33,3 (3/9)	0 (0/9)	0 (0/9)
Total	%8 (39/486)	%21,5 (104/486)	%25,1 (122/486)	%3,9 (19/486)	%5,3 (26/486)

Data are shown as % (ratio)

## Brain & Development

### MANAGEMENT OF SPINA BIFIDA IN AN EXTREME PRETERM – DO WE UNDERSTAND FETAL/NEONATAL SKIN HEALING? (708)

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#### Introduction /Case Report

##### Background -

Presentation of spina bifida aperta (SBA) in extreme preterm born infants is rare. Due to clinical instability and skin immaturity, early surgical intervention carries additional risk to the infant. Experience of treatment of the extreme preterm with SBA is limited to iatrogenic preterm delivery following fetal surgery. In these patients fetal patch coverage of the lesion obviates the need for early postnatal surgery.

Aim - We present our experience of managing wound healing in an extreme preterm with SBA.

##### Case Report

Animal studies have suggested that a fetus with SBA may be subject to further damage from the intrauterine environment; a so called “secondary hit”.

Open fetal surgery performed at 25th C) and head circumference 22cm (9th C). He was noted to have an open low lumbar myelomeningocele with marked lower limb muscular hypotrophy. The lesion was immediately covered with sterile gauze. He was placed in a plastic bag and given surfactant following intubation at 5 minutes of age.

During the initial few weeks he developed a left sided intraventricular haemorrhage with parietal parenchymal infarction. Due to skin immaturity the neurosurgical team decided to manage his SBA conservatively, not for primary closure. The lesion was left to allow granulation healing and dressed with moist sterile gauze and tegaderm. Over 7 weeks the dressing was changed every 5 days and demonstrated re-expansion of a meningocele without major CSF leakage. Cranial US revealed herniation of the cerebellum (Arnold Chiari II malformation) and mildly progressive ventricular dilatation. He had no episodes of CNS infection. At 32 weeks CGA the placode was felt to have some granulation but no epithelialisation.

He underwent primary closure and reservoir insertion at 33+6 weeks CGA. Following this he has required daily CSF taps due to progressive ventriculomegaly.

##### Conclusions

Initial conservative interim management of SBA in the extreme preterm over a period of 7 weeks is feasible. It prevents a “secondary hit” from intervention related complications due to skin immaturity and an unstable clinical condition. However in contrast to the early experiences following fetal endoscopic surgery with minimally invasive collagen patch coverage, conservative management of SBA as described is not followed by secondary skin coverage of the lesion.

Picture



## Pulmonology / Mechanical ventilation

Is it beneficial to treat ureaplasma urealyticum in ventilated preterm infants? (457)

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### Introduction /Case Report

Cochrane review does not demonstrate a reduction in chronic lung disease (CLD) when intubated preterm infants are treated with erythromycin prophylactically before U. urealyticum results are known or when ureaplasma colonized intubated preterm infants are treated with erythromycin. Even though the benefit on CLD is not clear, it is often tested and/or treated in ventilated preterm infants. The rationale in treating the infection/colonisation in preterm infants is to facilitate extubation or weaning the ventilator requirement.

Aim: To evaluate the efficacy of treating ureaplasma infection or colonisation with erythromycin in ventilated preterm infants.

### Patients and Methods

Retrospective observational study of 4 years (from Feb 2011 to Jan 2015) in a busy non-surgical neonatal intensive care unit of all the positive ureaplasma cases in preterm infants. Test for Ureaplasma is done by PCR technique on the endotracheal/nasopharyngeal aspirate. Treatment dose of erythromycin was given for 2 weeks.

### Results

Total number of positive ureaplasma cases in study period: 27. Median gestational age: 25 weeks. Median Birth weight: 750 grams. Median age of test/diagnosis: 14 days. Maximum respiratory support required, Ventilation: 85%(23/27), Continuous Positive Airway Pressure(CPAP): 7%(2/27), High flow/Vapotherm: 7%(2/27).

PDA present: 85%(23/27), medical treatment: 9/23, Surgical ligation: 5/23, Both(medical & surgical ligation):5/23.

Steroids used for extubation: 44%(12/27).

Erythromycin treatment given in: 85%(23/27), mean age of treatment: 17 days.

In 5 cases erythromycin treatment for ureaplasma was given preceding extubation. In 18 cases either PDA treatment or dexamethasone was used after erythromycin treatment to facilitate extubation.

Discharged on Home Oxygen: 41% (11/27).

### Conclusions

In 22% of the ventilated preterm infants with ureaplasma infection/colonisation, erythromycin treatment may have facilitated extubation.

Large randomised control trials are needed to evaluate the true effect of erythromycin treatment on ventilated preterm infants in facilitation of extubation.

## Pulmonology / Lung injury

### EFFECT OF EARLY VERSUS LATE VITAMIN D SUPPLEMENTATION IN VERY LOW BIRTH WEIGHT INFANTS ON CHRONIC LUNG DISEASE (451)

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#### Introduction /Case Report

Neonatal chronic lung disease (CLD) is an important cause of morbidity and mortality. Vitamin D is known for its role in bone metabolism, but physiology suggests it influences lung fibroproliferation, remodelling and function by various cytokines, cellular elements, oxidative stress and protease/antiprotease levels. There is emerging evidence implicating vitamin D's association with chronic inflammatory lung diseases like asthma. An animal study speculates that decreased vitamin D levels may contribute to the pathogenesis of bronchopulmonary dysplasia. The aim is to evaluate whether early supplementation of Vitamin D in Vitamin D deficient very low birth infants has an impact in CLD.

#### Patients and Methods

Retrospective observational study on very low birth weight (VLBW) infant's (<1500grams) over 18 months from Nov 2013 to Mar 2015 in a tertiary NICU. VLBW with low vitamin D levels (500IU) or rapidly rising. The definition of chronic lung disease used is the requirement of oxygen at 36 weeks (corrected gestation) in <32 weeks gestation at birth. Microsoft Excel was used for prevalence and population study, and Fischer's exact test.

#### Results

24 VLBW infants had low vitamin D levels in study period. All the infants were supplemented with high dose Vitamin D (1500 units/day). Prevalence of CLD in early supplementation group (n=13) is 38%, compared to the prevalence of 72% in the late supplementation group (n=11) (Fischer's exact test p= 0.122). There was no statistical difference between both groups regarding gestation (p=0.318) and weight (p=0.214). (Table 1)

#### Conclusions

Despite the small population size, incidence of chronic lung disease is high in late supplementation of Vitamin D group (not statistically significant). Larger randomised control trials are needed to establish the role of Vitamin D deficiency and chronic lung disease.

Table

	Early supplementation group (n=13)	Late supplementation group (n=11)	Unpaired t-test p value
Gestation mean	26,69	25,73	0,318
Weight mean	841,77	722,55	0,214
Mean age of testing (days)	29,54	52,58	<0.001

Epidemiology / Nosocomial infection and colonization

NEONATAL AMOEBIASIS MAY NOT BE AS RARE AS WE THOUGHT, A CASE SERIES (211)

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### Introduction /Case Report

Entamoeba Histolytica (EH) is the protozoan parasite responsible for dysentery and amoebiasis. It can cause invasive intestinal and extraintestinal disease. It is responsible for up to 100,000 deaths every year worldwide.<sup>1,2</sup> Over the years, only a handful of cases of neonatal and infantile amoebiasis that has been reported.<sup>3,4,5</sup>

This is to highlight a higher incidence of this infection in this age group than previously thought.

### Case Report

A total of six babies presented to us at the Neonatal Intensive Care Unit (NICU) at Mediclinic City Hospital in Dubai over a period of 24 months. All of them but one shared a universal symptom of passing stool mixed with fresh blood. Other symptoms were variable according to gestation and the age at presentation.

The first baby was a 25 week preterm baby. He became unwell at the age of 2 weeks. He developed bloody stool associated with abdominal distension. He required to be re-ventilated.

Other two babies were preterm babies born at 26 and 25 weeks. However, they developed the infection at a corrected gestation of 38 and 44 weeks respectively. They remained well with no other associated symptoms.

The other two babies were term well babies who were reported to pass fresh blood mixed with their stool shortly after birth while on the postnatal ward. Interestingly, with one of these two babies, there was a history of confirmed neonatal amoebiasis with his older sibling. The sibling was born two years ago in a different Middle Eastern country. This was suggestive of ongoing maternal carriage status.

The last baby was a 23 weeks and 6 days of gestation. He developed small bowel perforation as a complication of Necrotising Enterocolitis. His infection has manifested by sudden increase in his ileostomy output associated with raised C-reactive protein.

The diagnosis of amoebiasis was confirmed by the detection of EH antigens in stool (chromatographic immunoassay) in all babies. All these babies had normal platelets count and coagulation profile. Their parents and household contacts were tested for entamoeba in stool.

All babies were successfully treated with metronidazole. Their stool testing after treatment was negative for EH.

### Conclusions

Neonatal amoebiasis appears to be commoner than previously reported. It should be suspected in every baby presenting with passing fresh blood in their stool.

The diagnosis may be reliably and specifically made using rapid EH antigen detecting test.6

Picture



## Pulmonology / Lung injury

Single centre experience of using Montelukast in extreme preterm infants (496)

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### Introduction /Case Report

Bronchopulmonary dysplasia (BPD) remains a significant problem in extreme preterm (EP) population. Montelukast, a leukotriene inhibitor, appears to be a logical choice for prevention or treatment of evolving or established BPD in ELBW babies due to known pathophysiology of BPD.

Phase 1 and II trials have been conducted and cohort studies are published (Rupprecht et al), but definitive randomised trials are pending. We would like to share our experience of using monteleukast in 8 babies with severe evolving or established BPD.

Aim: To assess the clinical outcomes in extreme preterm babies treated with montelukast at a tertiary NICU.

### Patients and Methods

During a period of 9 months (01/08/14 to 11/05/15), eight extreme preterm babies were identified as receiving montelukast during their admission.

The montelukast was used as a last resort in babies with evolving or established severe chronic lung disease with radiological changes of significant lung disease unresponsive to routine medical treatment including postnatal steroids. Babies were ventilated, on nasal CPAP or high flow oxygen with significant oxygen requirement. Montelukast was administered at a dose of 2mg/kg or 2 mg once daily orally at mean gestation of 54 days (range day 22 - day 106 of life).

The hospital notes & electronic records of these babies were searched to identify the details of pregnancy, condition at birth, need for respiratory support and neonatal morbidity.

### Results

The mean gestation was 25+6 weeks (range 23-27) & mean birth weight was 727 gms (range 590-905 gms). 5 babies survived & 3 died. Of 3 babies who died 2 had an antenatal history of oligohydramnios. 2 babies had APGAR scores < 3 at 1 & ≤ 5 at 5 minutes. No baby received chest compressions or resuscitation drugs.

All babies received surfactant & postnatal dexamethasone, 2 received prednisolone. The mean ventilation days were 42.5 (range 29-69). 2 babies had chest drain for pneumothorax, 4 had high flow oxygen at 36 weeks corrected gestation.

All 6 had a patent ductus arteriosus, 5 had ibuprofen & 2 had surgical ligation. 1 baby had necrotising enterocolitis, 4 had culture positive sepsis, 5 had retinopathy of prematurity (3 had Laser). No baby had cystic PVL & 1 had intraventricular bleed.

4 went home in oxygen & on montelukast & 1 is still inpatient. No obvious side effects were noted.

#### Conclusions

At least half of patients in our cohort of patients could be discharged home. No unusual side effects were noted. Montelukast may be tried in an extreme preterm neonate dependent on significant respiratory support for severe chronic lung disease unresponsive to postnatal steroids and other treatment modalities. Further phase 3 clinical trials are needed to establish safety and efficacy.

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

Trends in pharmacological management of patent ductus arteriosus in a tertiary neonatal unit (532)

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### Introduction /Case Report

Patent ductus arteriosus is a common finding in extremely preterm babies and can be challenging to manage. Pharmacotherapy for the closure of PDA has been around for decades and recently the production of indomethacin has ceased. This has impacted on the options available for the pharmacological management of PDA in preterm babies.

### Patients and Methods

We aim to review the trends in pharmacological management of PDA in a tertiary neonatal setting. The badger electronic patient record was reviewed for babies who had their PDA treated with either indomethacin or ibuprofen in the last six years (April 2009-March 2015).

### Results

The following table shows the demographic and outcome data of babies that had PDA treatment.

	Ibuprofen (n=50)	Indomethacin (n=67)
Time period in months	27	31
(n per month treated)	(1.8)	(2.2)
Median gestational age	25.5	25
(range in weeks)	23-29	22-29
Median birth weight (grams)	697.5	755
(range in weight)	535-1380	480-1430
No. of courses	55.6	80.3
PDA ligation	13 (26%)	11 (16%)
CLD	34	28
NEC	14	15
IVH	8	13
IVH ≥ Grade 3	2	3
Died	5	12
Survived to discharge	45 (90%)	55 (82%)

## Conclusions

Currently, there is only one pharmacological agent available for the management of PDA in preterm babies. Although the population of babies being treated for PDA remains the same, the babies requiring PDA ligation have increased since the move towards ibuprofen.

Brain & Development / Early developmental care

## IMPROVING INFUSION THERAPY IN NEONATOLOGY (387)

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### Introduction /Case Report

Individual doses of infusions can be calculated as “the rule of six”, where an individual dose is diluted in a fixed volume (i.e 50 ml), giving a variety of concentrations, or with calculation of dose as the volume of standard concentrations. In both cases manual calculation is needed to know which dose the individual patient gets. Errors are common, and in the tiny neonate this may have serious consequences

### Patients and Methods

Modern syringe and infusion pumps (smart pumps) enables pre-made drug protocols with standard concentrations, and the option of dosing of medications and infusions either as ml/kg or as dose/weight/time. The pump calculates and the display shows which dose the patient gets at any time. Preset upper and lower limits for infusions can be set.

### Results

Examples of protocols from our 5 years' experience will be presented.

### Conclusions

In modern neonatology such pumps should be used to reduce the risk for errors in infusion therapy.

Protocols should be designed in close cooperation between neonatologists, nurses, pharmacists and medical engineers.

Nutrition and gastroenterology / Breast feeding

THE PROCEDURE OF DONOR'S HUMAN MILK SUPPLEMENTATION - THE BENEFITS FOR PRETERM INFANT'S HEALTH AND THE ECONOMICAL EFFECT FOR THE HOSPITAL (788)

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Introduction /Case Report

More and more is known about the health benefits of exclusive human milk feeding for preemies. Although, there is still lack of information on the economic effects, resulting from the implementation procedure of donor's milk supplementation in hospital neonatal ward.

Patients and Methods

Since the opening, in the middle of 2013, the Human Milk Bank in L. Rydygier's Provincial Polyclinical Hospital in Torun (the HMB), each preterm hospitalized there, who has required supplementation, has got donor's milk (i.e. 329 babies for 1,5 year).

Results

After 1,5 year of the HMB activity we analysed the expenses of the Department of Neonatology and NICU in this Hospital on antibiotics, immunoglobulin and parenteral nutrition, per one premature, born before 33 gestation age. We also examined the length of the supplementation. In the first year of HMB activity we observed a decrease in the expenses: 56,3% on antibiotics, 72,2% on immunoglobulin and 38,5% on parenteral nutrition, and in the second year, respectively: 44,6% , 85,6% and 40,3% cost reduction, compared to the period before the implementation of this procedure. The median length of donor's milk supplementation in the first year of the HMB activity was 4 days, and in the second year- 3 days.

Conclusions

The results show that the implementation of donors' milk supplementation procedure has given both, the health benefits for preemies as well as savings for the hospital, that give strong support for breastfeeding of preterm infants. Shortening of the supplementation length can indicate the result of better promotion of premature' own mother's milk feeding.

Epidemiology / Host responses and early diagnosis of infection

A RISK FACTORS IN EARLY NEONATAL SEPSIS (703)

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### Introduction /Case Report

Neonatal sepsis is important cause of morbidity and mortality in early neonatal period. Clinical manifestation of early neonatal sepsis are unspecific, so it is very difficult to recognised it on time. There are many risk factors that influenced on appeared early neonatal sepsis. Early diagnostic and appropriate therapy can save a life of newborn baby.

### Patients and Methods

The p̄spective study on 95 newborn over 34 gestatio age divided in two group: I-A: blood culture proven systemic infection, I-B: systemic infection widouth proven blood culture, but presence clinicaly sings of SIRS. II group: control group. We monitored the risk factors that influenced the apperence of infection with laboratory parametars that referes to infection: CRP, white blood cels, and blood plateles as wellas blood cultures in IA group. We monitored parametars in first second and third day of living.

### Results

Levels of CRP in I group including subgroups werw statistically significantly higher in the first, second and third day in compared with the control group( $p<0,001$ ). Number ofwhite blood cells is not statistically significant from the groups( $p<0,05$ )

The greatest impact as risk factors have vaginal discharge, maternal urinaru infection and premature rupture membrans in our reserch( $p<0,001$ )

### Conclusions

Infection in neonatal period is manifested by nonspecific signs with RD symptoms mostly, but also with bloted stomach and hypotonia. Every newborn baby with risk factors is on antibiotic, because delaying therapy in neonates significantly increased the risk of disease progresion. By monitoring CRP concentration in semples to estimate the initial adaptation of antibiotic therapy and sensivity of bacteria.

Epidemiology / Early origins of adult disease

## CONGENITAL ADRENAL HYPERPLASIA WITH NON-FUNCTIONAL MUTATIONS IN BOTH ALLELES IN A CLINICALLY UNAFFECTED INFANT (877)

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### Introduction /Case Report

Results in neonatal screening programs aiming at detection of congenital adrenal hyperplasia (CAH) can only report elevated levels of 17-hydroxy-progesterone (17-OHP) without being able to differentiate presence or absence of salt loss. In a newly established neonatal screening system in Lao PDR the information about presence or absence of salt loss would largely facilitate management of these infants.

### Case Report

The first specimen of suspected CAH in samples sent from Lao PDR was investigated for known mutations in CAH associated with salt loss. Molecular genetic diagnosis revealed mutations associated with loss of function in both alleles, however, the infant was clinically unaffected even without any corticosteroid substitution therapy. Further genetic studies were performed in order to ascertain the identity of this infant and to exclude confusion of samples. All four blood samples were derived from the same infant. 17-OHP was elevated on all four occasions above the screening cut-off level.

### Conclusions

Although molecular genetic methods can theoretically predict loss of function in CAH, our infant was clinically unaffected even without any corticosteroid substitution at 13 months of age. We speculate that in CAH remaining enzyme activity can be sufficiently high despite the presence of loss of function mutations in order not to affect infants clinically.

Circulation, O2 Transport and Haematology / Organ blood flow and autoregulation

THE USE OF NEAR INFRA RED SPECTROSCOPY AND NON-INVASIVE CARDIAC OUTPUT MONITORING TO ASSESS THE HAEMODYNAMIC CHANGES IN INFANTS UNDERGOING THERAPEUTIC HYPOTHERMIA (275)

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### Introduction /Case Report

Severe perinatal asphyxia in term infants occurs in 1-2/1000 live births. These infants are considered for therapeutic hypothermia (TH) as a neuro-protective measure. The impact of therapeutic hypothermia on cardiac output, systemic vascular resistance and brain tissue oxygenation in this population is gaining interest. Non-invasive cardiac output monitoring has gained interest in the assessment of neonatal haemodynamics. In addition, non-invasive Near Infrared Spectroscopy (NIRS) can be used for the measurement of cerebral regional oxygenation (CrO<sub>2</sub>). In this case report, we present continuous haemodynamic and NIRS data in an infant undergoing TH and during rewarming.

### Case Report

This infant was born to a Gravida 5 female. There was a 48 hour history of decreased fetal movements and meconium stained liquor. The cardiocograph demonstrated variable decelerations. The infant delivered vaginally. She was limp and apnoeic at delivery with an Apgar score of 5 and 5 at 1 and 5 minutes respectively. A capillary blood gas at 21 minutes of age showed pH 6.88, a base excess of -18.9 and a lactate of 28. The infant was encephalopathic on examination and the decision was made to begin TH. The infant was then transferred to a tertiary Neonatal Intensive Care Unit and arrived at hour 10 of TH. NIRS and non-invasive cardiac output monitoring (NICOM) was commenced at that time).

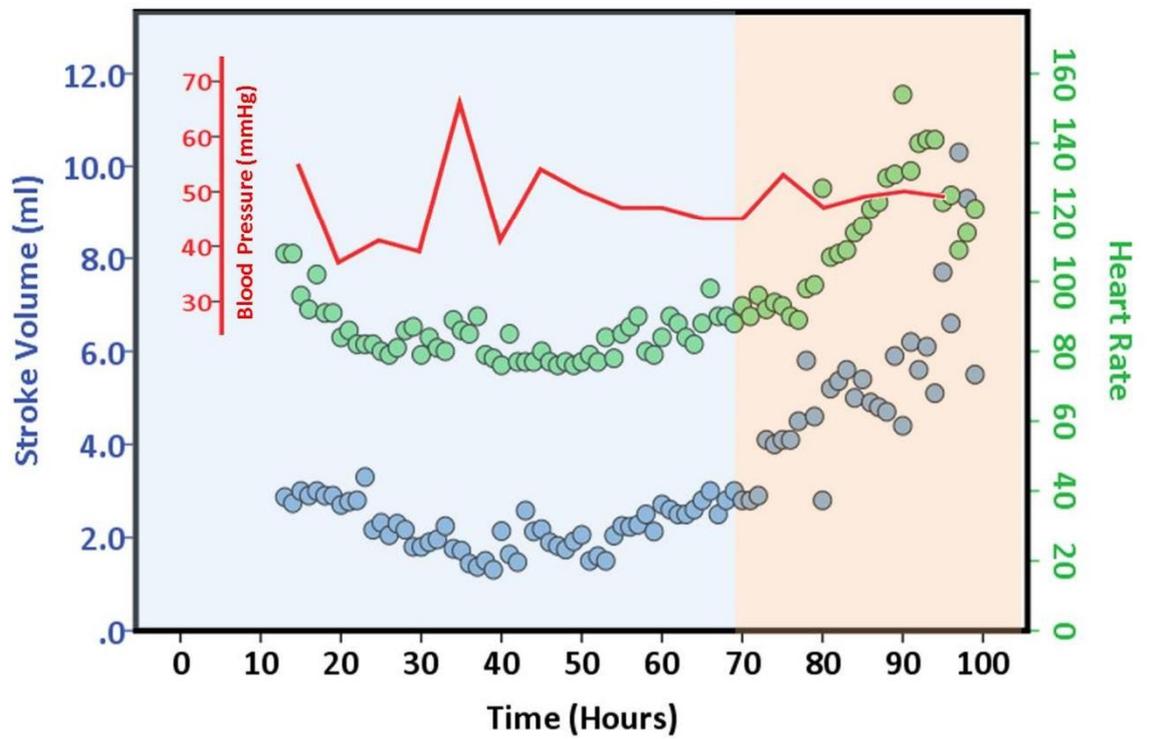
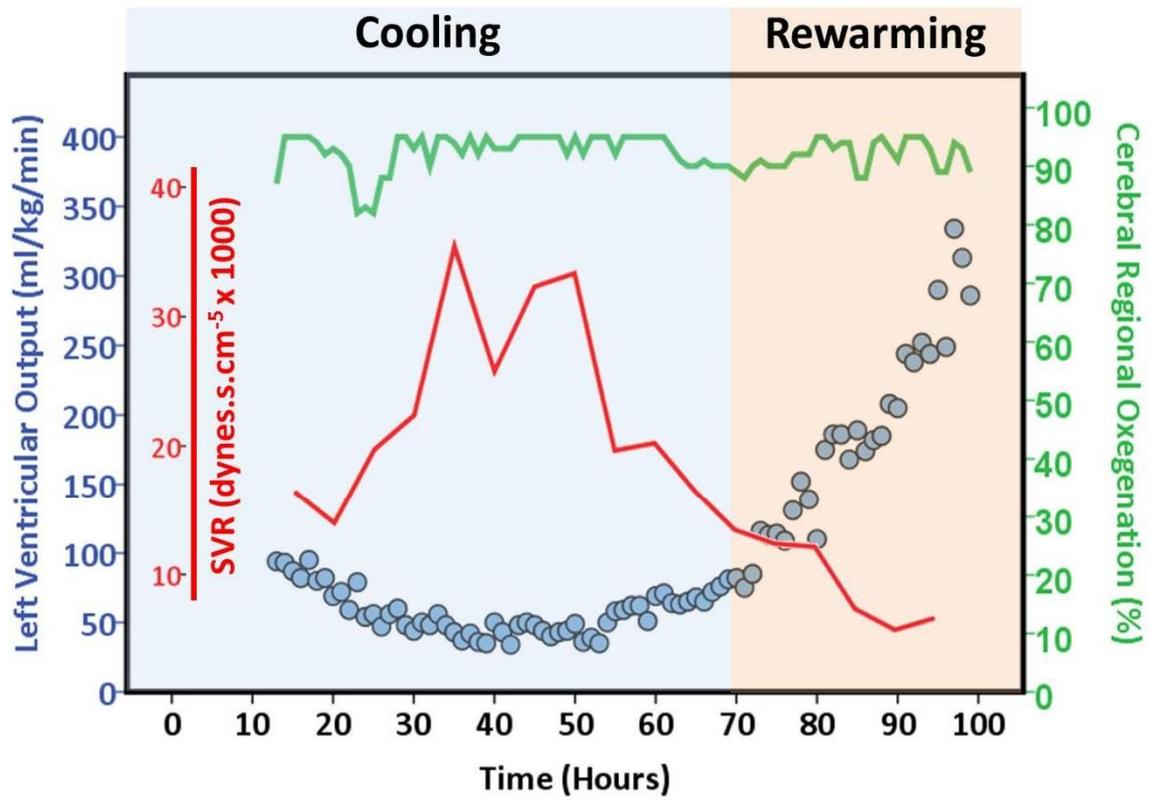
Focal seizures were noted at 20 hours of TH and the infant was commenced on phenobarbitone and midazolam. The infant became hypotensive at 26 hours of TH and was commenced on dopamine. The infant developed Persistent Pulmonary Hypertension at 32 hours of TH and was commenced on inhaled Nitric Oxide.

As demonstrated in the figure, cardiac output initially fell until hour 40 of TH when it began to plateau and recover before rewarming was commenced. The improvement in cardiac output was due to a combination of an increasing heart rate and stroke volume. The administration of Dopamine was associated with an increase in SVR and blood pressure but not cardiac output, SVR began to increase during the early stages of TH and slowly recover before re-warming was commenced. NIRS recorded CrO<sub>2</sub> demonstrated a fall during the initial seizure period.

### Conclusions

This data, for the first time, shows the effect of therapeutic hypothermia on both cardiac performance and brain tissue perfusion. It is hoped that following further research into the area, NICOM and NIRS can guide clinical management of infants undergoing therapeutic hypothermia. Monitoring the haemodynamic status of infants undergoing TH in real time may pave the way for more goal directed therapeutic interventions.

Picture



Nutrition and gastroenterology / Metabolism

## CONTINUOUS VENOVENOUS HEMODIAFILTRATION IN NEONATAL METABOLIC DECOMPENSATION (816)

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### Introduction /Case Report

The accumulation of toxic metabolites leads to the neurological deterioration of newborns with inborn error of metabolism (IEM) and is associated with high morbidity and mortality. Aggressive and adequate management of acute metabolic crises with restriction of protein intake, stabilization of patient, reversal of catabolism, and removal of toxic metabolites are essential steps. Continuous hemodiafiltration (CHDF) is a modality choice to treat acute metabolic decompensation in IEM. Here we aimed to report our neonatal cases, to whom we performed CHDF.

### Patients and Methods

This study is performed in Istanbul Medeniyet University, Goztepe Research and Education Hospital. We retrospectively searched our patient files with IEM, who were hospitalized in NICU between January 2010 and December 2014. Demographic characteristics, postnatal day of hospitalization, day of onset of symptoms, family history, parental consanguinity, laboratory findings such as serum aminoacid levels, serum ammonia levels, biochemical parameters before and during CHDF, total CHDF duration were recorded in patient data sheet. During the study period 14 patients received CHDF in our NICU.

### Results

We reached to the medical reports of 9 cases with neonatal metabolic decompensation and treated with CHDF. 8 of them received CHDF due to hyperammonemia, while the last 1 was treated for hyperleucinemia. 8 of them were referred to our hospital on  $12\pm 3$ rd days (min-max: 2,5 – 44th days) with the suspicion of IEM. Three were diagnosed as propionic acidemia, 2 were OTC, and 2 were type-1 citrullinemia, 1 of them was argininosuccinic acidemia and 1 of them was MSUD. We used Prisma and M-10 filter kit (Gambro, Meyziu, France) in two patients and Prisma-flex and HF-20 filter kit (Gambro, Meyziu, France) in seven patients. The patients maintained stable vital signs without hypotension and electrolyte imbalance during CHDF, except for one patient, who was severely hypotensive beside therapy and CHDF was terminated.

### Conclusions

Patients received CHDF for a mean of 48hrs. Mean ammonia levels were  $>2000 \mu\text{mol/l}$  at the beginning and decreased  $<500 \mu\text{mol/l}$  after 24hrs of CHDF. But this successful descent didn't prevent mortality of 8 patients who were referred with severe hyperammonia after several days. In countries where consanguineous marriages are habitual, rare and fatal IEM are very common. Early diagnosis and intervention during early neonatal period is life-saving and preventive for permanent brain damages.

Circulation, O2 Transport and Haematology / Transfusion and volume therapy

False positive neonatal toxoplasma serology following Fresh Frozen Plasma transfusion (324)

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## Introduction /Case Report

Congenital Toxoplasmosis in a neonate is a serious infection resulting from the vertical transmission of *Toxoplasma gondii*.

This is a rare case of false positive toxoplasma serology in a neonate after receiving Fresh frozen plasma. Transfusion-associated toxoplasmosis has been described in neonates but never from Fresh frozen plasma transfusion. Maternal ante-natal saved serology and baby's serology after three months were negative for toxoplasma indicating that it was a false positive toxoplasma serology.

We decided to present this case because of the rare presentation of findings, difficulty in interpretation of serology results and the sensitiveness of the diagnosis to the parents.

## Case Report

A male infant was born at term following emergency caesarean section for foetal distress. He was symmetrical IUGR. Weight was 2500 grams (0.4th centime ) and head circumference was 31.5 cm ( 2nd centile). He was born in a good condition with Apgars of 8 and 9 at 1 and 5 minutes respectively. Maternal medical and ante-natal history was unremarkable.

He was admitted to the neonatal unit at 4 hours of age in view of hypothermia of 35.50 C, hypoglycaemia of 1.6mmol/L, tachypnoea and prolonged bleeding from heel prick. The hypoglycaemia was corrected with IV fluids and his temperature normalised within few hours after admission. The coagulation screen was deranged. The prothrombin time was 26 seconds, INR was 2.2, activated partial thromboplastin time was 61 seconds and Fibrinogen was 0.4 g/l. This was corrected with vitamin K and a transfusion of FFP on day 1. His platelet count at admission was 58,000 and his platelet count improved spontaneously.

Cranial ultrasound scan done on day 2 showed speckles of intracranial calcification. Subsequently, serology for Toxoplasmosis was requested in view of the baby being Symmetrical IUGR, having a low platelet count and intracranial calcification. Both the IgM and IgG were positive. A blood sample from baby was sent for PCR but was deemed not suitable for analysis. PCR assay was inhibited by substances within the blood sample. Unfortunately, there was no blood sample from the baby prior to FFP to be tested for Toxoplasmosis serology. It was difficult to interpret the serology results and we were indecisive to start treatment. We decided to wait for serology results of mother's saved sample during pregnancy. Maternal ante-natal (saved blood sample) and post-natal Toxoplasmosis serology were tested and negative. Urine CMV PCR was negative.

Since maternal serology was negative, the baby's protective antibodies were most likely acquired from the FFP. The Blood transfusion service were confident the treatment and storage of FFP prior to transfusion prevents transmission of Toxoplasmosis.

The baby's Toxoplasmosis serology at 3 months was negative for both IgM and IgG and he did not show any signs of Toxoplasmosis infection. This indicates that the baby's initial positive Toxoplasmosis serology must have been acquired from FFP he received.

## Conclusions

Neonatal Toxoplasmosis serology has to be interpreted cautiously and should correlate with maternal serology. False positive Toxoplasmosis serology may follow transfusion of Fresh Frozen Plasma. Fresh Frozen Plasma is treated to remove Toxoplasmosis parasites. However blood donors with recent Toxoplasmosis infection may still have IgM antibodies. Antenatal maternal Toxoplasmosis serology will help to clarify the false positive serology.

## Epidemiology

### RESULTS OF OUR CENTER IN THE COMPARISON OF VERMONT OXFORD NETWORK CENTERS (872)

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## Introduction /Case Report

University of Debrecen, Medical Health and Science Center, Department of Neonatology and Pediatric Neurosurgery Center has been part of the Vermont Oxford Network (VON) since 2012. We are the only one VON center in Hungary.

## Patients and Methods

Data were collected on infants between 401-1500 grams or where the gestational age was between 22 weeks till 29 weeks and 6 days who were admitted to our unit within 28 days of birth without having first gone home and this data were entered into an international database. The information generated by the Vermont Oxford Network can be used for comparisons among hospitals providing similar levels of care.

## Results

Based on these data in our department in the last 3 years were measured better survival rate and survival without known morbidity, lower incidence of CLD, NEC, Cystic PVL and late onset sepsis compared to the average values of VON centers. The number of patients who needed extreme long of stay and the average length of stay had proven to be less in our institution. The number of exclusively human milk fed infants at discharge was notably higher compared to the average of VON centers. Incidence of severe ROP and PTX was higher in our department. National Pediatric Neurosurgery Center is working at our university wich explains the higher occurrence of severe intraventricular hemorrhage. Significant number of patients were admitted to our department for ventriculosubgaleal or ventriculoperitoneal shunt insertion because of posthaemorrhagic hydrocephalus.

## Conclusions

Comparison to network benchmarks enables to measure and will help us to improve our practices in areas that will be beneficial to our patients.

Nutrition and gastroenterology / Micronutrients

## THE USE OF SPECIALIZED FORMULAS FOR PRETERM NEWBORNS WITH CONGENITAL DEVELOPMENTAL DEFECTS OF THE DIGESTIVE TRACT (497)

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### Introduction /Case Report

Enteral feeding in preterm newborns experienced surgery on congenital developmental defects (CDD) of the digestive tract (DT) requires supply of essential ingredients to ensure biologically valuable psychophysical development. Breast milk is the base of natural feeding. In case of digestive disorders caused by DT CDD and surgery, changes of the intestinal functional state are found (insufficient breaking down, assimilation, absorption of nutrients, peristalsis), stipulating the necessity to use special formulas.

To analyze the use of the element amino acid formula «Nutrilon® Amino» in preterm newborns afflicted with CDD of the DT in the post-operative period.

### Patients and Methods

26 preterm newborns were observed after surgery on CDD of the DT. The control group included 25 healthy newborns. Laboratory findings of the functional intestinal state included: the level of albumin, alpha-1-antitripsin, secretory immunoglobulin A, fecal elastase 1, PMN-elastase, calprotectin by means of enzyme-bounded immune-sorbent method (ELISA), Community laboratory Cottbus, Germany; the content of lipids, starch and undigested food remains in coprogram and spectrum of intestinal microbiocenosis.

### Results

The results obtained were indicative of a positive effect after using the formula «Nutrilon® Amino» in preterm newborns which was proved by satisfactory food tolerance (absence of regurgitation, flatulence, stasis, frequent or delayed stools, pathological changes in coprogram) 10 days after use. Normalization of the functional state of the intestine was proved by the laboratory findings of coprofiltrate, disappearance of the signs of inflammation and decreased permeability of the intestinal mucus in particular, which was proved by normalization of the following signs:  $\alpha$ 1-antitripsin, calprotectin, albumin and sIgA, elastase level, PMN-elastase). The indices of coprogram and microbiocenosis of the intestine in infants corresponded to the norm.

## Conclusions

The element amino acid formula «Nutrilon® Amino», containing 100% protein replacement by essential and non-essential amino acids (AA), easily assimilated lipids, carbohydrates, vitamins and minerals, promotes normalization of food tolerance in preterm newborns undergone surgery on CDD of the DT enabling to ensure metabolic homeostasis corresponding to the growth and development of the body.

Circulation, O2 Transport and Haematology / Transfusion and volume therapy

PLATELETS FOR NEONATAL TRANSFUSION – STUDY 2: A RANDOMIZED CONTROLLED TRIAL TO COMPARE TWO DIFFERENT PLATELET COUNT THRESHOLDS FOR PROPHYLACTIC PLATELET TRANSFUSION TO PRETERM NEONATES (659)

SF Fustolo-Gunnink 1; JG van der Bom 1; P Clarke 2; A Curley 3; K Fijnvandraat 4; R Khan 5; E Lopriore 6; P Muthukumar 2; HV New 7; S Stanworth 8; V Venkatesh 9; T Watts 10; K Willoughby 5; A Deary 9

1 Sanquin Blood Supply Foundation, the Netherlands; 2 Norfolk and Norwich University Hospitals NHS Trust, Norwich, United Kingdom; 3 The National Maternity Hospital, Dublin, Ireland; 4 Academic Medical Center Amsterdam, the Netherlands; 5 Cambridge University Hospitals NHS Trust, United Kingdom; 6 Leiden University Medical Center, Leiden, the Netherlands; 7 Imperial College Healthcare NHS Trust/NHS Blood and Transplant, London, United Kingdom; 8 Oxford University Hospitals NHS Trust, Oxford, United Kingdom; 9 NHSBT Cambridge, Cambridge, United Kingdom; 10 Guys and St Thomas NHS Trust, United Kingdom.

### Introduction /Case Report

Preterm neonates with severe thrombocytopenia ( $<50 \times 10^9/L$ ) often receive platelet transfusions, with the aim to prevent major bleeding. However, the efficacy and safety of prophylactic platelet transfusions is unknown, resulting in significant variation in transfusion practices worldwide. No randomized controlled trials support current transfusion guidelines and several observational studies suggest that widely used transfusion thresholds can be lowered without increasing bleeding risk. The objective of this study is to assess whether a higher prophylactic platelet transfusion threshold is superior to a lower threshold in reducing the proportion of neonates who experience a major bleed.

### Patients and Methods

International, randomized, parallel group, superiority trial comparing clinical outcomes in 660 preterm neonates allocated to receive prophylactic platelet transfusions below thresholds of  $25 \times 10^9/L$  or  $50 \times 10^9/L$ . Neonates with a gestational age of  $<34$  weeks at birth and a platelet count of  $<50 \times 10^9/L$  are included. Weekly cerebral ultrasound scans and daily observational bleeding assessments using a validated bleeding assessment tool are performed. Extensive educational packages have been developed to support participating centers. The primary outcome measure is a composite of mortality and the occurrence of a major bleed within the first month after randomization. Neurodevelopmental follow up at 2 years corrected age will also be assessed.

### Results

The trial is ongoing: 373 neonates have now been randomized by 44 centers in the United Kingdom, Ireland and the Netherlands. An interim independent safety analysis done after 100 randomizations allowed recruitment to continue. Maintaining high inclusion rates has been challenging due to variable rates of thrombocytopenia and eligible babies per center, but recruitment is satisfactory and is now rising. Trial quality is monitored and maintained through regular principal investigator and research-nurse meetings. If superiority is demonstrated, the incidence of bleeding can be reduced by implementing higher transfusion thresholds. If superiority is not demonstrated, the potential benefits of the lower threshold may include

fewer transfusions, reduced donor exposure, lower risk of transfusion related adverse effects, including errors in processing and administration, and reduced costs.

## Conclusions

This is the first randomized controlled trial assessing currently used platelet transfusion thresholds in neonates and an example of successful international collaboration in neonatal research. Enrolment is expected to finish in 2017. The results of this trial will have important implications for neonatal transfusion practices.

NOREPINEPHRINE FOR THE MANAGEMENT OF HYPOTENSION IN PRETERM AND FULL-TERM NEONATES (760)

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Introduction /Case Report

Hypotension represents a serious complication in critically ill newborns. Severe hypotension is associated with a higher incidence of intraventricular haemorrhage and an adverse neurodevelopmental outcome. Early initiation of inotropic and/or vasoactive agents is recommended to increase cardiac output and thereby oxygen delivery to the tissue. Dopamine and dobutamine are the most commonly used pharmacological agents in the treatment of newborn hypotension. Norepinephrine can be suggested as an alternative medicine in the management of hypotension in neonates. In this retrospective observational study, we evaluated the haemodynamic effects of norepinephrine in neonates with hypotension.

Patients and Methods

A retrospective cohort study from June 2012 until December 2013 in a neonatal intensive care unit was performed. All neonates treated with norepinephrine for the management of hypotension were included. The initial dosage of norepinephrine varied from 0,04 to 0,1 mcg/kg/min; the rate of infusion was adjusted to reach the targeted mean blood pressure. Haemodynamic parameters were recorded just before and 4 hours after starting norepinephrine. Furthermore, the same parameters were also recorded just before and 4 hours after the effective dosage of norepinephrine. The primary outcome measure was the change in blood pressure. Secondary outcomes were effects on the cardiac function, effects on the pulmonary condition, effects on tissue perfusion and adverse effects during hospitalization.

Results

In total 17 infants were analysed with a median gestational age of 33+6 weeks. Before starting norepinephrine the infants received a mean dosage of dopamine of  $11 \pm 5$  mcg/kg/min and/or dobutamine of  $9 \pm 5$  mcg/kg/min. After starting norepinephrine the mean systemic blood pressure increased from  $33 \pm 8$  to  $37 \pm 6$  mmHg ( $p=0,01$ ) within the first 4 hours of norepinephrine infusion. Blood lactate concentration decreased from  $3,7 \pm 2,8$  to  $2,7 \pm 2,0$  mmol/l ( $p=0,088$ ). Urine output increased from  $2,2 \pm 2,3$  to  $4,1 \pm 3,6$  ( $p=0,017$ ). The mean norepinephrine dosage to correct the systemic hypotension was  $0,3 \pm 0,3$  mcg/kg/min. The mean systemic blood pressure increased from  $35 \pm 7$  to  $43 \pm 11$  mmHg ( $p=0,002$ ) within the first 4 hours after the effective dosage of norepinephrine. Despite an initial correction of hypotension, 7 infants died later.

Conclusions

Treatment with norepinephrine in the management of hypotension resulted in a sufficient increase of systemic blood pressure. Moreover, a decrease in blood lactate concentration and an increase in urine output suggest that norepinephrine may have improved cardiac function and tissue perfusion. A

prospective cohort study has started to echocardiographically evaluate the effect of norepinephrine on central blood flow.

Table

Table 1. Haemodynamic parameters just before and 4 hours after starting norepinephrine

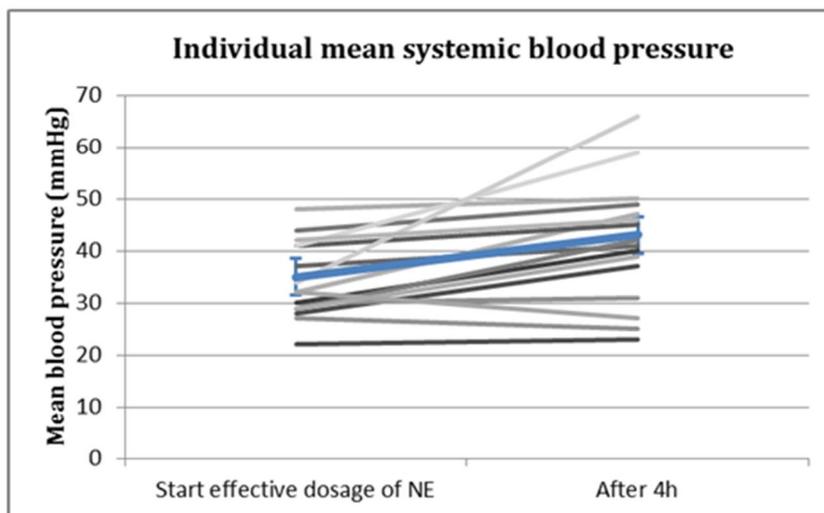
Characteristics	Start NE (N=17)	After 4h (N=17)	p value
MBP (mmHg)	33±8	37±6	0,013*
Heart rate (bpm)	161±33	161±30	0,554
pH	7,16±0,1	7,18±0,1	0,649
Lactate (mmol/l)**	4,0±3,0	2,9±2,1	0,088
Urine output (ml/kg/h)	2,2±2,3	4,1±3,6	0,017*

Data are expressed as mean±SD. NE, norepinephrine; MBP, mean blood pressure; bpm, beats per minute.

\* A significant difference after the initiation of treatment with norepinephrine

\*\* Data missing for 2 infants

Picture



Individual mean systemic blood pressure measured just before and 4 hours after the effective dosage of norepinephrine. The blue line represents the mean systemic blood pressure of all infants (±SD, outer dots). NE, norepinephrine.

Pulmonology / Delivery room management

## CAFFEINE AUGMENTS RESPIRATORY EFFORT OF PRETERM INFANTS AT BIRTH (460)

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### Introduction /Case Report

Preterm infants are most vulnerable immediately after birth. Intubation and mechanical ventilation are now avoided as the focus of respiratory care has shifted to non-invasive respiratory support. Although most preterm infants breathe at birth, their respiratory effort is often weak. Caffeine is a safe and effective treatment to stimulate breathing in the NICU, but the effect has not been investigated directly after birth. We aimed to investigate the effect of caffeine on the respiratory drive in preterm infants at birth.

### Patients and Methods

Infants <30 weeks GA receiving caffeine base (10 mg/kg) directly after birth were compared to infants receiving caffeine after arrival in the neonatal unit (standard care) in a randomized controlled trial. Respiratory function measurements (gas flow, heart rate, oxygen saturation and supplemental oxygen) were recorded using a monitor (Advanced Life Diagnostics, Weener, Germany). The primary outcome was the minute volume achieved during spontaneous breathing at 7-9 minutes of age. Respiratory rates, tidal volumes, rate of rise to the maximum tidal volume (respiratory effort) were also calculated. Data from 27-29 week infants are reported herein.

### Results

Fourteen infants at 27-29 weeks GA were included; 7 infants received caffeine at birth (at mean(sd) 4:22(1:22) min) and 7 infants received standard treatment (median (IQR) GA (28(27-28) vs 29(28-29) weeks; ns, birthweight 1042(820-1527) vs 960(740-1400) grams;ns). There was a trend towards a higher minute volume at 7-9 minutes after birth in the caffeine at birth group (mean (SD) (258(58) vs 182(69) ml/kg/min;  $p=0.08$ ). Although the respiratory rate was not different between groups (42(9) vs 35(10) breaths/min;ns),  $V_{ti}$  was significantly higher in the caffeine at birth group (5.9(2.8) vs 4.9(2.8) ml/kg), as was the rate of rise to the maximum tidal volume (18.0(8.5) vs 13.2(6.5) ml/kg/sec). While, the oxygen saturation was similar (89(5) vs 88(8)%;ns), the caffeine at birth group had a lower  $FiO_2$  (27.7(7.9) vs 44.4(30.1)) and a higher pulse rate (156(17) vs 146(10) bpm).

### Conclusions

In preterm infants, caffeine administration during transition at birth augments the respiratory drive, resulting in lower oxygen requirements.

Pulmonology / Delivery room management

## EVALUATION OF ELECTIVE FAMILY CENTERED CAESAREAN SECTIONS IN A TERTIARY CARE HOSPITAL IN THE NETHERLANDS (507)

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### Introduction /Case Report

Since July 2014 elective family centered caesarean sections (FSCSs) are performed in singletons >38 weeks of gestation. In FSCSs the infants are placed on mothers chest directly after birth, enabling direct skin-to-skin contact and breastfeeding within 30 minutes. We aim to evaluate the FSCSs to assess the safety of FSCSs in this target group.

### Patients and Methods

Pulse oximetry data of infants born after FSCS were collected and compared to data of regular caesarean sections (CS) performed at infants >38 weeks of gestation in 2013. Pulse oximetry data of the first 10 minutes, percentage of hospitalization at the NICU, and first temperature at the maternity were obtained.

### Results

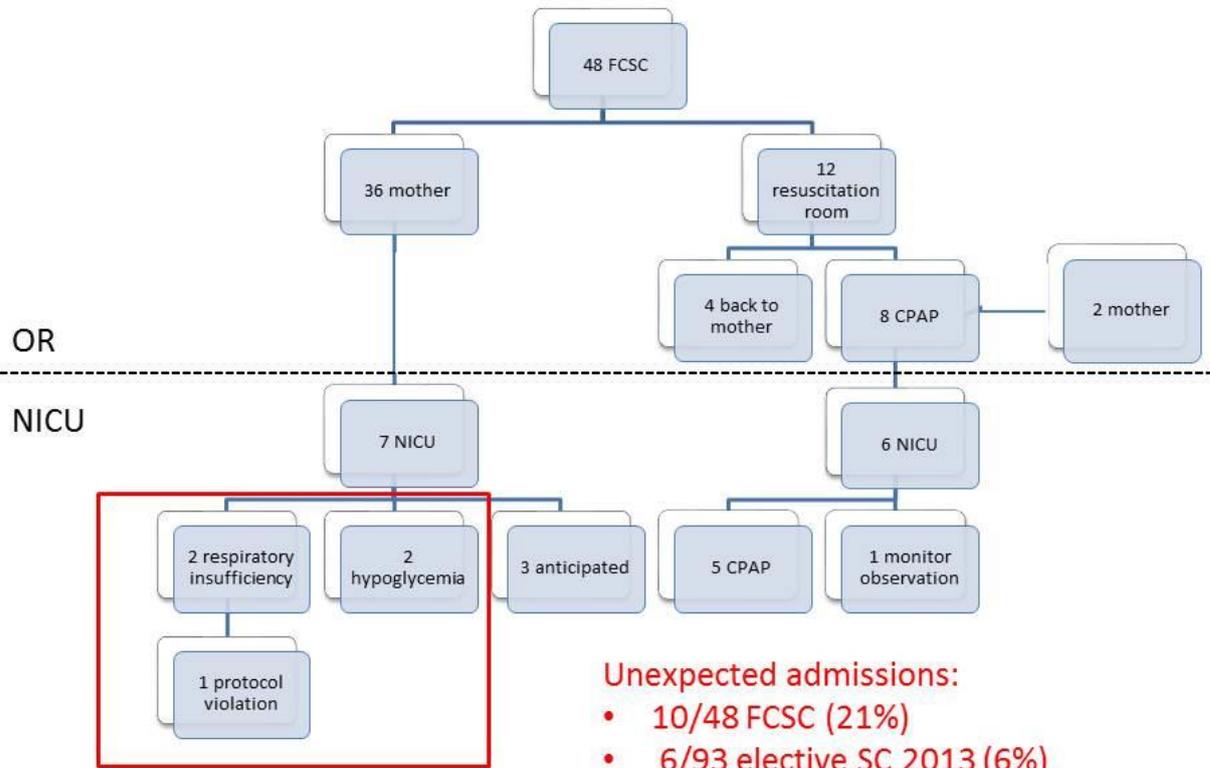
48 FSCSs were performed, of which 36 stayed with their mother during the procedure, and 12/48 infants (25%) were assessed in the resuscitation room, with 8 infants needing CPAP. 6/12 infants could go back to their mother and 6 were admitted to the NICU with CPAP (5/6) and/or monitor observation. 7/36 infants that stayed with their mother were admitted to the NICU after the procedure: 2 with hypoxemia (1 protocol violation due to hypoxemia directly after birth), 2 with hypoglycaemia and 3 were anticipated. Hypothermia did not occur at arrival at the maternity ward. In total 13/48 (27%) infants with FSCS were admitted to the NICU, of which 10 unexpected (21%). In the cohort of elective CS in 2013 6% infants were unexpectedly admitted to the NICU. There was no significant difference in SpO<sub>2</sub> and heart rate values, nor in gestational age, birth weight and Apgar scores between the two cohorts.

### Conclusions

After FSCS more unexpected admissions to the NICU occurred (21% versus 6% in the regular CS group). Infants needing respiratory support are well recognized when adhering to the protocol. Monitoring of these infants is necessary to guarantee safety. Hypothermia did not occur and Apgar scores were good. There was no clinical significant difference in heart rate and SpO<sub>2</sub> between infants with FSCS or regular elective CS.

Picture

CPAP: Continuous Positive Airway Pressure  
FCSC: Family centered Caesarean Section  
NICU: Neonatal Intensive Care Unit  
OR: Operating Room



Epidemiology / Host responses and early diagnosis of infection

## EVALUATION OF THE RELATIONSHIP BETWEEN INFLAMMASOMES' FUNCTIONS AND THE RISK OF LATE-ONSET SEPSIS IN PRETERM INFANTS. (548)

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### Introduction /Case Report

Inflammasomes are multiprotein complexes that regulate activation of the cysteine protease caspase-1. Activated caspase-1 cleaves the cytokine precursors: pro-interleukin 1 $\beta$  (pro-IL-1 $\beta$ ) and pro-IL-18. This process is critical for the release of their biologically active forms (IL-1 $\beta$  and IL-18) and triggers proinflammatory and antimicrobial responses. Till now there have been no studies evaluating the role of inflammasomes in pathogenesis of sepsis in preterm babies.

### Patients and Methods

43 preemies without symptoms of early-onset sepsis (gestational age  $\leq$  32 weeks, mean birth weight 1062g) were enrolled into the study. Blood samples were collected on the 5th day of life (5th DOL). During hospitalization in NICU subjects underwent prospective monitoring for signs of late-onset sepsis (LOS). 3 subgroups of samples were obtained: A1—collected on the 5th DOL from newborns without LOS (n=24), B1—collected on the 5th DOL from newborns with at least 1 episode of LOS (n=19), B2—collected from group B1 with initial LOS symptoms. The percentage and absolute number of monocyte subsets in the peripheral blood and the level of IL-1 $\beta$  cytoplasmic expression after LPS stimulation was analyzed by flow cytometry. Study supported by National Science Center, Poland: grant number: DEC-2012/07/B/NZ5/01221

### Results

Groups A1 and B1 were comparable regarding birth weight, gestational age and absolute counts of monocyte subsets. Significant difference with respect to the percentage of non-classical monocytes with intracellular IL-1 $\beta$  expression after LPS stimulation (67 vs. 30%; p=0.02) was observed between them. Mean fluorescence intensity (MFI) of IL-1 $\beta$  after LPS stimulation in monocytes from the A1 was higher than from the B1 group (classical: 727 vs. 173; p=0.04; intermediate: 656 vs. 108; p=0.09; non-classical: 632 vs. 263; p=0.016). At the beginning of LOS significant increase in the number of intermediate monocytes was noticed (562 vs. 83/ul; p=0.012; B2 vs. B1) and the higher percentage of intermediate (72 vs. 45%; p=0.031) and non-classical (73 vs. 30%; p=0.0063) monocytes with intracellular IL-1 $\beta$  expression and higher MFI of IL-1 $\beta$  (984 vs. 108; p=0.029 and 540 vs. 263, p=0.004, respectively) was observed (B2 vs. B1).

### Conclusions

In preemies with LOS during hospitalization, in all monocytes' subsets an initially lower level of IL-1 $\beta$  expression (MFI), and lower percentage of IL-1 $\beta$ (+) non-classical monocytes was observed, what may suggest, that inflammasome function in preterms prone to bacterial infection is not fully developed. Relatively high IL-1 $\beta$  production in children without septic symptoms during hospitalization may be connected with protection against sepsis in vivo.

## Epidemiology

### COMPARATIVE STUDY OF FREQUENCY AND SEVERITY OF NEONATAL JAUNDICE WITHOUT A KNOWN ETIOLOGY IN TWO GROUPS OF TERM NEONATE BORN VIA CESAREAN SECTION AND VAGINAL DELIVERY (022)

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## Introduction /Case Report

Neonatal jaundice has a significant prevalence, and in severe cases, causes permanent neurological Sequela. Many studies have carried out on neonatal jaundice and its predisposing and exacerbating factors. On the other hand, delivery method (cesarean vs vaginal) has been suggested as a predisposing factor for many of neonatal complications in many studies. The aim of this study is to investigate and compare frequency and severity of neonatal jaundice without a known etiology in two groups of term neonate born via cesarean section and vaginal delivery.

## Patients and Methods

Samples included 182 term 7 days old neonates with minimum serum bilirubin of 5 mg/dl. Half of these neonates were born via cesarean delivery and half of them born via vaginal delivery. All of these neonates had neonatal jaundice without a known etiology. The data of the two groups was compared with statistical tests.

## Results

Mean serum bilirubin in the neonates was 9.60 mg/dl (SD=3.21 mg/dl). Mann-Whitney test showed that there is not any significant relationship between serum bilirubin value and the delivery method (P=0.53). Bilirubin value in the group with the family history of jaundice in siblings was significantly higher than the group without the family history (P=0.003). Mothers with the age of < 20 years had the least serum bilirubin levels (P=0.01). Serum bilirubin level did not have significant relationship with neonatal sex. Neonatal bilirubin levels had a significant relationship with the type of cesarean indications (P=0.01).

## Conclusions

There is not any significant relationship between serum bilirubin level in neonates and type of delivery method (vaginal vs cesarean). However, the results of investigations in this field are controversial and additional studies are recommended.

## Epidemiology

### COMBINED EVALUATION OF CORD BLOOD VITAMIN D LEVELS IN HEALTHY NEWBORNS: SIX-MONTH FOLLOW-UP OUTCOMES (064)

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#### Introduction /Case Report

Vitamin D, one of the oldest known hormones, is does not only have an effect on calcium homeostasis and bone formation, but also on hormone secretion, immune functions, cell proliferation, and differentiation . It has been suggested to play a role in a number of autoimmune diseases, in particular, thanks to its modulator effect on immune system. However, recent studies have shown that vitamin D deficiency may cause vulnerability for infection development in newborns . The current study aimed to evaluate the possible effects on child development of cord blood vitamin D levels of healthy babies born to healthy mothers and the rate of infections within the first six months of life.

#### Patients 265and Methods

This prospective study included a total of 81 healthy term newborns to healthy mothers who gave birth after the completion of the 37th week of pregnancy with a birth weight of > 2500 g. A cord blood sample of 2 mL was drawn immediately after birth from the cord blood for 25(OH) vitamin D analysis. Babies were initiated on a vitamin D prophylaxis at a dose of 400 IU/day, when they were 15 days old with a six-month follow-up. The daily amount of time that the babies spent outdoors in sunny weather for six months, the amount of time keeping the head upright, the number of infections within the first six months, type of feeding, and the weight of the babies at six months were recorded. Venous blood samples were obtained for the 25(OH) vitamin D analysis, when the babies were 6 months old.

#### Results

The mean birth wee

k and birth weight of the babies were  $39\pm 0.8$  weeks and  $3341\pm 347$  g, respectively. The mean cord blood and six-month vitamin D levels were  $7.0\pm 6.6$  ng/mL and  $39.7\pm 12.3$  ng/mL, respectively. The number of babies keeping the head upright at two months, three months, and four months were 28 (34.6%), 38 (46.9%), and 15 (18.5%), respectively. Forty babies (49.4%) had only one infection and seven (8.6%) babies had two episodes of infections, whereas 34 (42%) babies had no infection episodes within the first six months. There was no association between the cord blood vitamin D levels and season of birth, number of infection episodes, and the amount of time keeping the head upright. In addition, vitamin D levels at six months were not associated with the number of infection episodes, amount of time keeping the head upright, gender, duration of sun exposure, and season of birth.

#### Conclusions

In conclusion, our study results suggest that vitamin D deficiency as assessed in the cord blood samples is unlikely to be associated with early or late neonatal sepsis and increased number of infections within the

first six months of life. Although vitamin D gene polymorphism may play a role in asymptomatic individuals. Further large-scale, randomized-controlled studies are required to establish a conclusion.

Circulation, O<sub>2</sub> Transport and Haematology / Microcirculation and oxygen transport

## CEREBRAL AND HEPATIC REGIONAL OXYGEN SATURATION IN NEONATES WITH POST-ASPHYXIA ENCEPHALOPATHY ON BRAIN HYPOTHERMIA (673)

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### Introduction /Case Report

Brain and liver are large organs receiving 40% and 20% of total blood flow of the body, respectively. Previous studies have reported regional oxygen saturation (rSO<sub>2</sub>) at the head, peri-renal or abdominal region using near-infrared spectroscopy in the newborn. However, no data on rSO<sub>2</sub> at the hepatic region have been reported. The aim was to measure cerebral and hepatic regional oxygen saturation simultaneously and to study the relationship with other circulatory indices.

### Patients and Methods

The subjects were 5 newborn infants admitted to the NICU of Tokai University Hospital in the period 1/2013-12/2014 who underwent hypothermia therapy for hypoxic ischemic encephalopathy (HIE) following severe asphyxia. Their gestational age ranged 35-41 weeks, birth weight 2076-3256g and 0-5 postnatal days. The rSO<sub>2</sub> was measured using INVOSTM 5100C (Covidien Japan, Tokyo, Japan). Regional tissue saturation of the head (rSO<sub>2</sub>-H) and the liver (rSO<sub>2</sub>-L) were continuously monitored and recorded. The averaged values for each day were calculated and studied for correlation with mean blood pressure (MBP), arterial oxygenated hemoglobin concentration (O<sub>2</sub>Hb), and resistance index of anterior cerebral artery (ACA-RI).

### Results

Compared with values in uncomplicated stable newborns, rSO<sub>2</sub>-H was significantly higher (61-95%, median 88%) during hypothermia and tended to remain high (57-95%, median 92%) after re-warming. In contrast, rSO<sub>2</sub>-L tended to be low only during hypothermia (49-75%, median 61%; 51-77%, median 72%). Both rSO<sub>2</sub>-H and rSO<sub>2</sub>-L showed a positive correlation with O<sub>2</sub>Hb ( $r^2=0.29$ ,  $p<0.01$ ;  $r^2=0.57$ ,  $p<0.001$ ; respectively) but not with MBP or ACA-RI.

### Conclusions

1) High rSO<sub>2</sub>-H in neonates with HIE under hypothermia therapy may indicate increased cerebral blood flow in the phase of post-ischemic reperfusion. Low rSO<sub>2</sub>-L may be linked to decreased oxygen delivery due to impaired hepatic and systemic circulation as well as anemia. 2) The rSO<sub>2</sub>-H and rSO<sub>2</sub>-L monitoring is a useful tool for the assessment of systemic and cerebral circulatory status and hence for the management of HIE.

Table

	Day2 (during hypothermia)			Day4 (after re-warming)		
	rSO <sub>2</sub> -H	rSO <sub>2</sub> -L	H/L	rSO <sub>2</sub> -H	rSO <sub>2</sub> -L	H/L
HIE n=5	88 (61-95)	*61 (49-75)	*1.4 (1.2-1.6)	92 (57-95)	72 (51-77)	1.3 (1.1-1.6)
Control n=12	78 (67-91)	78 (68-84)	1.0 (0.9-1.1)	69 (69-72)	71 (66-79)	1.0 (0.9-1.1)

median (range) \*p <0.05

## Pulmonology / Surfactant

### WALK THE TALK! WHY IS IT SO HARD TO DO? (168)

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#### Introduction /Case Report

Recent guidelines confirm that right surfactant dose (poractant alpha, curosurf<sup>®</sup>, Chiesi Pharmaceuticals, Parma, Italy) in respiratory distress syndrome (RDS) is 200mg/kg (Grade A recommendation). Our mobile NICU performs newborns transfers from more than 30 maternity hospitals to one NICU, representing the quarter of the greatest region of France. The aim of this study was to evaluate if the amount of surfactant instilled in preterm babies with RDS before or during the transfer was in compliance with guidelines and if the new guidelines changed team practices.

#### Patients and Methods

We retrospectively analyzed the doses of poractant alpha instilled during the 24 first hours of life in preterm neonates with RDS, by local pediatric team (LPT) or by the transfer team (during 2011-2014). Data were extracted from data sheets filled by transfer team and confirmed cross-matching with hospital institutional database.

We considered dose of 200mg/kg  $\pm$  10% as correct and classified doses in categories: under 150mg/kg (110%).

#### Results

258 surfactant instillations were performed by local team and 327 by the transfer team. Results are shown in Table 1. About half of patients received the good dose. Even when LPT uses very low dose, the transfer team performs supplementary dose only in 4% of the cases (n=13). 40% and 25% of patients were undertreated by LPT and the transfer team, respectively. When comparing doses instilled by years, we could not highlight any change in terms of doses, even in 2014 (new European guidelines published in May 2013). Economic reason (use only half of a package), miscalculation of the weight or ignorance of guidelines could be explanations.

#### Conclusions

The dose of surfactant instilled, despite recommendations, remains insufficient in 20 to 40% of the cases for outborn preterm babies. Even if larger studies could specify reasons of this, new packaging and wider guidelines diffusion could improve practices.

Table

Table 1:

	<b>Local Pediatric Team</b>			<b>Transfer team</b>		
	(n)	(%)	Lack (mg)	(n)	(%)	Lack (mg)
<b>&gt;110% dose</b>	34	13%		68	21%	
<b>90%≤doses≤110%</b>	120	47%		177	54%	
<b>75%≤ dose&lt;90%</b>	60	23%	59 [38-72]	56	17%	53 [30-80]
<b>&lt;75% dose</b>	44	17%	146 [106-210]	13 + 13	4% + 4%	94 [48-220]
<b>Total</b>	258	100%		327	100%	

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

Double Trouble in a Bubble (759)

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### Introduction /Case Report

We present term infant of a diabetic mother, with a rare complication of respiratory distress syndrome - a large tension pneumopericardium, together with a pneumothorax, requiring urgent pericardiocentesis.

### Case Report

A baby boy born at 37 +4 weeks gestation by normal vaginal delivery after induction for maternal gestational diabetes. He was in good condition at birth but reviewed at 1 hour of age as he was grunting, commenced on CPAP at 5cms. He continued to deteriorate and his oxygen requirements increased, grunting persisted and he became agitated on CPAP and so changed to Vapotherm at 8L/M at 16 hours of age.

This support continued until the baby was 47 hours old when he had a sudden and severe collapse, saturations dropped to 40-55%, in 100% Oxygen via Vapotherm, blood pressure was unrecordable, he had weak pulses, and poor perfusion. Gases showed mixed acidosis with rising lactate.

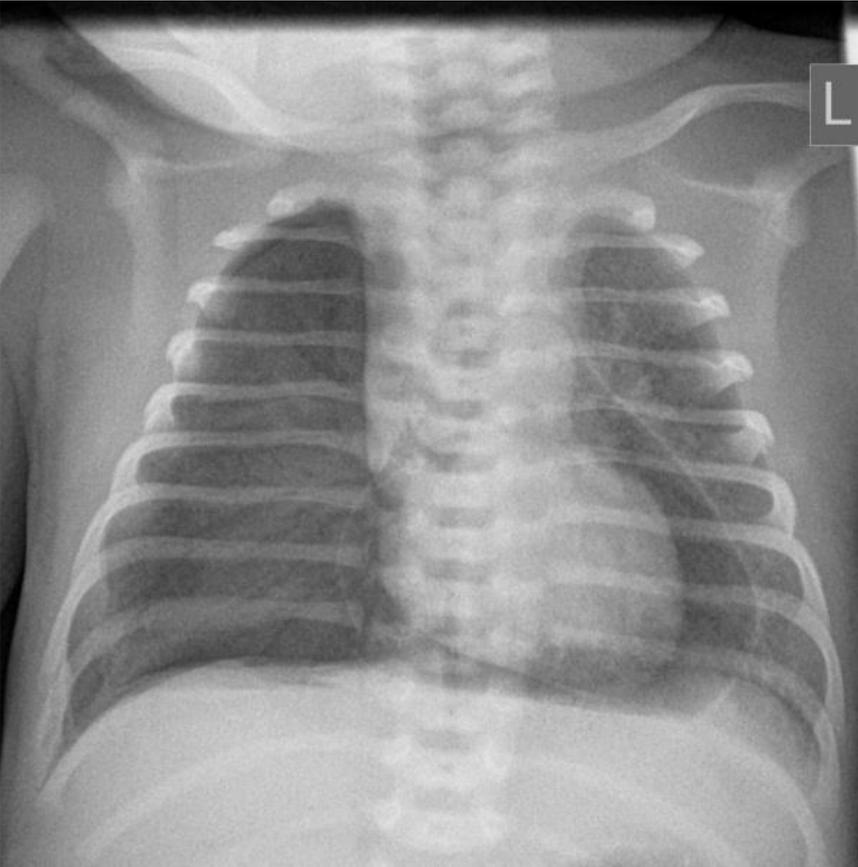
The chest X-Ray showed a right sided pneumothorax and a significant pneumopericardium, with the heart encapsulated in a bubble of air. The heart size was significantly smaller than on the initial film, demonstrating tamponade.

The pneumopericardium was drained, under sterile conditions, using 22g cannula inserted to left of xiphisternum, at an angle of 30 degrees to the skin, aiming for the left shoulder tip, 15ml of air was aspirated. The baby was then intubated and ventilated, paralysed and a drain inserted to right sided pneumothorax, arterial access was obtained. The baby stabilised and repeat CXR showed resolution of the pericardial air and successful drainage of the pneumothorax. Baby was extubated successfully two days later, and discharged home four days after that.

### Conclusions

It is important to recognise the rare complication of a tension pneumopericardium as it requires urgent intervention. Pericardiocentesis is a life saving and straightforward procedure, but is rarely performed on neonatal units.

Picture



## Epidemiology

### RENAL REPLACEMENT THERAPY IN NEWBORNS – 30 YEARS OF EXPERIENCE IN UHC ZAGREB (746)

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## Introduction /Case Report

Acute kidney injury (AKI) is a common occurrence in critically ill neonates in the intensive care unit. Over the past several decades, the epidemiology of acute kidney failure (AKF) in neonates (defined as need for dialysis) has changed significantly, as well as survival. We analysed change of indications, method of renal replacement therapy (RRT) and survival in Croatia over the past three decades in newborns.

## Patients and Methods

Medical records of newborns from 1982 and 2014 were investigated to discover patients who needed RRT before age of 30 days. Age, gender, diagnose, method of dialysis, and survival were recorded for all patients

## Results

: Acute dialysis was done in 47 newborns. Most of them were boys (63.8%). Until 2004, only available method was acute peritoneal dialysis and over the past decade in 90% of cases we used continuous RRT. Before 2005 the most common indication for acute dialysis were sepsis (41.9%) and AKF after surgery for congenital heart defect (CHD) (35.5%). Mortality is still high and was 68% before, and 56.3% after 2005.

## Conclusions

Survival of critically ill neonates in the ICU has improved over the past decades reflecting improvements in obstetric, delivery room and neonatal intensive care and that could be the reason that the indication for dialysis moved from sepsis and CHD to rare metabolic disorders and severe asphyxia with multiorgan failure. Unfortunately, mortality is still high possibly due to late introduction of RRT, which could be improved with new RIFLE classification

Pulmonology / Mechanical ventilation

## A RETROSPECTIVE STUDY OF EXTUBATION PRACTICES AND SUCCESS RATES IN A COHORT OF EXTREMELY PREMATURE INFANTS IN A TERTIARY NEONATAL CENTRE (589)

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### Introduction /Case Report

Extremely premature infants frequently receive invasive respiratory support. Mechanical ventilation can be damaging to the preterm lungs therefore, current emphasis is on early extubation to non-invasive ventilation such as continuous positive airway pressure to counter this. However extubation readiness is difficult to predict and very premature infants often require several extubation attempts before successfully transitioning on to non-invasive ventilation. Our goal was to review the attempts and success rates of extubation for a cohort of Scottish extremely preterm infants in a tertiary neonatal centre.

### Patients and Methods

This was a retrospective cohort study of the Badger electronic database for a large Glasgow tertiary neonatal centre between December 2010 to March 2015. Inborn and outborn infants with gestational ages between 23+0 and 28+6 weeks post menstrual age were included. Infants who died before 40 weeks corrected gestational age were excluded. The primary aim was to review extubation attempts in this cohort of infants. Outcomes that were assessed included: age at first extubation attempt, number requiring reintubation, time when reintubation was necessary, the number of extubation attempts and age when extubation was successful (defined as not requiring reintubation within 7 days) as well as the percentage requiring post natal steroids and the median number of courses they received.

### Results

115 infants were eligible for inclusion for this study. All of them were intubated at delivery. In the younger gestational age group (23-25 weeks gestational age at birth), the percentage successfully extubated at first attempt was low (0-16.7%) whereas this ranged from 42.9-59.3% in the higher gestational age group (26-28 weeks gestation at birth). The median day of successful extubation was higher in the 23-25 week gestation infants (day 20-36) compared to the more mature cohort (day 2-3). In the younger gestation group, the median number of extubation attempts was higher than in the older gestation group. Also if an infant required reintubation, a significant percentage (29.4-75%) of infants required to be reintubated within 24 hours regardless of gestation. Lastly, the number requiring post natal and DART courses were also higher in the 23-26 week gestation than the 27-28 gestation.

### Conclusions

Successful extubation of extremely preterm infants is challenging. Success rates decrease with decreasing gestation age. Vice versa, the number of extubation attempts and age at successful extubation decreases with increasing gestation age.

Table

Gestation (number of infants)	Age at 1 <sup>st</sup> extubation attempt days*	Infants successfully extubated on 1 <sup>st</sup> attempt n(%)	Age at successful extubation days*	Number of extubation attempts*	Extubation attempt duration if unsuccessful		Number requiring post natal steroids n(%)	Number of DART courses received*
					≤24 hours	>24 hours- <7 days		
23 (6)	16 (7-36)	1 (16.7%)	36 (32-42)	3 (1-5)	8 (100%)	0 (0%)	4 (66.6%)	1.5 (1-3)
24 (14)	6 (1-56)	1 (7.1%)	36 (2-66)	3 (1-5)	10 (52.6%)	9 (47.4%)	9 (64.3%)	1 (1-2)
25 (10)	2 (1-22)	0 (0%)	30 (2-45)	3 (2-7)	16 (84.2%)	3 (15.8%)	4 (40%)	2 (1-2)
26 (28)	3 (1-65)	12 (42.9%)	20 (1-65)	2 (1-5)	16 (69.6%)	7 (30.4%)	9 (32.1%)	1 (1-3)
27 (30)	2 (1-26)	15 (50%)	3 (1-45)	2 (1-4)	12 (75%)	4 (25%)	4 (13.3%)	1
28 (27)	2 (1-13)	16 (59.3%)	2 (1-54)	1 (1-5)	4 (66.7%)	2 (33.3%)	0 (0%)	0
All (115)	2 (1-65)	45 (39.1%)	23 (1-66)	2 (1-7)	72 (47.1%)	41 (26.8%)	30 (26%)	1 (1-3)

\* Median (range)

Epidemiology / Host responses and early diagnosis of infection

FATAL NEONATAL SEPSIS CAUSED BY NEISSERIA MENINGITIDIS: A CASE REPORT (373)

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### Introduction /Case Report

There are rare case reports in the literature about meningococemia cases that are seen during neonatal period. However, sufficient information about the general frequency is not available. Although it's incidence differs according to the annual epidemics and regions, it is estimated that the meningococcal meningitis comprises 0.54% of the neonatal meningitis cases. We describe a neonate N. Meningitis sepsis who admitted at postnatal 10th day.

### Case Report

Our case is a 10-day-old male patient. The neonate was admitted to NICU with fever and difficulty in breathing (respiratory distress). At the initial examination cutis marmoratus detected. He was hypotonic and had poor sucking. Axillary fever was 38.8 C, heart rate was 190/min, respiratory rate was 55/min and arterial blood pressure was 100/60 mmHg. The initial laboratory tests: complete blood count and biochemistry, C-reactive protein, urine analysis and chest X-ray did not reveal any abnormality. The patient was accepted as septicemia and respiratory insufficiency. He was intubated and intravenous ampicillin and cefotaxime therapy was administered. CSF evaluation revealed normal values. During the second hour of hospitalization, hypotension and bradycardia developed. But at the 5th hour of hospitalization, baby developed generalized purpuric eruption [Figure 1]. Leucopenia and thrombocytopenia, deterioration in coagulation tests and a rise in C-reactive protein value has been detected. Antibiotic treatment was changed to vancomycin and meropenem. However, at the 12th hour, with severe bradycardia, cardiac arrest developed. The child did not respond to cardiac resuscitation. The baby had an autopsy. Neisseria meningitidis [untypeable] was isolated in the blood and tissue cultures.

### Conclusions

During neonatal period, in case of sepsis/septic shock that respond poorly despite to early, fast and appropriate treatment, N. meningitidis should be considered even if there are no specific clinical findings.

## Pulmonology / Non-invasive ventilation

Retrospective Pre-audit Survey of HHHFNC Usage in Infants born at  $\geq 30$  weeks Gestation (113)

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### Introduction /Case Report

HHHFNC (Humidified Heated High Flow Nasal Cannula) introduced in our unit in 2008. Gradually it became one of the main modes of non-invasive respiratory support. However, the general feeling was; HHHFNC, on occasions, was applied to late preterm, near term and term infants when they could have managed with other modes of non-invasive respiratory support such as Low-Flow Nasal Cannula (LFNC), ambient oxygen or its application could have delayed the initiation of mechanical ventilation in infants with severe respiratory failure.

### Patients and Methods

It was a retrospective study, targeted patients admitted to Neonatal Intensive Care Unit (NICU), Norfolk and Norwich University Hospital (NNUH) from 01/01/2014 till 01/04/2014. Its inclusion criteria were; 1- patients born at  $\geq 30$  weeks gestation, 2- received HHHFNC as initial support, 3- no major or incompatible with life congenital abnormalities. Badger-net system used to identify eligible candidates. Originally, 22 were selected, 3 of them excluded. Hence, 19 patients were included in the final analysis.

### Results

All the patients were presented with respiratory distress signs. Grunting was the most common symptom. However, 90% of medical records did not contain detailed description of the clinical respiratory status of the patients. 85% had blood gases analysis prior to initiation of HHHFNC; only 10% of them were arterial blood samples. 50% of pre-HHHFNC blood gases analyses showed acidaemia secondary to respiratory failure. 58% required  $\leq 0.30$  FiO<sub>2</sub> at the initiation of HHHFNC. 21% of patients required mechanical ventilation; 75% of them were the most premature i.e.  $< 34$  weeks gestation at birth.

### Conclusions

Initial symptoms and their severity (Mild, moderate or severe) together with indications for initiation of HHHFNC therapy should be clearly stated. Documentation must also show unequivocal management plans with clear display of thinking process. In other word, is HHHFNC is the appropriate respiratory support; could other mode of respiratory support such as LFNC alleviate patient's symptoms? Or application of mechanical ventilation is required.

## Pulmonology / Delivery room management

A review of delivery room respiratory support for a cohort of Scottish preterm infants (401)

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### Introduction /Case Report

Mechanical ventilation is damaging to preterm infants' lungs. Current emphasis is on either avoiding it completely or extubating early to non-invasive support. Studies have shown that preterm infants who are managed in the delivery room with non-invasive ventilation (NIV) have similar or improved respiratory outcomes compared to those who receive invasive respiratory support. We aimed to review the respiratory support given to a cohort of Scottish preterm infants in the delivery room and in the first 72 hours of life, with a view to ascertaining current practice.

### Patients and Methods

A retrospective review was performed using admission documentation on the Badger neonatal electronic database. Advice regarding data protection was sought and approved. Data was collected on preterm infants born over a three year period (01/01/12-31/12/14) in a level 3 neonatal unit in Glasgow, Scotland. Infants born at 23+0 to 30+6 weeks post menstrual age were included. Demographics relating to the cohort were gathered, including gestation and birth weight. Information relating to their respiratory management was collected, including number intubated in the delivery room, reasons reported for intubation, whether NIV was given in the delivery room and whether intubation was required in the first 72 hours of life in NICU. An excel spreadsheet was used to collate and analyse the information

### Results

145 infants were included in the review. Gestation specific results are presented in the table. 69% (n=100) were intubated in the delivery room, all of whom received endotracheal surfactant. The most common reported indication for intubation was respiratory distress and apnoea, with 45% (n=45) intubated for this reason. Elective intubation was the indication reported in 40% (n=40) of infants who were intubated. Elective intubation was more common in infants less than 28 weeks gestation. 33% (n=48) of the total were initially managed on NIV in the form of mask continuous positive airway pressure, the majority were above 29 weeks gestation. 35% (n=17) of those receiving NIV were intubated after NICU admission in the first 24 hours of life. Of those who received NIV, 48% (n=23) were not intubated in the first 72 hours, all of whom were above 28 weeks gestation.

### Conclusions

Of this cohort, almost 70% of infants were intubated in the delivery room. 40% of those intubated were reported as being elective intubations. One third of infants were trialled on NIV in the delivery room. Infants transferred to NICU on NIV were stable, and less than half required intubation in the first 24 hours of life. Where clinical condition allows, NIV can be considered as first line respiratory support in preterm infants.

Table

Gestation	No. of Babies	Median weight in grams (range)	Intubated in the delivery room (no.)	All reported reasons for intubation (no.)				NIV in delivery room (no.)				
				Resp Distress	Low SaO2	Low Heart Rate	Elective	Total received NIV in delivery room	% intubated in delivery room who received NIV first	% receiving NIV in delivery room intubated in NICU in...		% receiving NIV in delivery room NOT intubated in first 72hrs
										first 24hr	24-72hr	
23+0 - 23+6	5	690 (630-750)	100% (5)	20% (1)	0	0	80% (4)	0	0	0	0	0
24+0 – 24+6	7	720 (500-890)	86% (6)	14% (1)	0	14% (1)	71% (5)	14% (1)	0	100% (1)	0	0
25+0 – 25+6	5	860 (715-910)	100% (5)	20% (1)	0	20% (1)	60% (3)	0	0	0	0	0
26+0 – 26+6	16	965 (770-1230)	94% (15)	25% (4)	6% (1)	13% (2)	56% (9)	6% (1)	0	100% (1)	0	0
27+0 – 27+6	20	1090 (780-1220)	95% (19)	30% (6)	10% (2)	30% (6)	30% (6)	15% (3)	4% (2)	33% (1)	0	0
28+0 – 28+6	28	1130 (750-1660)	79% (22)	46% (10)	9% (2)	18% (4)	27% (6)	21% (6)	0	0	0	100% (6)
29+0 – 29+6	34	1235 (820-1747)	41% (14)	64% (14)	18% (4)	0	18% (4)	62% (21)	21% (3)	33% (7)	5% (1)	48% (10)
30+0 – 30+6	30	1490 (920-1900)	47% (14)	40% (8)	20% (4)	25% (5)	15% (3)	53% (16)	21% (3)	31% (5)	6% (1)	44% (7)
<b>Total</b>	<b>145</b>		<b>69%</b> <b>(100)</b>	<b>45%</b> <b>(45)</b>	<b>13%</b> <b>(13)</b>	<b>19%</b> <b>(19)</b>	<b>40%</b> <b>(40)</b>	<b>33%</b> <b>(48)</b>	<b>8%</b> <b>(8)</b>	<b>35%</b> <b>(15)</b>	<b>4%</b> <b>(2)</b>	<b>48%</b> <b>(23)</b>

Pulmonology / Placenta and prenatal factors

## CHORIOAMNIONITIS, MECHANICAL VENTILATION AND SEPSIS AS MODULATORS OF BRONCHOPULMONARY DYSPLASIA (034)

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### Introduction /Case Report

The histologic chorioamnionitis is associated with reduced risk of respiratory distress syndrome (RDS), but increases the risk of bronchopulmonary dysplasia (BPD), suggesting that intrauterine infection accelerates lung maturation but increases the vulnerability to early lung postnatal injuries. The objective of this study is to investigate the presence of bronchopulmonary dysplasia in premature infants of mothers with histological chorioamnionitis and correlate postnatal outcomes such as sepsis, need for mechanical ventilation and patent ductus arteriosus as taxpayers in chronic lung injury.

### Patients and Methods

An observational retrospective cohort of neonates with 26-32 weeks, born from April to November 2011. Statistical analysis was performed using SPSS version 16.0 software, and used the chi-square tests of association, t-Sudent, the hazard ratio with confidence interval. The significance level was 0.05.

### Results

We studied 51 preterm infants, and 23 underwent antenatal infection. Mothers with chorioamnionitis had a higher number of previous pregnancies were less submitted to cesarean section. Receiving corticosteroids as were mothers without infection. Newborns who underwent maternal infection, were born with gestational age and lower weight but a smaller number needed resuscitation at birth. Had 10 times more early-onset sepsis, a higher incidence of patent ductus arteriosus and a 2 times greater tendency to develop bronchopulmonary dysplasia.

### Conclusions

The chorioamnionitis is a contributing factor for bronchopulmonary dysplasia but the small sample size limited the findings of this study.

## Epidemiology

Sexual dimorphism and the placenta – results from the ROLO kids study (265)

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## Introduction /Case Report

### Aim

To assess the association between placental size and shape and neonatal and infant anthropometry at 6 months and to assess any discrepancy in male and female neonatal and infant outcomes.

### Patients and Methods

Data from the ROLO/ROLO Kids [Randomised COntrol Trial of LOw Glycaemic Index in Pregnancy] study were analysed. Neonatal anthropometric and skinfold measurements were recorded as markers of adiposity in 265 neonates and 280 infants. Placental weights were available for 301 and morphology for 123. Pearsons' correlation and simple linear regression were performed to examine the association between these placental factors and weight and anthropometry at birth and 6m in the entire cohort and in gender selective analysis.

### Results

Trimmed placental weight was associated with birth weight in the total, male and female cohorts [ $p = <0.001$ ] and numerous neonatal anthropometric measurements. Trimmed Placental weight was also associated with weight at 6 months in the total and male cohorts [ $p = 0.003$ ,  $p = 0.018$ ] respectively and other markers of infant anthropometry. This association was not determined in the female infant cohort outside of length at 6 months.

### Conclusions

The placental phenotype is associated with anthropometry at birth and this association persists to early infancy more dynamically in males than females, suggesting that sexual dimorphism needs to be taken into account in assessing the impact of the placental on infant anthropometry.

Table

**Table 1: Association of trimmed placental weight and neonatal and infant anthropometry: Simple Linear Regression – total neonatal and infant cohort**

<b>Total Neonatal/Infant Cohort</b>				
<b>Variable</b>	<b>B</b>	<b>SE B</b>	<b>p</b>	<b>R<sup>2</sup></b>
Birth Weight	0.124	0.011	<b>0.000</b>	0.312
Length	0.007	0.002	<b>0.000</b>	0.019
OFC	0.002	0.001	<b>0.036</b>	0.053
Abdominal Circumference	0.006	0.002	<b>0.008</b>	0.090
Thigh Circumference	0.004	0.001	<b>0.003</b>	0.115
Waist Hips Ratio	0.007	0.002	<b>0.010</b>	0.085
Infant Length	0.008	0.002	<b>0.000</b>	0.114
Infant weight	0.005	0.002	<b>0.003</b>	0.078
Infant Thigh	0.007	0.003	<b>0.010</b>	0.059
Infant Chest	0.006	0.003	<b>0.027</b>	0.041
Infant Hip	0.007	0.003	<b>0.028</b>	0.040
Infant Mid Upper Arm Circumference	0.004	0.002	<b>0.015</b>	0.051
<b>Total Male Neonatal/Infant Cohort</b>				
Birth Weight	2.811	0.309	<b>0.000</b>	0.367
Length	0.005	0.002	<b>0.041</b>	0.096
Birth Subscapular	0.004	0.002	<b>0.026</b>	0.140
Infant Weight	0.006	0.002	<b>0.018</b>	0.104
Infant Chest	0.008	0.004	<b>0.022</b>	0.097
Infant Mid Upper Arm Circumference	0.005	0.002	<b>0.038</b>	0.076
<b>Total Female Neonatal/ Infant Cohort</b>				
Birth Weight	2.017	0.331	0.000	0.215
Length	0.008	0.003	0.009	0.230
Thigh Circumference	0.007	0.002	0.002	0.289
Infant Length	0.007	0.003	0.018	0.095

Simple Linear Regression was used in this analysis and only statistically significant associations were included in this table.  $p < 0.05$  was considered statistically significant. Abbreviations: TNF- $\alpha$  = Tumour Necrosis Factor alpha, IL-6 = Interleukin 6

## Pulmonology

### TERM NEONATES WITH PULMONARY HAEMORRHAGE: A RETROSPECTIVE STUDY (525)

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#### Introduction /Case Report

Pulmonary haemorrhage (PH) is a potentially life threatening condition seen in preterm infants. There has been no recent study describing this condition in term infants.

#### Patients and Methods

A retrospective observational study from April 2012 to April 2015, to describe the risk factors for PH in term infants admitted to Nottingham University Hospitals, UK. PH was defined as the presence of blood in the trachea associated with significant clinical deterioration. In non-ventilated infants, need for ventilation was considered significant. In already ventilated infants, need for an increase in ventilator pressures by more than 2cm H<sub>2</sub>O and / or increase in FiO<sub>2</sub> of 10% was considered as significant.

Patients were identified by neonatal admission database (Badger). Notes of these patients were reviewed for inclusion criteria, background information, associated risk factors and outcomes.

#### Results

Over the period of three years, 12 term infants (4.7 per 1000 term admissions) developed PH (median birth weight 3.57kg and median gestation 39 weeks). PH presented at a median age of 7 hours (IQR 16.25) with 5 cases presenting in the first hour of life. Nine babies received resuscitation at birth; seven of them were diagnosed as hypoxic-ischaemic encephalopathy (table 1). Four had sepsis with PPHN. One case presented unexpectedly with collapse at 5min of age with no risk factors for HIE or sepsis.

#### Conclusions

Pulmonary Haemorrhage at term was seen in three settings; (1) HIE complicated by coagulopathy, (2) Sepsis with PPHN and (3) sudden unexplained collapse with PH. PH at term has a mortality of 33.3% in this series. A larger prospective study needs to be undertaken to characterise PH in term infants, particularly those presenting suddenly with collapse, shortly after birth.

Table

**Table 1: Factors associated with PH and the risk of death**

<b>Risk factor</b>	<b>Survived</b>	<b>Died</b>	<b>p value</b>
HIE (any)	4	3	0.407
Hypothermia	4	2	1
CRP>10	6	1	0.09
Coagulopathy	6	3	1
PPHN	5	0	0.038
MAS	4	0	0.08
Surfactant before PH	2	0	0.27
Inotropes before PH	5	2	0.67
Median age at PH (IQR)	12 (14.75)	0.5665(18.63)	0.83

CRP C-Reactive protein, PPHN Persistent Pulmonary Hypertension, MAS Meconium Aspiration Syndrome IQR Inter Quartile Range

Circulation, O2 Transport and Haematology

## CONSERVATIVE MANAGEMENT OF PATENT DUCTUS ARTERIOLES IN PRETERM INFANTS (634)

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### Introduction /Case Report

Recent systematic reviews showed that randomized controlled trials performed to date do not provide clear evidence supporting treatment of patent ductus arteriosus (PDA) in premature infants. The objective of this study is to test whether conservative management of PDA in extremely low gestational age newborns (ELGANs) is detrimental to morbidity by comparison of periods of conventional treatment and conservative management.

### Patients and Methods

We retrospectively reviewed all preterm infants who were born with gestational age < 28 weeks or birth weight < 1,000 g, and had hemodynamically significant PDA (HS-PDA). The policy for management of HS-PDA has changed from conventional pharmacologic and/or surgical treatment (July 2009 to December 2011; period 1) to a conservative approach (January 2012 to June 2014; period 2). We compared baseline characteristics and morbidity of infants with HS-PDA between these periods.

### Results

There was no difference between the periods with regard to baseline characteristics. There was no difference with regard to mortality, intraventricular hemorrhage, and necrotizing enterocolitis. However, bronchopulmonary dysplasia (BPD) and composite BPD or death were less frequent in period 2 compared to period 1. After propensity score-adjusted regression analysis, period 2 was associated with a decreased incidence of BPD (adjusted odds ratio [OR]: 0.4; 95% confidence interval [CI]: 0.2–0.7) and composite BPD or death (adjusted OR: 0.4; 95% CI 0.3–0.8) compared to period 1.

### Conclusions

Conservative management for PDA in ELGANs was not associated with detrimental short-term outcome and might be associated with a decreased incidence of BPD or composite BPD or death.

## SHOULD DOPAMINE BE THE FIRST LINE INOTROPE IN TREATMENT OF NEONATAL HYPOTENSION: REVIEW OF EVIDENCE (453)

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### Introduction /Case Report

Hypotension is a common feature in the preterm infant(1). The normal range of blood pressure in newborns, term or preterm, remains unknown(2). The principle aim of treating hypotension is to prevent end organ damage. Although there is no evidence to establish particular undesirable effects cause by low blood pressure(3,4), it is associated with increased mortality, periventricular leucomalacia(5) and neurodevelopmental morbidity(6). The aim is to determine, after systematic review of evidence, if dopamine is effective in treating hypotension and safe to use comparing to other inotropes, hence if dopamine would make a good first line drug therapy for hypotension in the neonatal population.

### Patients and Methods

For the purpose of this article, the definition of hypotension stated by the authors of their respective articles has been used.

Data sources: Medline, and EBM-Cochrane Database of Systematic Reviews were used to search treatment for hypotension in newborn infants. All searches were done using MeSH terms "Hypotension" (Major), "Dopamine" (explode), "Dobutamine" (explode), "Hydrocortisone" (explode), "epinephrine" (explode), "norepinephrine" (explode). Results were limited to "Human" and "Age Group Newborn Infant birth to 1 month".

Study selection: We included in this review only studies with high levels of evidence (1 and 2). All abstracts were read and screened by two reviewers separately and only the ones with high quality evidence were included.

### Results

The search resulted in 86 articles. After reviewing all the articles, only 9 were included. Articles with high levels of evidence only targeted preterm infants, no results fitting our criteria were found for term infants. (Table 1)

Dopamine has been shown to increase blood pressure more effectively than dobutamine(7,8), and hydrocortisone. There is no statistical difference in long term neurological outcome between dopamine and dobutamine(7). There were noted to be transient endocrine effects with dopamine comparing to dobutamine(9), however these normalized one day after stopping dopamine. There is no data regarding long term side effects of steroids(10). Dopamine and Adrenaline have been shown to be equally effective(11), but epinephrine has transitory adverse effects on the lactate and carbohydrate metabolism(12). There were no statistically significant studies with Norepinephrine.

## Conclusions

Dopamine has been shown to be equally (adrenaline) or more effective than other inotropes (dobutamine, hydrocortisone) in raising blood pressure. We consider it to be a safe drug to use and after having reviewed the evidence would recommend it as a first line therapy in treating hypotension in the preterm infant. We are unable to comment on the use of noradrenaline, and on the use of dopamine in a term infant.

Table

	Citation	Study group	Study type (level of evidence)	Outcome	Key result
<b>All inotropes</b>					
Cardiovascular support for low birth weight infants and cerebral hemodynamics: a randomized, blinded, clinical trial	Pellicer <i>et al</i> (2005)	Low Birth Weight (LBW)	RCT double blinded	Quantitative changes in cerebral perfusion and blood pressure.	Among hypotensive LBW infants, cardiovascular support with low/moderate-dose dopamine or low-dose epinephrine increased cerebral perfusion, and were as effective in increasing mean blood pressure.
Treating hypotension in the preterm infant: when and with what: a critical and systematic review.	Dempsey and Barrington (2007)	Preterm	Critical systematic review	Pharmacological intervention improving clinical outcomes	Clinical outcomes of treatment have not been looked into, therefore no superiority of any treatment.
<b>Dopamine</b>					
A meta-analysis of dopamine use in hypotensive preterm infants: blood pressure and cerebral hemodynamics.	Sassano-Higgins <i>et al</i> (2011)	Preterm infants	Meta analysis	Dopamine effect on. Hypotension, Cerebral Blood Flow (CBF), and central nervous system injury	Dopamine increases mean arterial blood pressure with a greater overall efficacy than dobutamine ( $r=0.26$ ; 95% CI=0.20 to 0.32), colloid ( $r=0.60$ ; 95% CI=0.41 to 0.74) and hydrocortisone ( $r=0.40$ ; 95% CI=0.034 to 0.67). CBF increased following dopamine administration (5 studies; N=75; $r=0.36$ ; 95% CI=-0.059 to 0.67). There were no statistically significant differences in adverse neurological outcome between dopamine and dobutamine
<b>Dopamine and Dobutamine</b>					
Dopamine versus dobutamine for hypotensive preterm infants.	Subhedar NV, Shaw NJ (2003, 2009)	Preterm infants	Cochrane review	Effectiveness and safety of dopamine and dobutamine in the treatment of systemic hypotension	Dopamine was more successful than dobutamine in treating systemic hypotension (RD - 0.23, 95% CI -0.34 to -0.13). No significant difference between dopamine and dobutamine in terms of tachycardia, or poor outcome (neonatal mortality, periventricular leukomalacia).

Dopamine vs dobutamine in very low birthweight infants: endocrine effects.	Filippi et al (2007)	Very Low Birth Weight (VLBW)	Prospective RCT (non-blinded)	Endocrine effects of dopamine and dobutamine in hypotensive VLBW	Suppression of TSH, T4 and PRL was observed in dopamine-treated newborns but rebound was observed from the first day onwards after stopping dopamine. Dobutamine administration did not alter the profile of any of the hormones.
<b>Dopamine and steroids</b>					
Corticosteroids for treating hypotension in preterm infants.	Ibrahim H; Sinha IP; Subhedar NV (2011)	Preterm infants	Cochrane review	Effectiveness and safety of corticosteroids used either as primary treatment of hypotension or for the treatment of refractory hypotension	Persistent hypotension was more common in hydrocortisone treated infants compared to dopamine (RR 8.2, 95% CI 0.47 to 142.6). No statistically significant effects on any other short or long-term outcome.
Hydrocortisone for hypotension and vasopressor dependence in preterm neonates: a meta-analysis.	Higgins S et al (2010)	Preterm	Meta analysis	1. Efficacy of hydrocortisone for treatment of hypotension. 2. Reduction of vasopressor requirements in preterm infants	Random effects meta-analysis showed that hydrocortisone increases blood pressure (r=0.71, 95% CI=0.18 to 0.92) and reduces vasopressor requirement (r=0.74, 95% CI=0.0084 to 0.96).
<b>Dopamine and Adrenaline</b>					
Dopamine vs epinephrine for cardiovascular support in low birth weight infants: analysis of systemic effects and neonatal clinical outcomes.	Valverde et al (2006)	LBW	RCT	Short-term medium-term morbidity between dopamine group and adrenaline group	Significant increase of mean blood pressure throughout the first 96 hours with no differences between groups. However, epinephrine produced a greater increase in heart rate than dopamine, infants had higher plasma lactate, and lower bicarbonate and base excess, higher blood sugars. For medium-term morbidity, there were no differences in neonatal clinical outcomes in responders.
Adrenaline for prevention of morbidity and mortality in preterm infants with cardiovascular compromise.	Paradis et al (2004, Rv 2009)	Preterm	Cochrane review	Effectiveness and safety of adrenaline compared to no treatment or other inotropes in reducing mortality and morbidity.	Only infants >1750g are included in this review. Both adrenaline and dopamine significantly increased heart rate and mean BP, with no statistical difference and had no significant effect on left or right ventricular output.

## Pulmonology / Non-invasive ventilation

A retrospective study of heated, humidified high-flow nasal cannula use as a respiratory support for weaning from nasal continuous positive airway pressure in premature infants (214)

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## Introduction /Case Report

The use of nasal continuous positive airway pressure (NCPAP) for noninvasive respiratory support (NRS) of preterm infants was widely applied in the NICU. The step-down respiratory support as traditional nasal cannulae(N/C) was commonly used if the infants' respiratory condition was stable under NCPAP. Heated, humidified high-flow nasal cannula (HHHFNC) is commonly used in recent years as a NRS alternative in the NICU. But its role of the respiratory care in NICU was controversial. The aim of this study is to describe the efficacy of HHHFNC when the patients in our NICU were applied different weaning protocol. The nasal CPAP would be re-used if the use of the traditional nasal cannula failed.

## Patients and Methods

This retrospective study enrolled preterm(GA < 37 wk), low birth weight ( $\leq 2500$  g) infants who were admitted to NICU of Shin Kong Wu Ho-Su Memorial Hospital and have applied HHHFNC as a NRS. In period 1, HHHFNC was applied after weaning failure from NCPAP to N/C; in period 2, HHHFNC was applied as soon as possible if stable condition under NCPAP. HHHFNC failure was defined as apnea, bradycardia, and decreased O<sub>2</sub> saturation occurred within 3 d after shifting to HHHFNC. We analyzed the demographic data, including gender, gestational age, birth weight, 1 and 5 minute APGAR score, and also compared post-menstrual age, current weight when HHHFNC were applied. Primary outcome was weaning failure rate. Secondary outcome were days of HHHFNC use, ventilator support, ICU stay, and hospitalization.

## Results

We enrolled 15 infants who were treated with HHHFNC. In period 1, 4 infants were included. In period 2, 11 infants were included. There is no difference in gender, gestational age ( $29 \pm 3.7$  versus  $27.7 \pm 2.8$  weeks), birth weight ( $1340 \pm 769$  versus  $1135 \pm 334$  gm), 1-minute and 5-minute APGAR score. The days of ventilator support before switch to HHHFNC ( $82.8 \pm 52$  versus  $50.3 \pm 37.9$ ), days of ICU stay ( $88 \pm 46.3$  versus  $60.9 \pm 39.5$ ), and days of hospitalization ( $111 \pm 59.6$  versus  $83 \pm 48.6$ ) were higher in period 1 compared to period 2, but there was no statistical significance. In period 1, HHHFNC success rate was 100%; in period 2, HHHFNC success rate was 9/11 (82%).

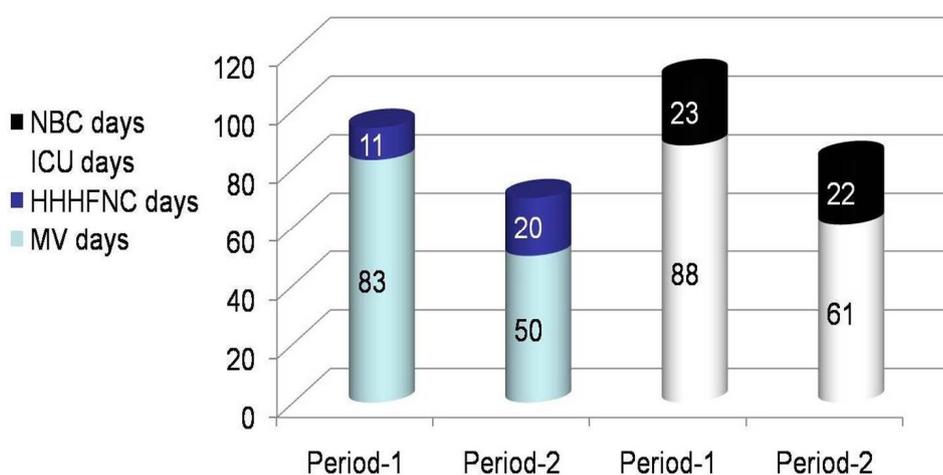
## Conclusions

Early HHHFNC use in NICU compared to NCPAP seemed to shorten ICU stay and hospital days. Heated, humidified high-flow nasal cannula use could be a better respiratory support for fast weaning from nasal continuous positive airway pressure in premature infants. Larger prospective studies are required to confirm our preliminary results.

Table

	Period 1, N=4	Period 2, N=11	P value
Male, (n, %)	2 (50%)	6 (54.5%)	.876
Gestational age, (mean $\pm$ SD, wk)	29 $\pm$ 3.7	27.7 $\pm$ 2.8	.851
Birth weight, (mean $\pm$ SD, gm)	1340 $\pm$ 769	1135 $\pm$ 334	.753
1-min Apgar score, (median IQR 25th-75th)	5.5 (3.5-7)	5 (4-6)	1.000
5-min Apgar score, (median IQR 25th-75th)	7.5 (6.5-8.5)	8 (6-8)	.476
Cesarean section (n, %)	1 (25%)	9 (81.8%)	.039
<b>When shift to HHHFNC</b>			
Postmenstrual age, (mean $\pm$ SD, wk)	41.8 $\pm$ 5.9	34.7 $\pm$ 2.7	
Current Body weight, (mean $\pm$ SD, gm)	3393 $\pm$ 745	1875 $\pm$ 430	
<b>Primary outcome</b>			
Weaning failure (n, %)	0/4 (0%)	2/11 (18%)	

Picture



## Epidemiology

Post discharge growth assessment in VLBW infants : Comparisons among the Korea, CDC and WHO standards (783)

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## Introduction /Case Report

In the assessment of the growth failure, we frequently find the variation in the results of the growth failure depending on which growth chart is used. We evaluated and compared the post-discharge growth patterns regularly, using three different growth charts, namely WHO, CDC, and Korean standard in Korean VLBW infants.

## Patients and Methods

For 81 infants, measurement of weight and height was made every 3 months until 24 months of age. Growth failure was defined as below the 10th percentile. Comparisons between SGA and AGA infants were done. Repeated measured ANOVA was used for comparing the difference by the time among three standards. At PCA 40 weeks, 58.4% showed growth failure in weight, and 50.5% in height.

## Results

A significant catch-up growth ensued thereafter, and at PCA 24 months, growth failure rate was 24.3% in weight and 18.1% in height. For SGA infants, at PCA 40 weeks, 71.2% showed growth failure in weight, and 77.5% in height. At PCA 24 months, growth failure in weight and height for the SGA infants were higher than AGA infants (29% vs 18%,  $p=0.045$ ; 37% vs 10%,  $p=0.038$ ). Catch-up growth in height was more severely impaired than in weight. When the growth patterns were serially compared among the Korean, WHO, or CDC standard, there were significant differences among the three standards ( $p<0.001$ ).

## Conclusions

For assessment of growth failure, it is important to recognize the differences depending on which growth pattern standard is used. More careful monitor of the growth and active intervention will be necessary in SGA infants.

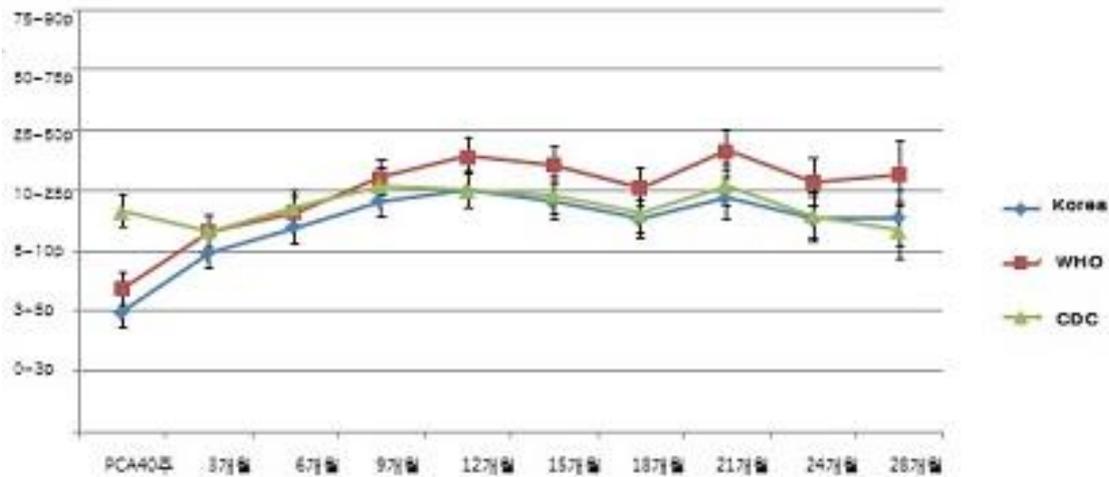
Table

<b>Weight</b>	At birth	PCA 40wk	6month	12month	24month
<10p	21%	58%	40%	31%	24%
SGA	100%	81%	55%	47%	29%
Non-SGA	0%	53%	38%	27%	21%
ELBW(<1000g)	17%	75%	52%	40%	42%
1000-1500g	25%	43%	23%	18%	10%
Male	58%	69%	60%	55%	54%

<b>Height</b>	At birth	PCA 40wk	6month	12month	24month
<10p	21%	55%	42%	35%	18%
SGA	100%	75%	59%	51%	37%
Non-SGA	0%	49%	38%	30%	13%
ELBW(<1000g)	17%	72%	58%	45%	25%
1000-1500g	25%	30%	18%	12%	8%
Male	58%	64%	51%	58%	50%

Picture



## Pulmonology / Lung injury

### RECURRENT PNEUMONIA ASSOCIATION IN TWO SIBLINGS WITH GUANIDINOACETATE METHYLTRANSFERASE (GAMT) DEFICIENCY SUSPICION. CASE PRESENTATION (690)

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#### Introduction /Case Report

Guanidinoacetate methyltransferase (GAMT) deficiency (OMIM 601240, chromosome 19p13.3) is a part of the recently described primary deficiencies of creatin synthesis, with autosomal recessive transmission. The well known neurological signs are due to the role of creatin (Cr) and guanidinoacetate (GAA) in the CNS. But little is known about the possible connection between this deficiency and other pathologies (ie. malformations) and organs stricken (ie. lung). We monitored descendants of a family with suspected GAA deficiency.

#### Case Report

The 1st case was a full term born, AGA, male, G V P V from parents 28 resp. 33 year old, smokers and coffee consumers, grade II/III relatives with low socio-economical status, having other 4 healthy kids. At birth no neurological signs, phenylketonuria (PKU) and congenital hypothyroidism (CH) screening being normal. Fed mixt. At the age of 5 weeks admitted (in Marghita) due to Bronchiolitis with moderate respiratory insufficiency, with normal neurological development at that time. By the time gradually developed neuro-psycho-motor retardation, but the mother did not appeal to a medical advice. At 7 months was admitted again with altered general condition due to atelectatic pneumonia of the upper left lobe, but this time with evident psycho-motor retardation, microcephaly, central blindness, spastic tetraparesis, right eye convergent strabism. TORCH infection was excluded. After two weeks admitted again with Bronhopneumonia and the above mentioned neurological signs. At 8½ and 9½ months age, admitted for pneumonias of the left inferior lobe. Every time discharged clinically and radiologically clear. At 10 months admitted for Bronhopneumonia and deceased after irresuscitable cardio-respiratory stop. At 9 months mass-tandem spectrometry (MS/MS) based extended metabolical screening was done which revealed a high value of GAA (9,99 µmol/L). Because the result came after infants death, we could not do confirmation tests and substitution treatment. In the absence of a thoracic CT/MRI under anaesthesia (no informed consent could be taken from the mother who was permanently absent from the hospital) we could not differentiate weather the repeated pneumonias were due to respiratory malformations or crico-faringian incoordination.

Genetic advice was given, mother delivered two more boys, GAA was monitored for them also (taking count by the fact that GAA could be elevated in grade I. relatives of a proband). One of them (GA 29/30 wks, G VI P VI, BW 1500g, Apgar 5/6) with normal PKU and CH screening, had a light increase in GAA (4,17 µmol/L) interpreted as transitional GAMT deficiency of the premature (at 14 months admitted for viral pneumonia with perfect neurological status). The other full term borne (G VII P VII, AGA, Apgar 9/10)

without perinatal problems and normal PKU and CH screening, had a normal GAA values by MS/MS screening and normal neuro-psycho-motor development at the age of 1 year.

The 2nd case from this family with a suspicion of GAMT deficiency was a girl, born at full term (G VIII P VIII, AGA, Apgar 9/10), with premature rupture of the membranes (over 32 hours). A mild hypotonia was interpreted first in a septic condition. An inspiratory stridor was interpreted first as a possible laryngomalacia. Mother didn't come back for neurological evaluation and GAA screening. At 6 weeks admitted for viral pneumonia with altered general condition, moderate persistent hypotonia, cephalic crying which rise a suspicion of GAMT deficiency. Empirical substitution treatment with creatine (300 mg/kg/day) was begun. Substitution with ornitine and an arginine restrictive diet couldn't be realized due to the low socio-economical conditions and the absence of a specific national program. Significant improvement of the neuro-psycho-motor retardation under the substitutive treatment had strengthen our suspicion of GAMT deficiency and permitted temporizing the GAA screening (in progress). At age 7 months admitted with severe Bronchopneumonia. After initial good outcome she presents cardio-respiratory stop finished with death.

GAA screening by MS/MS was done in Szeged, Hungary, from dry-blood spot collected on a filter paper (Schleicher&Schuell 903). The rest of the family could not be tested for GAA because of the financial limits.

## Conclusions

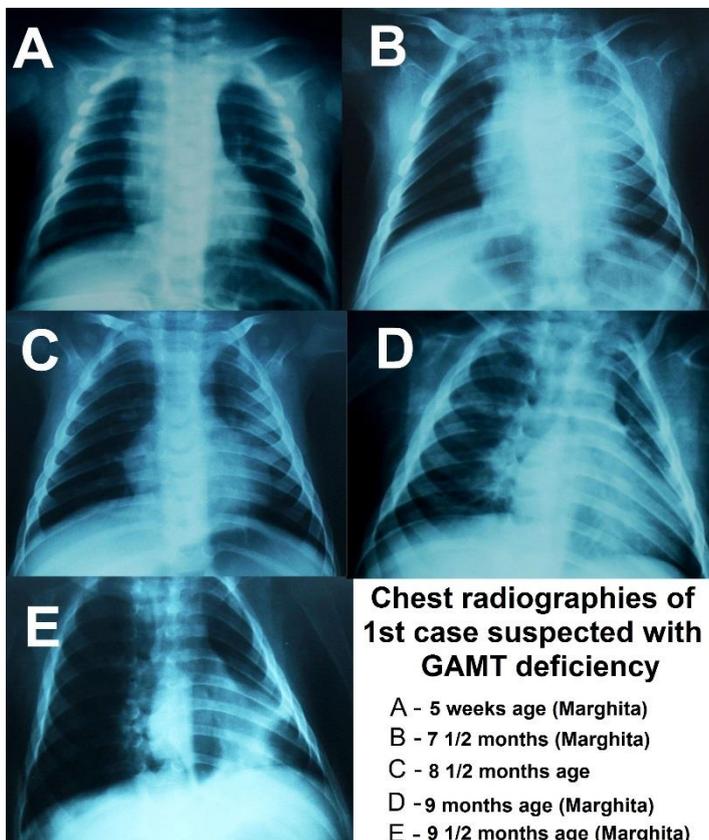
Descendants of this family were monitored in scarce technical conditions (MS/MS-based extended metabolical screening is a hardly accessible investigation in Romania) and unsatisfactory parental collaboration. Cases come from, probably, the first family from Romania with a suspicion of GAMT deficiency in association with pneumonias. Association between GAMT-deficiency and other pathologies needs more attention in the future.

Table

Vér	Vizelet	
GAA μmol/l	GAA/Kreatinin mmol/mol	Kreatin/Kreatinin mol/mol
9.99		
Normál tartomány		
< 15 év: 0,23 -- 3,29	0 -11 év: 10-103 > 11 év: <66	0 - 4 év: < 0,80 5-11 év: < 0,47 >11 év: < 0,06
Vér	Vizelet	
GAA μmol/l	GAA/Kreatinin mmol/mol	Kreatin/Kreatinin mol/mol
4.17		
Normál tartomány		
< 15 év: 0,23 -- 3,29	0 -11 év: 10-103 > 11 év: <66	0 - 4 év: < 0,80 5-11 év: < 0,47 >11 év: < 0,06

Increased GAA in 1st case (MS/MS, upside)  
Slightly elevated GAA in premature brother (downside)

Picture



Pulmonology / Mechanical ventilation

## STUDY OF CORRELATION BETWEEN GAS TRANSPORT COEFFICIENT (DCO<sub>2</sub>) AND pCO<sub>2</sub> IN VENTILATED NEONATES (258)

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### Introduction /Case Report

In high frequency ventilation pulmonary gas exchange is dependant on frequency (f - Hz) and amplitude (delta P) which has an impact on the CO<sub>2</sub> clearance. The elimination of CO<sub>2</sub> is represented by DCO<sub>2</sub> (gas transport coefficient) expressed as {VT<sub>2</sub> (tidal volume) X frequency} in some ventilators.

On our NICU, we have been using the trend of DCO<sub>2</sub> to monitor ventilation in babies on HFOV and use DCO<sub>2</sub> value associated with normocarbina in a baby as a rough guide. If the DCO<sub>2</sub> value changes rapidly, we encourage our medical and nursing staff to review the baby and do a blood gas.

We did not find any recent published literature reviewing the use of DCO<sub>2</sub> in clinical practice.

### Patients and Methods

We prospectively collected demographic, ventilator setting and blood gas data of neonates ventilated with SLE5000 on HFO mode between February 2014 to February 2015. We analysed the data using SPSS version 20 for deriving the correlation coefficient.

### Results

We collected and analysed 126 blood gas results and simultaneous HFOV parameters including dCO<sub>2</sub> from 15 babies. The birth weight ranged from 450 grams to 3775 grams and gestation ranged from 23 – 40 weeks.

Pearson correlation coefficient r (p value) between DCO<sub>2</sub> (Hz ml<sup>2</sup>/kg) and amplitude (delta P) 0.677 (<0.001); Gestation 0.377 (<0.001); weight 0.425 (<0.001); Frequency (Hz) -0.716 (<0.001); pCO<sub>2</sub> -0.196 (0.028); lactate 0.333 (<0.001).

### Conclusions

This study shows that using DCO<sub>2</sub> as a trend for assessing pCO<sub>2</sub> is useful in clinical practice.

DCO<sub>2</sub> values had strong positive correlation with statistical significant result with amplitude, gestation, weight, lactate and strong negative correlation with statistical significant result with frequency.

There is negative correlation between DCo<sub>2</sub> and pCo<sub>2</sub>, is approaching strong statistical significance in this sample size. We would need a larger sample to establish strong statistical significance.

Pulmonology / Apnea and respiratory control

VARIATIONS IN TIMING OF CAFFEINE THERAPY IN VLBW INFANTS – A SINGLE CENTER EXPERIENCE (809)

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### Introduction /Case Report

Administration of methylxanthines to preterm infants is common practice. The current evidence supports beneficial effects of caffeine on apnea of prematurity and on respiratory and neurodevelopmental outcome. However, there is ongoing debate on several practical aspects of caffeine therapy such as optimal timing, dosing schemes, and route of administration.

### Patients and Methods

We retrospectively analyzed the current practice of caffeine therapy at the two sites of the perinatal center of the Charité University Medical Center, Berlin, Germany. The Charité is a tertiary center with a total of >4000 births/year and >180 very low birth weight infants (VLBWI). All VLBWI admitted in between January 1st and December 31st 2012 were evaluated regarding the timing of treatment initiation, route of administration, dosing regimens, and duration of therapy.

### Results

Caffeine therapy was predominantly initiated within the first 72 hours of life as caffeine citrate. However, there was variation in timing of initial treatment, especially in ventilated infants. Furthermore, the recommended loading dose (20 mg/kg) was inconsistently administered, although adherence to a maintenance dose of 10 mg/kg was relatively consistent. Significant variability existed regarding the route of administration and the duration of treatment. Furthermore, caffeine-dosing schemes seemed to habitually differ with regards to whether the daily dosage was divided into several proportions or given as a single dose.

### Conclusions

Our results indicate a still high variability in regard to several practical aspects of caffeine therapy in VLBW infants. This illustrates the critical need for further prospective trials on these practical issues.

## Epidemiology

### Risk factors for recurrent miscarriage (382)

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## Introduction /Case Report

Routine screening for parental chromosome abnormalities, uterine anomalies and thyroid disorders is often carried out in women with recurrent miscarriage (RM) but its significance is controversial and mostly justified in a research setting. Our aim was to estimate the occurrence of paternal chromosome abnormalities, uterine structural anomalies and thyroid disorders in women with RM because such data have not until now been available in Hungarian population.

## Patients and Methods

201 women with RM presenting to the National Committee for Recurrent Miscarriage at the 2nd Dept Obstet Gynecol Semmelweis University between 2012 and 2015 for consultation were involved in this retrospective study. Data on the uterine anomalies investigated by hysteroscopy, 3-D ultrasonography, hysterosalpingography or hysterosalpingosonography, on the parental chromosome abnormalities, on the thyroid function characterized by TSH, T4 and T3 concentrations, and on the thyroid autoimmunity shown by anti-TPO and anti-TG antibodies were obtained from the medical files. Hypothyresosis was defined as TSH > 2.5 mU/ml.

## Results

Out of 201 couples maternal and paternal chromosome abnormalities were found in 3% and uterine structural anomalies in 13.9% (uterine septum in 5.4%, uterus arcuatus in 1.5%, uterus bicornis in 1.5%, submucosal fibroids in 2.5% and intrauterine synechiae in 1%). Thyroid disorders occurred in 48.7% of the women with RM and among them 26.3% showed only hypothyresosis and 19.4% only autoimmunity, and 3% suffered from both disorders.

## Conclusions

Thyroid disorders and uterine structural anomalies are regarded as frequent risk factors for RM and the parental chromosome abnormalities may be rare risk factors.

## Pulmonology / Surfactant

### LUNG LAVAGE WITH DILUTE SURFACTANT VERSUS BOLUS SURFACTANT FOR MECONIUM ASPIRATION SYNDROME: A RANDOMISED CONTROLLED TRIAL (418)

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## Introduction /Case Report

The aim of this study to compare the effect of lung lavage with dilute porcine surfactant and bolus surfactant administration in the treatment of infants with meconium aspiration syndrome (MAS).

## Patients and Methods

In this prospective randomized controlled study, ventilated infants with MAS with a gestational age  $\geq 36$ , birth weight  $\geq 2000$  g were included. Infants were randomized into two groups; in group 1, two sequential 15 mL/kg aliquots of dilute porcine surfactant (Curosurf, Chiesi Farmaceutici S.p.A., Parma, Italy) with a phospholipid concentration of 5 mg/ml were instilled into the lung. In group 2, 100 mg/kg of porcine surfactant were administered as a bolus. The study groups were compared with regard to efficacy, morbidity and mortality.

## Results

Thirty-three infants were randomized. Median duration of mechanical respiratory support was similar in infants who underwent lung lavage and bolus surfactant (3 versus 3.5 days,  $p=0.36$ ). Similarly, duration of oxygen therapy and hospitalization were not significantly different between lung lavage and bolus surfactant group (5 versus 7 days,  $p=0.48$ , 12.5 versus 12 days  $p=0.88$ , respectively). There were no differences in high frequency ventilation and nitric oxide requirement between the groups. Mortality and pneumothorax also did not differ between the groups.

## Conclusions

Lung lavage with dilute surfactant therapy does not alter the neonatal outcomes in terms of the duration of respiratory support, need of high frequency ventilation and nitric oxide, mortality and duration of hospitalization in ventilated infants with MAS.

Circulation, O<sub>2</sub> Transport and Haematology / Placenta and prenatal factors

#### BLOOD GAS DIFFERENCES BETWEEN UMBILICAL ARTERY AND VEIN IN TERM NEWBORNS (719)

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#### Introduction /Case Report

Background: The evaluation of differences in umbilical arterial-venous blood analysis can be useful to assess fetal status at delivery but also placental respiratory ability.

Aim: To obtain reference values for blood gas analysis, electrolytes, hematocrit (Htc) and glucose in the umbilical artery and vein of healthy term newborn.

#### Patients and Methods

Blood samples were taken from umbilical cord of both artery and vein in 102 healthy term newborns (mean GA: 38 wks; mean BW: 3219 g). Samples were analyzed using IRMA TruPoint Blood Analysis System with CC type cartridges.

#### Results

Significantly lower pH, lower pO<sub>2</sub>, higher pCO<sub>2</sub>, higher HCO<sub>3</sub><sup>-</sup> (p< 0.0001) and higher base excess (p=0.011) values were found in artery cord blood compared to vein. Furthermore

Na<sup>+</sup> and glucose concentrations were higher in vein than artery (p <0.0001). No significant difference were detected in the hematocrit, potassium and calcium levels between artery and vein cord blood.

#### Conclusions

The higher concentrations of Na and glucose in the umbilical vein compared to artery express maternal contribute mediated by placenta. Umbilical arterial venous differences reflects placental respiratory function. Both arterial and vein cord blood gas analysis are easy to be collected and can be crucial to ascertain intrauterine wellbeing and placental respiratory ability at birth.

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

## SEVERE LEFT VENTRICULAR FAILURE IN A TERM NEWBORN INFANT (159)

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### Introduction /Case Report

We present the case of an infant who was born at term with no significant antenatal history and an uneventful pregnancy.

Following delivery the infant was cyanosed with intermittent respiratory effort. His colour did not improve with facial oxygen and he was transferred to the neonatal unit where he was found to have a loud systolic murmur and oxygen saturations of 53% in room air.

He was intubated which resulted in a rapid improvement of his oxygen saturations though his lung fields appeared clear on a chest radiograph. His murmur persisted and on echocardiogram he was found to have mitral regurgitation and severe impairment of his left ventricle with a significantly raised troponin.

### Case Report

A baby boy was born at term weighing 3.2kg. He was the firstborn child of a well mother with no significant family history. The pregnancy had proceeded uneventfully and no concerns had been raised by mother or the midwifery team looking after her.

During labour a dose of diamorphine was given for pain relief and the baby was born two hours later. The neonatal team were asked to attend following delivery due to poor respiratory effort by the newborn and cyanosis. After giving mask ventilation the baby's heart rate improved but he remained cyanosed despite being in 100% oxygen. A loud systolic murmur was noted and he was transferred to the neonatal unit.

On arrival he had saturations of 53% in room air. This improved to only 65% in 100% facial oxygen though his work of breathing was not marked. His respiratory rate was 30-50 breaths per minute with no other signs of respiratory distress.

Cardiovascular examination at this point revealed a grade 3 systolic murmur but palpable femoral pulses and a mean non-invasive blood pressure of 44mmHg. His first blood gas result showed a pH of 7.15, a pCO<sub>2</sub> of 11Kpa and a lactate of 4.2.

At this stage the diagnosis was unclear. A newborn baby was presenting with low saturations showing little improvement with facial oxygen which would point to a cardiac cause for his cyanosis. However, the blood gas had revealed a mixed acidosis with an increased pCO<sub>2</sub>, suggesting a respiratory component to his presentation and the possibility of respiratory distress syndrome or sepsis.

Due to the blood gas interpretation and the likelihood of a respiratory pathology he was intubated, given a dose of surfactant and placed on a ventilator. His oxygen requirement improved rapidly to air and he began saturating consistently above 95%. Despite this rapid improvement his chest radiograph showed clear lung fields with no evidence of surfactant deficiency, and a normal cardiac silhouette.

At this stage the pathology which caused the baby to present with such severe cyanosis was not obvious. His murmur persisted on repeated examinations, and with the absence of any obvious respiratory cause an echocardiogram was performed.

The echo raised concerns that the aortic valve may be bicuspid and there was also moderate mitral regurgitation. But the more pressing finding was a severely impaired and dilated left ventricle, with a normally functioning right ventricle. The aortic arch was found to be normal and though the coronaries were difficult to visualise they were thought to be normally sited.

The diagnostic focus was now on identifying the cardiac pathology for the baby's presentation. The focal severe impairment of the left ventricle and abnormal aortic valve raised the possibility of a severe or critical aortic stenosis, but the flow across the valve was so poor at this stage that the diagnosis could not be confirmed. Another differential for focal ventricular impairment is myocardial infarction, an important diagnosis to consider as its management is very different, especially with regard to the use of inotropes in supporting cardiac function.

Blood troponin levels were subsequently performed and these were raised at 446ng/L (normal range 0-40ng/L). It was therefore felt that he had suffered a myocardial infarction which had affected a large proportion of his left ventricle. He was commenced on dobutamine at 5mcg/kg/minute for myocardial support and his blood pressure and lactate were maintained within normal limits.

Despite this diagnosis there still remained significant concern regarding his left ventricular outflow tract, so his case and images were discussed with the local cardiac centre. He was commenced on heparin due to the possibility of coronary vessel obstruction, but this was discontinued the next day following a repeat troponin that was falling (355ng/L) and an improvement in his left ventricular function on repeat echocardiogram performed at eighteen hours of age.

The baby continued to improve and his inotropes were discontinued after twenty-four hours. He was extubated on day two of life and commenced on milk feeds which were well tolerated. He remained in air following extubation and was cardiovascularly stable with normal blood pressure and lactate following cessation of the inotropes. A further echocardiogram performed on day three of life demonstrated a normal aortic valve and only a mildly impaired left ventricle. The coronary ostia were clearly identified and were normal.

The diagnosis therefore was of severe left ventricular impairment as a result of myocardial infarction, though the underlying cause of this has not yet been clearly defined. His rapid improvement after intubation was felt to be as a result of improved cardiac output following sedation and subsequent ventilation.

Following his rapid improvement he was commenced on captopril and after a further four days was discharged home. He has continued to have investigations as an outpatient including thrombophilia screening which has returned normal results. A further echocardiogram at three months of age now shows normal biventricular function and he continues to thrive. He will continue to have cardiology follow-up but no clear cause for his myocardial infarction has been identified to date.

## Conclusions

This case demonstrates the range of diagnoses in infants presenting with left ventricular failure. As well as coronary vessel abnormalities and critical aortic stenosis it is important to identify myocardial infarction. Rapid identification helps direct treatment, especially the use of inotropes which would be contraindicated

in critical aortic stenosis. Neonatologists should be aware of these differentials and the need for urgent investigation.

## Brain & Development / Neurodevelopmental Outcome

### IS HYPERGLYCEMIA ASSOCIATED WITH THE DEVELOPMENT OF RETINOPATHY OF PREMATURITY IN PRETERM INFANTS? (029)

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#### Introduction /Case Report

Previous predictive models of hyperglycemia as a risk factor for retinopathy of prematurity (ROP) did not include death as a competing outcome. Moreover, these models typically did not include postnatal age and therefore could not quantify the variable contribution of exposures to ROP risk factors over time. The objective of the study is to identify risk factors for ROP surgery, and the competing outcome of death, by postnatal day and to identify if persistent hyperglycemia (blood sugar > 200 mg/dL) requiring treatment with an insulin infusion during the early neonatal period was significantly associated with the composite primary outcome of ROP surgery or death before hospital discharge.

#### Patients and Methods

Univariate analysis was used to identify all the factors that influenced the risk for ROP surgery or death in 216 infants of <29 weeks gestational age. A total of 111 (51%) of 216 infants required ROP surgery or died before hospital discharge. A series of multivariate regression models were then developed separately for each of 3 time periods: postnatal days 14, 28, and 36 weeks corrected age using previously identified significant risk factors, and the models were examined using a C statistic (area under the curve). Infants were included in the model if they survived through the day of prediction, and the risk factors included for prediction were also present prior to that day.

#### Results

Infants who required ROP surgery or died before hospital discharge were smaller and more premature, were the product of multiple gestation, were more likely to have severe IVH, NEC, blood culture proven sepsis, longer (>14 days) stay on mechanical ventilation, and were more likely to have hyperglycemia treated with an Insulin infusion and hypotension treated with vasopressors or hydrocortisone during the first 2 weeks of life. Multivariate regression analyses identified birth weight, gestational age, multiple gestation, and the continued need for mechanical ventilation, but not hyperglycemia treated with an insulin infusion, were independently associated with an increased risk of the composite primary outcome for all 3 time periods evaluated. Prediction did not improve with advancing postnatal age, with a C-statistic ranging from 0.825 on Day 14, 0.851 on day 28, and 0.827 at 36 weeks.

#### Conclusions

Persistent hyperglycemia requiring treatment with an insulin infusion was not independently associated with an increased risk of ROP surgery or death. Hyperglycemia likely reflects the degree of prematurity as the birth weight/gestational age were the major variables driving the composite primary outcome.

## Brain & Development / Neurodevelopmental Outcome

### INTRODUCING PRECHTL'S METHOD ON QUALITATIVE ASSESSMENT OF GENERAL MOVEMENTS IN A NEONATAL INTENSIVE CARE UNIT, LEADING THE WAY IN THE MIDDLE EAST (278)

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#### Introduction /Case Report

Prechtl's method on qualitative Assessment of General Movements (GMs) has been validated as a specific predictor of neurological impairment in preterm, term and young infants.<sup>1,2,3</sup>

We would like to demonstrate the feasibility of introducing this method in a Tertiary Neonatal Intensive Care Unit (NICU) for the first time in the Middle East.

#### Patients and Methods

Training on using Prechtl's method was undertaken. The hospital has funded the purchase of a video camera that is required for the assessments. Guidelines were drawn up to identify babies to be targeted by the assessment. Information leaflet was produced. Parents of targeted babies were approached for consent. None declined.

We aimed at obtaining 2-3 video recordings at: 32-36 weeks Post Menstrual Age (PMA), 40-44 weeks PMA and 52 weeks PMA. All recordings were uploaded on a secure hospital computer. A special register for babies included in the assessment was maintained. The outcome of the assessments was plotted on an Individual Developmental Trajectory. Each result was communicated to the parents.

#### Results

Assessments commenced in October 2013. Over a period of 18 months, a total of 15 babies were assessed. It was possible to obtain at least two recordings for each baby. 13 babies were preterms. One baby was diagnosed with Hypoxic Ischaemic Encephalopathy (HIE) and the other baby was a late preterm with small intraventricular haemorrhage. All assessments were normal except one. This baby has shown abnormal GMs (Poor Repertoire). Unfortunately, it was not possible to continue the assessments due to relocation to a different country.

All babies are regularly attending the neonatal follow up and physiotherapy clinics. Their development is appropriate for their corrected gestation.

#### Conclusions

This assessment method was successfully implemented in an NICU setting. It proved to be highly accepted by the parents. This may be because it provides quicker answers to parents about their babies' neurological outcomes. As previously reported, the method has shown a very high predictive value in all babies undergone the assessment.<sup>4,5,6,7,8</sup>

Picture



## Brain & Development / Neurodevelopmental Outcome

### GROSS MOTOR ABILITIES ASSESSED BY ALBERTA INFANT MOTOR SCALE IN VERY PRETERM GREEK INFANTS UP TO 19 MONTHS OF CORRECTED AGE (345)

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#### Introduction /Case Report

The Alberta Infant Motor Scale (AIMS), a norm-referenced measure to assess the gross motor abilities of infants from birth to independent walking, has been mainly studied in full-term infants.

#### Patients and Methods

AIMS scores obtained at supine, prone, sitting and standing position, as well as total AIMS scores, were monthly evaluated up to 19 months of age in a cross-sectional cohort of 403 very preterm Greek infants (III grade, or central nervous system infection were excluded.

#### Results

AIMS scores at supine, prone, sitting and standing position were significantly lower in preterm than full-term infants up to 9, 16, 16 and 19 months of corrected age, respectively. Total AIMS scores were significantly lower ( $p < 0.001$ ) in preterm than term infants at each month up to 19 months of corrected age and correlated negatively with RDS ( $b = -1.71$ ; 95% CI: -2.50, -0.91), IVH ( $b = -1.10$ ; 95% CI: -1.86, -0.35), ROP ( $b = -1.33$ ; 95% CI: -2.23, -0.44), and being born SGA ( $b = -1.89$ ; 95% CI: -3.61, -0.17) in multivariate linear regression analysis.

#### Conclusions

Total AIMS performance of very preterm infants is lower than that of full-term peers even at 19 months of corrected age. The influence of neonatal morbidity factors including RDS, IVH and ROP, as well as being born SGA, should be taken into account when performing AIMS in infants born prematurely.

## Brain & Development / Structural and Functional Brain Imaging

### 'FEED AND WRAP' OR SEDATE AND IMMOBILISE FOR NEONATAL BRAIN MRI? LOCAL EXPERIENCE AND A UK NATIONAL SURVEY (339)

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#### Introduction /Case Report

Successful neonatal brain Magnetic Resonance Imaging (MRI) relies on having a settled infant to permit acquisition of good quality images. Unsettledness may cause motion artefact that can lead to diagnostic error and uncertainty; sometimes scans are unsuccessful and require costly rescheduling with concomitant parental anxiety. Use of premedication to assist neonatal MRI is controversial. Our aims were: i) to review local experience and success of MRI in epochs before and after introducing routine use of chloral hydrate sedation and a vacuum body splint-immobilisation device for MRI, and ii) to survey current UK practices regarding use of sedation for MRI.

#### Patients and Methods

We retrospectively reviewed brain MRI radiology reports of neonates treated for neonatal encephalopathy. Scans done on intubated neonates, elsewhere, or after the neonatal period were excluded. In epoch 1 (Sept 2010-Sept 2013) standard practice was 'feed and wrap', whereas in epoch 2 (Oct 2013-Jan 2015) we used routine chloral hydrate sedation and the Med-Vac infant immobiliser. Two reviewers independently assessed MRI scan quality by grading the local consultant radiologists' reports using a simple scoring system: 0=no movement artefact; 1=minor movement artefact, not limiting scan interpretation; 2=significant movement artefact precluding full interpretation.

In Feb 2015 we telephone surveyed all 53 UK tertiary NICUs to ask about use of sedative premedication for neonatal brain MRI.

#### Results

Median postnatal age at first MRI was 9 days in both epochs. Median scan duration in epoch 2 was 55 min (range: 41-80 min), ~10-15 minutes longer than in epoch 1 due to research spectroscopy acquisition. No baby had any clinical instability associated with chloral sedation. Table 1 shows scan gradings of the 71 babies included (Cohen's  $\kappa = 0.65$ ). Movement artefact was reported on 52% of scans in epoch 1 compared with 0% in epoch 2. Five babies (10%) in epoch 1 required seven repeat scans between them due to prior artefacted scans, while none (0%) in epoch 2 needed a repeat.

Survey responses were obtained from all 53 (100%) units: 16 (30%) routinely used sedation; 31 (59%) sometimes used, and 6 (11%) never used. Of sedation-using units, chloral hydrate was the preferred drug in most (42/47; 89.0%).

## Conclusions

In our centre, routine chloral sedation combined with Med-Vac immobilisation has safely achieved a 100% success rate for completed MRI. The combination has permitted good quality clinical and research brain imaging by significantly reducing movement artefact has proved far superior to the 'feed and wrap' method.

## Table

Table 1 *MRI scan quality in two epochs graded using a simple scoring system*

<i>Scan quality grade</i>	<i>Epoch 1: "Feed and wrap" (n = 48)</i>	<i>Epoch 2: Routine Sedation &amp; Med-Vac<sup>1</sup> (n = 23)</i>
0 = No artefact	23 (48.0)	23 (100)
1 = Minor artefact	7 (14.5)	0 (0)
2 = Major artefact	18 (37.5)	0 (0)

Data are n (%)

Other / Quality improvement and Safety and Error Preventio

## FATAL UMBILICAL VENOUS CATHETERISATION: LESSONS TO LEARN (753)

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### Introduction /Case Report

Umbilical venous catheters (UVCs) are inserted on a daily basis on neonatal units throughout the world and provide a vital role in supporting neonates through intensive care. Serious complications appear to be relatively rare, but can be dangerous if unrecognised. We report a case of fatal UVC extravasation that presents some learning points.

### Case Report

A 31 week gestation baby boy (1780 g) had a UVC inserted within a few hours of birth for fluids and feeding. The position of its tip on x-ray (T12 vertebral level) was well below the diaphragm but was considered satisfactory. Parenteral nutrition (PN) was commenced.

On day 4, while the UVC was still in situ, the baby developed progressive abdominal distension and respiratory distress. Necrotising enterocolitis was suspected. An AXR was done, enteral feeds were stopped, and antibiotics started. By ~7 hours after first onset of abdominal distension the abdomen was severely distended compromising ventilation and he required intubation. He collapsed and had a long period of severe acidosis and clinical seizures. Resuscitation drugs, fluids, and blood products were administered, including through the UVC.

A repeat AXR done ~5 hours after first onset of abdominal distension showed the UVC tip at T12 level and ascites but no perforation (Fig 1). By ~9 hours after first onset of the abdominal distension, because of poor ventilation and marked respiratory acidosis, abdominal paracentesis was done with immediate improvement to oxygen saturation. 140 mL of creamy-coloured liquid suggestive of extravasated PN lipid solution. He was then transferred to a surgical centre.

The baby was flaccid and unresponsive on arrival suggesting severe encephalopathy. Cerebral function monitoring showed a persistent very low voltage trace. The baby developed progressive lactic acidosis, renal failure, clinical coagulopathy, and profound hypotension. He died aged 5 days following withdrawal of intensive care.

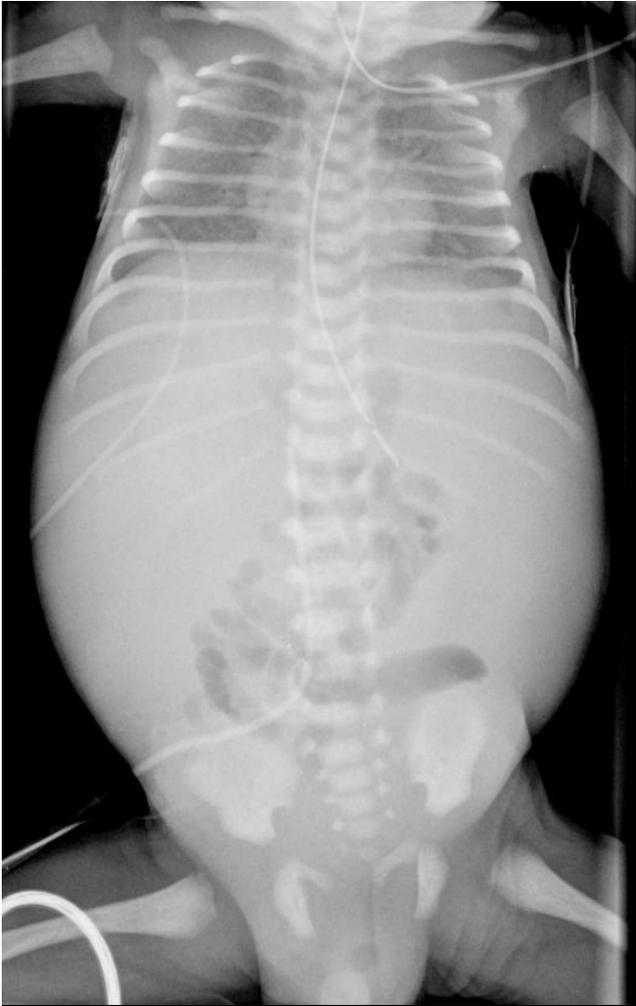
The primary diagnosis was intra-abdominal PN solution extravasation from the UVC causing progressive abdominal distension, severe respiratory embarrassment and ultimately cardiorespiratory collapse, protracted acidosis and fatal severe encephalopathy. A post mortem examination confirmed the cause of death as being intraperitoneal extravasation of PN solution.

### Conclusions

This case reminds practitioners of the potential dangers posed by UVCs. Extravasation is a relatively rare complication but can be fatal if unrecognised. Most extravasations occur with low-lying UVCs. Extravasation must always be considered in the differential diagnosis of necrotising enterocolitis in any baby with a UVC

in situ who develops abdominal distension. This case has prompted a national patient safety initiative in the UK.

Picture



## Other

Hypercalcemia in the course of subcutaneous fat necrosis in neonates after therapeutic hypothermia – report of 2 cases (495)

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## Introduction /Case Report

Subcutaneous fat necrosis (SCFN) is a rare, transient and self-limiting complication of birth asphyxia. It is characterized by painless nodules developing on the back, limbs and buttocks, which move freely over muscle and bone, with the overlying skin that may be of normal color or with erythematous discoloration. These lesions disappear spontaneously without scarring, but there may be systemic complications associated with SCFN. The most serious potential complication is hypercalcemia.

## Case Report

### Case 1

A female newborn weighing 4340 g delivered by cesarean section (indication: fetal life-threatening symptoms) at 37 weeks of pregnancy complicated by type C diabetes and Hashimoto's disease. She was born with Apgar score 0, 0, 0, 1 and 4 at 1, 3, 5, 10 and 15 minutes, respectively. Umbilical cord pH was measured at 6.71 (BE -21.2 mEq/l) and 6.78 (-21,0 mEq/l). Artificial ventilation in NICU was continued until day 10. Due to clinical symptoms of hypoxic ischemic encephalopathy whole-body cooling was initiated at hour 4, and continued for the next 3 days of life. Clinical and biochemical indicators of post-asphyxia multiple organ dysfunctions (renal, liver, heart insufficiency) were found. Subsequent cranial ultrasound scans revealed minor ischemic areas around cerebral ventricles. As of day 32, the infant presented reddish discoloration of the skin and subcutaneous nodules located primarily on her back and along the posterior side of her arms. Skin lesions were accompanied by the following abnormal results of laboratory tests: hypercalcemia (peak level of Ca<sup>2+</sup> at day 23: 2.9 mmol/l; reference range: 2.2-2.5 mmol/l), hypertriglyceridemia (peak triglyceride level at day 23: 217 mg/dl; reference range: below 150 mg/dl). Newborn was put on a low-calcium, low-vitamin D3 diet, and diuretics were administered. As a result, skin lesions were gradually resolving, and the Ca<sup>2+</sup> levels and lipid metabolism were normalized. The baby was discharged from hospital at day 42, with a good general health status.

### Case 2

A female full-term neonate weighing 5070 g was delivered by cesarean section in week 39 of pregnancy because fetal life-threatening symptoms. The pregnancy was complicated by maternal G2 diabetes. Child was born with Apgar score of 5, 2, 2, 5 and 6 at minute 1, 3, 5, 10 and 15, respectively. Umbilical cord pH was 6.79 (BE -18.9 mEq/l) and 6.98 (-15.0 mEq/l). After resuscitation neonate was transferred to the NICU, where artificial ventilation was applied until day 5. Because of the signs of serious intrauterine hypoxia therapeutic hypothermia (COOL-CAP) was applied. Biochemical indicators of post-asphyxia multiple organ dysfunctions observed. In the cranial ultrasound scan two weeks of the patient's life considerable leukomalacia. In her second month of physical examination revealed multiple subcutaneous painless nodules, ca. 0.5 – 1.0 cm in diameter, located on the thorax, the back, the extensor surface of arms, external side of thighs and on the buttocks. The clinical symptoms were accompanied by abnormal calcium and lipid metabolism. (total plasma calcium level was 3.10 mmol/l, and it peaked at day 35 of life at 4.0

mmol/l; triglyceride level was 386 mg/dl). The infant was put on a low-calcium/low-vitamin D3 infant formula, and steroid therapy was administered. No spectacular improvement in skin condition was achieved after two weeks of therapy (the lesions were still present at discharge from hospital). Total plasma calcium level at that point was 2.70 mmol/l and triglyceride level – 508.9 mg/dl. The patient was discharged from hospital at day 48 of her life, with recommendations low-calcium/low-vitamin D3.

## Conclusions

SCFN may represent a life-threatening complication of therapeutic neonatal hypothermia. It is advised that newborn infants treated with hypothermia for perinatal asphyxia should be regularly checked for the presentation of skin symptoms. Treatment for hypercalcemia involves a low-calcium diet, diuretics and corticosteroids. Blood calcium levels in patients with SCFN should be monitored once a week over the period of six months after the disappearance of skin lesions.

POSTHEMORRHAGIC VENTRICULAR DILATATION IN PRETERMS: ARE LINEAL MEASUREMENTS RELATED TO VENTRICULAR VOLUME? A STUDY THROUGH 3D ULTRASOUND (403)

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Introduction /Case Report

Post-haemorrhagic ventricular dilatation (PHVD) is usually monitored by conventional two-dimensional (2D) ultrasound after intraventricular hemorrhage in preterm infants. Linear measurements of the lateral ventricles are used for this purpose; however, given the complex morphology and disposition of lateral ventricles we wanted to know how good one, two or three of these measurements would reflect the dynamic and progressive change in volume in PHVD. The aims of this study were to determine the volume of the lateral ventricles using 3D ultrasound (3D US) in preterm infants with PHVD and evaluate the relationship between volume and ventricular linear measurements.

Patients and Methods

Serial 2D and 3D ultrasound was prospectively performed in very low birth weight infants with PHVD admitted to Neonatal Intensive Care Unit (NICU) at University Hospital Puerta del Mar, Cádiz, from January 2013 to December 2014. Ventricular index (VI), anterior horn width (AHW), and thalamo-occipital distance (TOD) were measured and used as ventricular linear measurements. Ventricular volume was calculated offline using virtual organ computer-aided analysis (VOCAL) with rotation steps of 15° (12 planes). Statistical analysis through Pearson correlation coefficient (r) and simple and multiple linear regression was performed. The intraclass correlation coefficient (ICC) was used to evaluate intra- and interobserver reproducibility.

Results

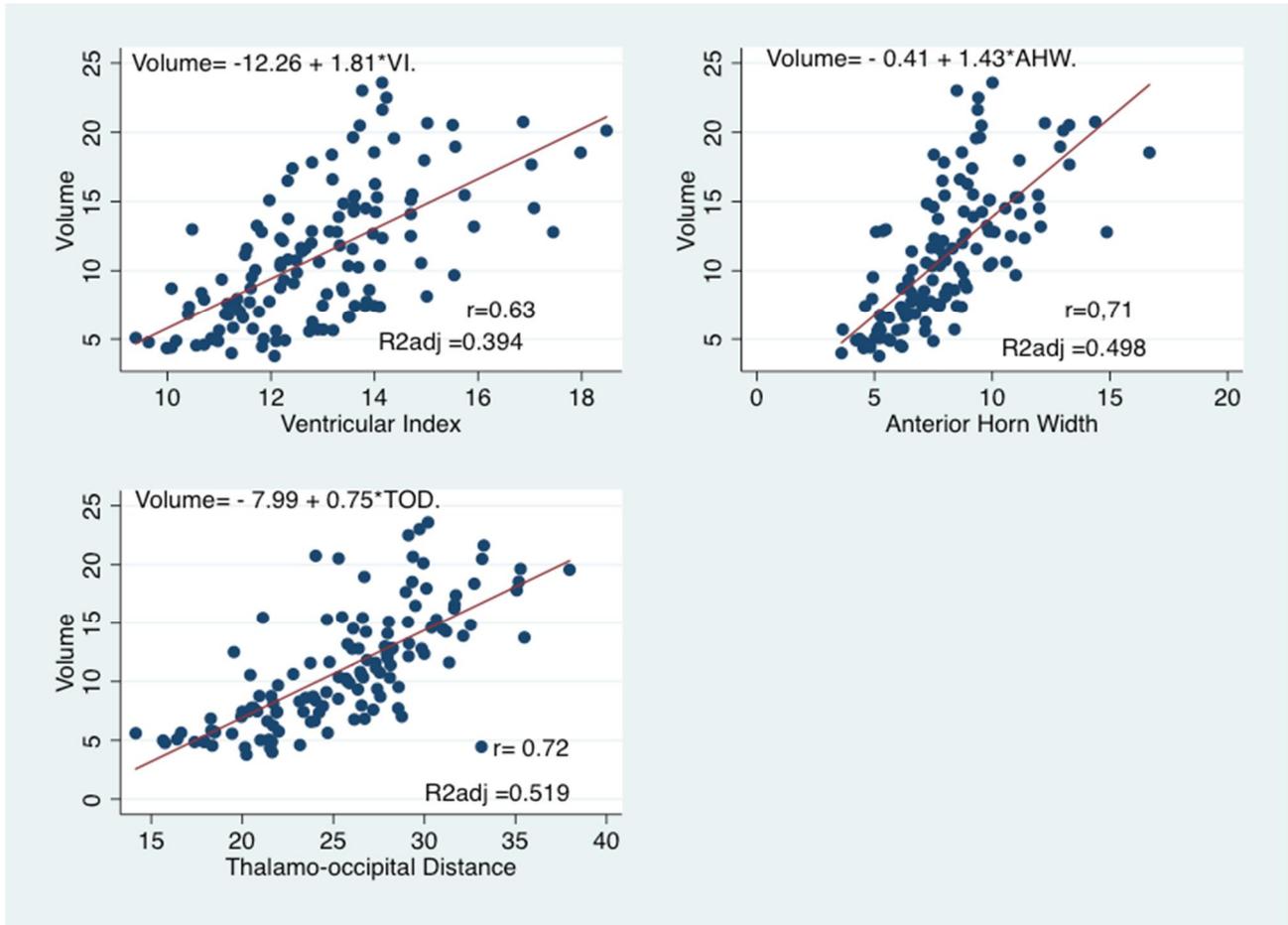
seven infants met inclusion criteria and were enrolled in the study. A total of 130 ventricles were measured. For volume and linear measurements, r ranged from 0.28 to 0.84. Each linear measurements was significantly associated with volume in simple linear regression models (Fig.1) and an equation was obtained through significant multiple linear regression model ( $F(3,126) = 128.92, p = 0.0000$ ): Ventricular volume (cm<sup>3</sup>) =  $-16.09 + 0.59 \cdot VI + 0.67 \cdot AHW + 0.56 \cdot TOD$ . This model, that includes VI, AHW and TOD, was better than those that included one or two linear measurements to explain ventricular volume ( $R^2_{adj} = 0.75$ ) There was no correlation of volume with head circumference. The ICCs for intra- and interobserver reproducibility were 0.9834 and 0.9287, respectively.

Conclusions

The lateral ventricular volumes of preterm infants with PHVD can be reliably determined using 3D ultrasound. We found that ventricular volume can be well estimated through three linear measurements: VI, AHW and TOD. The equation found through multiple linear regression could also be used as a prediction

model for ventricular volume. More studies are needed to address the importance of volume determination in monitoring PHVD in preterm infants.

Picture



Brain & Development / Neonatal Brain Injury and Neuroprotection

REGIONAL OXIMETRY IN NEONATES OF DIFFERENT GESTATIONAL AGE IN NICU (555)

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### Introduction /Case Report

The main strategy in modern neonatal intensive care is to prevent complications and improve the outcomes. Adequate respiratory support is one of the main factors for favorable prognosis in newborns of different gestational age (GA) in neonatal intensive care unit (NICU). It's well-known that inadequate ventilation can lead to hyperoxia or hypoxia, which cause an abnormal perfusion in different tissues and could result in complications. For that reason neonatologists try to find ways to monitor their patients to be ahead of evolving pathology and avoid the severe impact of negative events. Near-infrared spectroscopy (NIRS) allows monitoring of tissue oxygenation in real time.

### Patients and Methods

**PURPOSE:** Comparison of regional oximetry data in newborn babies based on GA, body weight and the need for respiratory support

We recruited 66 newborns in Moscow city hospital 24. For measuring the regional oxygen saturation we used Equanox Model 7600 device. Sensors were placed over the forehead for cerebral regional saturation (cSO<sub>2</sub>) and over the liver in the right upper quadrant for somatic regional saturation (sSO<sub>2</sub>).

Statistical analysis was performed using Statistica 8, results are expressed as Me [LQ;UQ].

26 healthy term newborns were examined as reference. 40 patients in NICU were examined as the main group. Based on GA they were divided into 2 subgroups: Group 1, 11 term babies and Group 2, 29 preterm newborns with GA 25-36 wks (32 [28;34]) (Tab.).

### Results

In reference group more often cSO<sub>2</sub> values were higher than sSO<sub>2</sub> (23 of 26 babies, 88,5%) (Pearson  $\chi^2$ (df=1)=9.6; p=0.002).

In Group 2 the proportion of patients with higher cSO<sub>2</sub> than sSO<sub>2</sub> values (53,6% vs 46,4%) was larger than in reference group (11,5% vs 88,5%) (Pearson  $\chi^2$ (df=1)=10.72; p=0.001).

In both groups of NICU patients sSO<sub>2</sub> values were lower comparing to reference group, but not significantly (Tab.)

Evaluation of somatic oxygenation depending on body weight showed decrease in sSO<sub>2</sub> values in VLBW infants (F(2,35)=4,6, p=0,02).

28 of 40 NICU patients received respiratory therapy: 13 diffuse O<sub>2</sub>, 7 continuous positive pressure (CPAP), 5 assisted ventilation (IMV) and 3 high frequency ventilation (HFV). In patients under CPAP cSO<sub>2</sub> values were significantly higher (F(5,60)=3,9, p=0,004) (Pic.)

sSO<sub>2</sub> values were lower among IMV patients (F(5,59)=2,9, p=0,02) comparing to all other groups.

### Conclusions

Decreased tissue oxygenation in VLBW patients is a result of poor perfusion (ischemia) and requires clinicians attention and therapy correction due to high risk of enterocolitis and other complications.

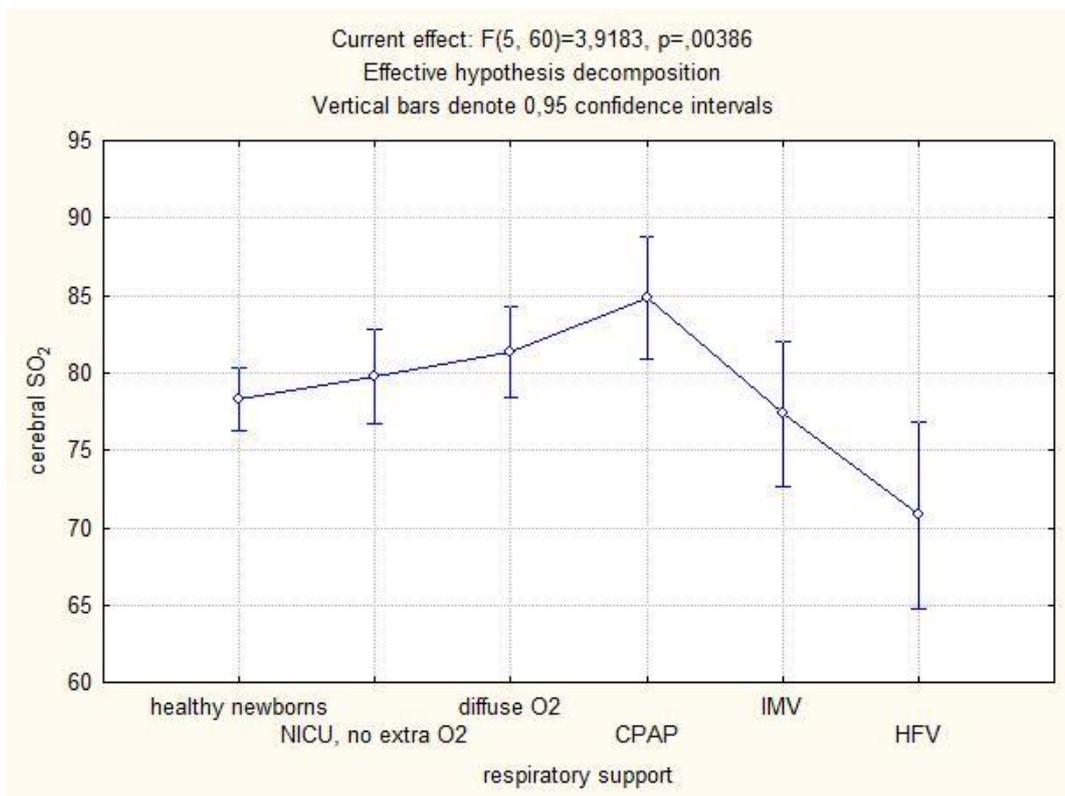
Our results forced to pay more attention to CPAP as potentially dangerous for cerebral hyperoxia.

NIRS provides information about the oxygen status of tissues/organs and allows clinicians to promptly change the therapy and improve the outcomes.

Table

	Reference Group (healthy term newborns)	NICU Group	
		Group I Term newborns	Group II Preterm newborns
Number of children	26	11	29
Weight, g Me [LQ;UQ]	3630g [3250;3800]	3410g [3180;3820]	1825g [1025;2125]
Apgar score at 1 min	8 [8;8]	7 [5;7]	6 [5;7]
Apgar score at 5 min	9 [9;9]	7 [6;8]	7 [6;7]
cSO <sub>2</sub> , Me [LQ;UQ]	78,4 [76; 80,5]	78,5 [77,5; 81,3]	82,25 [78,8; 84,5]
sSO <sub>2</sub> Me [LQ;UQ]	85 [80,5; 87,3]	81,5 [76,3; 86,5]	81,75 [76,1; 84,8]

Picture



Nutrition and gastroenterology / Nutrition of the Very Preterm

EFFECT OF ORAL VITAMIN A AND D SUPPLEMENTATION IN VERY LOW BIRTH WEIGHT INFANTS (010)

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### Introduction /Case Report

Very low birth weight (VLBW) infants are at risk for developing multiple vitamin deficiencies. Intramuscular vitamin A supplementation has shown to reduce bronchopulmonary dysplasia (BPD) and oxygen dependency at 36 weeks postmenstrual age in extremely low birth weight infants. Vitamin D plays major role in calcium metabolism and bone health. Recently, there are increasing data regarding vitamin D effect beyond bone health such as regulation of immune system. Currently, there are no intramuscular vitamin A and oral solution of vitamin D available in Thailand. Therefore, we conducted the study to evaluate efficacy of vitamin AD tab supplementation in VLBW infants.

### Patients and Methods

VLBW infants (BW<1500 g) were randomized at time of full feeding to received either oral vitamin AD tab (vitamin A 5000 IU and vitamin D 400 IU) three times per weeks for 4 weeks or standard care. Serum retinol was analyzed by HPLC methods and serum 25OH(D) was analyzed by CMIA methods (Architect-25 OH vitamin D, Abbott) at time of enrollment and 4 weeks later. Infants in both groups were received multivitamin supplementation (Multivitamin drop; vitamin A 2000IU and vitamin D 400IU/ml). Infants demographic data, growth parameter, vitamin level and clinical outcomes such as BPD, osteopenia of prematurity, etc. were collected. The primary outcomes were vitamin A and D status after 4 weeks of supplementation.

### Results

A total of 19 VLBW infants were randomized; 12 as intervention group and 7 as control group. Mean (SD) birth weight and GA were not different in both groups. (1107(278.23)g and 28.75 (1.87) weeks VS 1135.14 (198.87)g and 29(2.45) weeks in intervention and control group, respectively. Plasma retinol concentration after study completion were not significantly different in both groups; mean(SD) 16.11(4.74) VS 18.67(7.19) mcg/dL in intervention and control group, respectively. But plasma 25(OH)D concentration were significantly higher in intervention group after complete supplementation; mean(SD) 30.9(14.11) VS 18.99 (4.71) ng/ml,  $p=0.046$ . There were no significant different in terms of clinical outcomes such as BPD, osteopenia of prematurity etc.

### Conclusions

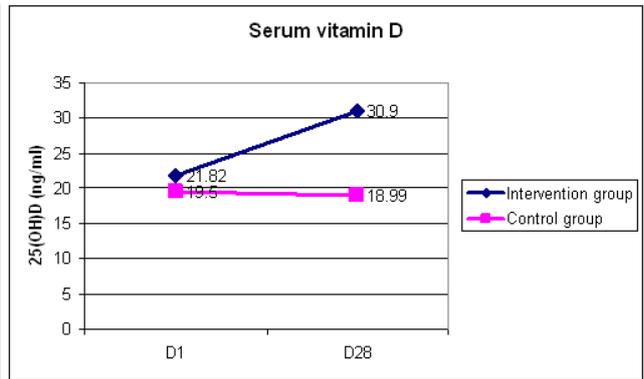
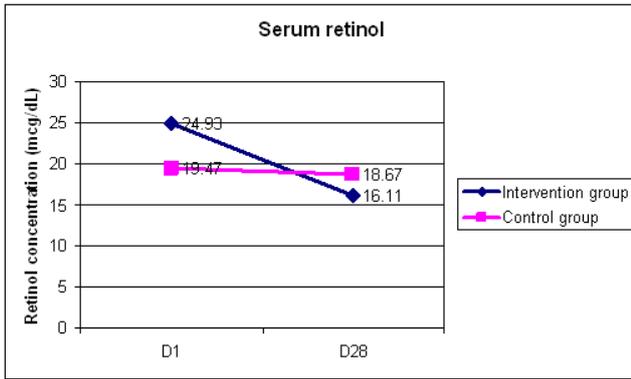
In this study, oral supplementation of vitamin AD tab failed to improve vitamin A status and reduce the incidence of BPD in VLBW infants. But this regimen did improve vitamin D status of these infants.

Table

	<b>Intervention group</b> (N=12) Mean (SD), N(%)	<b>Control group</b> (N=7) Mean (SD), N(%)	<i>p-value</i>
Birth weight (g)	1107 (278.23)	1135.14 (198.87)	0.818
GA (wk)	28.75 (1.87)	29 (2.45)	0.804
SGA	4 (33.3)	1(14.3)	0.603
ELBW	5 (41.7)	2 (28.6)	0.656
Antenatal steroid			
■ Complete	■ 6 (50)	■ 57.1 (4)	0.117
■ Partial	■ 5 (41.7)	■ 0	
■ No	■ 1 (8.3)	■ 3 (42.9)	
Apgar score ≤ 3			
■ At 1 min	■ 1 (8.3)	■ 1 (14.3)	■ 1.0
■ At 5 min	■ 1 (8.3)	■ 1 (14.3)	■ 1.0
Delivery room intubation	3 (25)	3 (42.9)	0.617
Days of intubation*	1 (0-42)	7 (0-23)	0.826
Breastmilk intake (%)*	86.97 (0-100)	100 (27.6-100)	0.72
TPN days*	9.5 (7-20)	11.0 (2-27)	0.966
BW at enroll	1238.33 (206.67)	1462.14 (334.2)	0.087
Maternal DM	8.3 (1)	0	1.0
Maternal HT	25 (3)	14.3 (1)	1.0

\* median (min-max)

Picture



Nutrition and gastroenterology

## THE USE OF DRIED BLOOD SPOTS CITRULLINE LEVELS AS A DIAGNOSTIC TOOL TO PREDICT MECONIUM OBSTRUCTION OF PREMATURITY (456)

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### Introduction /Case Report

Citrulline is a nonprotein amino acid synthesized in the enterocyte of small bowels. Recently studies have reported plasma citrulline levels correlate with function enterocyte mass and associated with necrotising enterocolitis in preterm neonates. This study aimed to define a normal DBS citruelline level in the premature population and determine a diagnostic tool to screen for meconium obstruction of prematurity (MOP).

### Patients and Methods

A retrospective cohort study was performed in 236 infants born at less than 32 weeks of gestation who were admitted to the neonatal intensive care unit (NICU) of Seoul University Hospital from Oct 2009 to Aug 2014. In this study, we collected citrulline concentrations routinely measured in dried blood spots (DBS) within 7 days after birth. Dried blood spots (DBS) sample were analyzed by Mass Spectrometry/Mass Spectrometry (MS/MS) method. Meconium obstruction and . DBS citrulline and other factors such as birth weight, gender, gestational age, meconium obstruction were analyzed to determine whether a correlation exists among the factors.

### Results

A total of 242 infants were included, with median birth weight of 1160 g and median gestational age 29.57 weeks. DBS citrulline is not associated with birth weight, gender, and gestational age. DBS citrulline levels decreased significantly when the patient presented meconium obstruction ( $p$ -value=0.037). In addition, DBS citrulline of preterm neonates who presenting complicated meconium obstruction treated with surgery were significantly lower as compared to healthy groups ( $p$ =0.0091).

### Conclusions

In our study, DBS citrulline levels are reduced in preterm infants with meconium obstruction in comparison to the control group. DBS citrulline monitoring, which are easily measured, may be useful in predicting early diagnosis of meconium obstruction of prematurity (MOP).

Nutrition and gastroenterology / Necrotising Enterocolitis

## LOW DIASTOLIC BLOOD PRESSURE IN TERM INFANTS WITH CONGENITAL HEART DISEASE AND SEVERE NECROTIZING ENTEROCOLITIS (505)

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### Introduction /Case Report

Necrotizing enterocolitis (NEC) is a devastating disease that affects term infants with congenital heart disease (CHD). Currently, the pathogenesis of the increased risk of NEC in term infants with CHD is unknown. One of the hypotheses states that low body perfusion due to retrograde diastolic flow in the ductus arteriosus, represented by a low diastolic blood pressure, results in ischemia of the bowel. Therefore, we aimed to explore whether diastolic blood pressure is lower in term infants with CHD who develop NEC (CHD+NEC) compared to term infants with CHD who do not develop NEC (CHD-NEC). Our second aim was to explore whether a low diastolic blood pressure is a predictor of severe NEC.

### Patients and Methods

Between December 2003 and December 2013, 565 infants with CHD and a gestational age >35 weeks were admitted to our NICU. Thirteen infants out of 565 infants developed NEC and were retrospectively included in this case-control study. We matched these infants 1:1, by type of CHD and date of birth, with infants from the same cohort who did not develop NEC. Diastolic blood pressure values, measured invasively or non-invasively, were collected at first day after admission, two days and one day prior to NEC onset. Severity of disease was assessed by Bell's stage. We used the Mann Whitney U test to assess differences in diastolic blood pressure between CHD+NEC and CHD-NEC, between CHD+NEC (Bell's stage 1 and 2) and CHD+NEC (Bell's stage 3) and between CHD-NEC and CHD+NEC (Bell's stage 3).

### Results

Median age of NEC onset was 5 days (interquartile range (IQR) 2.5-8). We found no significant differences in mean diastolic blood pressure between NEC cases and matched controls at the day of admission and two or one day(s) prior to NEC onset. However, when NEC cases were categorized by Bell's stage, diastolic blood pressure tended to be lower at day one of admission in infants with Bell's stage 3 (median 34.4 mmHg, IQR 34.2-36.5) compared with Bell's stage 1 (median 49.7 mmHg, IQR 41.6-57.8,  $p=0.08$ ) and compared with Bell's stage 2 (median 43.9 mmHg, IQR 39.7-47.1,  $p=0.07$ ). Furthermore, mean diastolic blood pressure in Bell's stage 3 patients ( $n=3$ , median 34.4 mmHg, IQR 34.2- 36.5) tended to be lower at the first day after admission than that of their matched controls (median 41.8 mmHg, IQR 40.3-45.9,  $p=0.05$ ).

### Conclusions

While low diastolic blood pressure might not be associated with the occurrence of any NEC in CHD patients, it may be associated with a complicated course of NEC. Therefore, diastolic blood pressure might be a predictor of severe NEC in infants with CHD

Nutrition and gastroenterology / Nutrition of the Very Preterm

OBSERVATIONAL STUDY EVALUATING NEED FOR EARLY SODIUM SUPPLEMENTS IN PRETERM INFANTS (554)

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### Introduction /Case Report

Poor weight gain is associated with adverse neurodevelopmental outcomes in premature infants below 32 weeks gestation.<sup>1</sup> Adequate sodium intake is essential for postnatal growth.<sup>2</sup> Recent studies have shown improved growth rates and neurodevelopmental outcomes with no increase in prematurity related morbidity from early sodium supplementation.<sup>3</sup> The European Society of Paediatric Gastroenterology, Hepatology and Nutrition recommend routine sodium supplementation of unfortified breast milk.<sup>2</sup> In this study we compared the need for sodium supplementation in preterm infants on expressed breast milk (EBM), with or without fortifier (BMF), mixed feeds and formula milk.

### Patients and Methods

Retrospective observational study of all preterm infants below 32 weeks gestation in a tertiary NICU between 01/01/2014 and 31/12/2014 (12 months) were included. Sodium supplementation was instituted when serum sodium fell below 135mmol/l. Data collection was done using BadgerNet records. Statistical analysis was conducted using Fisher's exact test and an unpaired t-test.

### Results

A total of 142 preterm infants were identified. 17 were excluded due to incomplete data, 125 babies were included in the analysis. Results and baseline characteristics are displayed in Table 1. Baseline characteristics were comparable across the groups. Mean weight at 36 weeks corrected gestational age was greater in those on formula (2267g) vs EBM 1835g ( $p=0.0002$ ) and vs EBM+BMF 2023g ( $p=0.0103$ ), but no difference in those who had mixed feeds. More EBM+BMF infants (81.8%) required sodium supplementation compared to formula fed infants (43%,  $p=0.0128$ ). A similar though not statistically significant trend was observed for EBM infants (69.4%,  $p=0.1225$ ), however this was not seen in the mixed feeding group.

### Conclusions

Preterm infants below 32 weeks on EBM +/- BMF needed sodium supplementation compared to those on formula. Early supplementation should be considered in preterm infants receiving fortified and unfortified breast milk as sodium content may be too low for nutritional demand. A large randomised controlled trial is needed to compare the effectiveness of early (pre-emptive) and late (once serum sodium falls below reference range) supplementation.

Table

**Table 1: Results comparing those fed exclusively on expressed breast milk (EBM), expressed breast milk with breast milk fortifier (EBM+BMF), mixed feeds (EBM, EBM+BMF & formula) and formula.**

	EBM	EBM+BMF	Mixed	Formula	p Value (<0.05)		
					EBM vs. Formula	EBM+BMF vs. Formula	Mixed vs. Formula
Total number of babies	36	33	40	16			
Mean gestation (weeks)	27+6	27+2	28+6	29+0	0.0719	0.0802	0.8695
Mean birth weight (g)	1018	1002	1116	1078	0.5025	0.3999	0.3597
Median no of days to reach full enteral feeds	15	15	12	13			
Percentage receiving diuretics for >72 hours	30.6%	39.4%	30%	25%	0.7522	0.3601	0.9999
Mean weight at 36/40 (g)	1835	2023	2096	2267	<b>0.0002</b>	<b>0.0103</b>	0.0677
Percentage receiving sodium supplements	69.4%	81.8%	52.5%	43%	0.1225	<b>0.0128</b>	0.7681

## Nutrition and gastroenterology / Micronutrients

Is vitamin D deficiency associated with chronic lung disease in preterm infants? (440)

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### Introduction /Case Report

Neonatal chronic lung disease (CLD) is an important cause of morbidity and mortality. Vitamin D is known for its role in bone metabolism, but physiology suggests it influences lung fibroproliferation, remodelling and function (1). There is evidence implicating vitamin D's association with chronic lung diseases like asthma (2). An animal study speculates that decreased vitamin D levels may contribute to the pathogenesis of bronchopulmonary dysplasia (3). The aim is to determine if there is an association between vitamin D levels in preterm neonates and chronic lung disease.

### Patients and Methods

Retrospective observational study on a preterm neonatal population (<37 weeks), over 18 months from Nov 2013 to Mar 2015 in a tertiary NICU. Preterm infants with vitamin D levels within the first 3 months of life were included. Vitamin D levels were only done if the Alkaline Phosphatase was high, or rapidly rising. In neonates with vitamin D levels measured, chronic lung disease status was identified. The definition of chronic lung disease used is the requirement of oxygen for more than 28 days. Analysis was done using the SPSS version 19. Parametric t-test was used to compare the means in both groups.

### Results

A total of 29 infants were included in the study. In the studied population, 25 infants had CLD, and 4 did not have CLD. The mean levels of vitamin D calculated in both groups independently, were lower than the normal reference range. Mean vitamin D levels were lower in the CLD group (mean vitamin D level= 52.64, SD= 12.42) than in the group without CLD (mean vitamin D level= 57.75, SD= 14.97). However, comparison of mean vitamin D levels between both groups was not statistically significant ( $p=0.463$ , parametric t-test). (Table 1)

### Conclusions

This pilot observational study showed vitamin D levels were lower in the chronic lung disease group, the results were not statistically significant. Future aim would be to do prospective studies with larger numbers. In order to detect a statistically significant difference (power=80%,  $p<0.05$ ), the number needed is 232 patients.

Table

	CLD (n=25)	No CLD (n=4)
Gestation mean	26,08	32,25
Weight mean	766,44	1703,75
Age of testing mean	41,56	36,25
Mean Vitamin D levels	52,64	57,75

## Nutrition and gastroenterology / Breast feeding

### CAN MOTHERS BEYOND ONE YEAR OF LACTATION BE DONORS OF HUMAN MILK FOR PREMATURE INFANTS (785)

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## Introduction /Case Report

The percentage of preterm infants - beneficiaries of the Human Milk Bank of Ludwik Rydygier's Provincial Polyclinical Hospital in Torun is 75% on average. The donors are usually women in the first year after delivery on time, or mothers of premature infants. In the Kuyavian-Pomeranian Voivodeship the percentage of women breastfeeding till 16-24 months after delivery is 5%. We decided to find out if their milk is also valuable for preemies.

## Patients and Methods

We have analysed the macronutrients and energy contents in 132 samples of expressed milk from 21 preemies' mothers, 96 samples from 12 term infants' mothers in the first 2-6 weeks of lactation, and 144 samples from 30 mothers beyond one year of lactation. We compared the results concerning fat, total nitrogen, carbohydrates and energy contents, using a human milk analyser (MIRIS).

## Results

Fat concentration in milk samples from compared groups was significantly different ( $F(2,60)=8.917$ ;  $p=0.0004$ ) - in milk samples from mothers over one year of lactation was higher than in milk samples from preterm infants' mothers or term infants' mothers'. Total nitrogen concentration significantly varied among compared groups ( $F(2,60)=5.367$ ;  $p=0.007$ ). Total nitrogen content in term infants' mothers' milk was significantly lower than in preterm infants' mothers' milk and in milk from mothers over one year of lactation. In case of energy contents we also observed significant differences among compared groups ( $F(2,60)=7.717$ ;  $p=0.001$ ). The energy contents in milk samples from mothers over one year of lactation was significantly higher than in both other groups. Carbohydrates content showed no significant differences between all analysed groups (Table 2).

## Conclusions

The results allow to conclude, that women beyond one year of lactation shouldn't be rejected as donors because the macronutrient value of their milk is appropriate to the needs of premature infants. In addition,

our results highlight the value of breastfeeding for as long as WHO recommended. It is desirable to conduct further research to evaluate bioactive content in milk obtained from such a subgroup of donors.

Table

Parameters	Total nitrogen [g/dL]	Energy [kcal/dL]	Lactose [g/dL]	Fat [g/dL]
mean ± SD	1.26-3.18	58.17-82.09	5.56-6.88	2.87-5.09
median	1.77	68.85	6.63	3.67
min-max	0.92-2.60	55.00-95.80	4.52-7.67	2.50-6.54
mean ± SD	1.02-1.42	51.78-71.40	5.07-9.29	2,21-4.23
median	1.20	58.82	6.66	3.26
min-max	0.90-1.65	46.63-75.89	5.10-13.59	1.80-4.66
mean ± SD	1.17-2.25	61.15-103.67	6.01-7.01	3.30-7.44
median	1.62	76.45	6.63	4.67
min-max	1.10-3.73	47.00-138.00	4.87-7.10	2.60-11.07
F(df); p	<b>F(2,60)=5.367; p=0.007</b>	<b>F(2,60);p=0.001</b>	F(2,60)=2.008; p=0.143	<b>F(2,60)=8.917;p=0.0004</b>
group1-group2; p	<b>0.503; p=0.004</b>	8.533; p=0.075	-	0.764; p=129
group1-group3; p	0.015; p=0.913	<b>-12.281; p=0.27</b>	-	<b>-1.382; p=0.010</b>
group2-group3; p	<b>-0.488; p=0.004</b>	<b>-20.814; p=0.0003</b>	-	<b>-2.146; p=0.0002</b>

Nutrition and gastroenterology / Necrotising Enterocolitis

INCIDENCE OF NECROTISING ENTEROCOLITIS (NEC) IN PRETERM INFANTS OF LESS THAN 32+0 GESTATION WITH A BIRTH WEIGHT BELOW THE SECOND CENTILE (693)

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### Introduction /Case Report

Infants with intrauterine growth restriction (IUGR) are at increased of NEC<sup>1</sup>. Mortality from NEC in very low birth weight (VLBW) infants is 10%<sup>2</sup>. This study determined the incidence of NEC in extremely preterm, growth restricted infants born in a non-surgical tertiary NICU.

### Patients and Methods

Infants born <32+0 weeks gestation between January 2010 to 2015 were identified on Badgernet. Data was collected for those with birth weight <2nd centile<sup>3</sup>.

### Results

Twenty nine infants were identified. Three were excluded due to congenital anomalies. The remaining 26 infants accounted for 3% of all NICU preterm admissions. Median gestation and birth weight were 27+1 and 617grams respectively. Twenty infants (77%) had abnormal dopplers. When enteral feeds were first commenced: 24 (92%) infants received maternal breast milk (MBM), one (4%) donor milk and one (4%) preterm formula. Median times to commencing and reaching full enteral feeds were six and 21.5 days respectively. Five (19%) had NEC with Bell staging 2 or 3. Of these, two (8%) underwent laparotomies. Three (12%) of the infants with NEC died. There was no difference in incidence of NEC between infants with birth weights below 0.4th or 2nd centile ( $p=1.0$ ). Twenty one (80%) infants survived to discharge and of these eleven (42%) were receiving MBM or MBM and formula.

### Conclusions

This study reported a 12% mortality due to NEC in extremely low birth weight high risk preterm infants compared with 10% in VLBW infants. Identifying protective factors in this high risk group would require further study.

Nutrition and gastroenterology / Metabolism

## RISK FACTORS FOR BONE MINERAL DISTURBANCES IN PREMATURE INFANTS (834)

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### Introduction /Case Report

Osteopenia of prematurity represents a postnatal delay in bone growth and mineralization. It's incidence is growing. Extreme prematurity and low birth weight, low dietary intake of calcium, phosphorus and vitamin D, prolonged total parenteral nutrition and delayed enteral nutrition, chronic diseases are known risk factors. The aim of this paper is to evaluate some of the ethiopathogenetic factors involved in bone mineralization disturbances in very low birth weight infants.

### Patients and Methods

An descriptive, exploratory retrospective study on 60 preterm babies with birth weight  $\leq 1500$  g and gestational age  $\leq 34$  weeks who were admitted to the Second Neonatology Department of Emergency University Hospital Cluj-Napoca from January 2000 to December 2003 has been conducted. Two groups of infants were included in our study: breast-feeding and formula-feeding. Data were collected from medical records and the same variables such as gestational age, birth weight, gender, the type of feeding (breastfeeding or formula), vitamin D administration, serum levels of calcium, phosphorus, alkaline phosphatase and wrist X-Ray changes were collected for all subjects included in the study. Statistical analysis has been conducted using Statistica program (v.8)

### Results

Rx changes characteristics to rickets were founded in 17 breast feeding infants (56.67%) and 8 formula feeding infants (26.6%); they had gestational age and birth weight significantly lower compared to those without rickets. Half of infants received vitamin D intramuscular (12 in breastfeeding group (40%) and 18 in formula feeding group (60%). All other infants received vitamin D per oral. No significant differences has been observed when mean of serum calcium, serum phosphorus or alkaline phosphatases were compared in the same feeding group between infants with positive Rx and infants with negative Rx ( $p \geq 0.1609$ ). Significant differences were identified between breastfeeding group and non-breastfeeding group for phosphorus at 8 and 12 weeks and alkaline phosphatase at 4, 8 and 12 weeks.

### Conclusions

Gestational age below 30 weeks and low birth weight are major risk factors for bone mineral disturbances in premature newborns. Unfortified human milk feeding and low serum phosphorus level could be important risk factors in these children

Nutrition and gastroenterology / Nutrition of the Very Preterm

## SURVEY IN THE USE OF LIPIDS IN PARENTERAL NUTRITION OF PREMATURE NEONATES AMONG LEVEL 2 AND 3 UNITS IN THE UNITED KINGDOM (354)

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### Introduction /Case Report

Parenteral nutrition (PN) is a vital component of treatment for premature or very sick neonates that cannot obtain adequate nutrition through the gastrointestinal tract. Lipids are important as they provide neonates with calories and necessary vitamins. There is no national guideline for the use of lipid infusions in parenteral nutrition. Different neonatal units follow local guidelines. Our aim was to try and investigate the variability of practice in the use of lipid infusion for parenteral nutrition amongst different level 2 and 3 neonatal units in the UK.

### Patients and Methods

We performed a telephone survey, where we have contacted all neonatal units of level 2 and 3 in the UK. We have asked from the staff to answer a short questionnaire regarding the policy in place for parenteral nutrition. We have received answers from 134 neonatal units (57.5% level 2 vs 42.5% level 3). The results were processed by using Microsoft word excel 2010 and IBM SPSS Statistics 20.

### Results

Intralipid was first choice for 66.4% of units, with SMOF lipid being a preferred choice by level 3 units (Intralipid/SMOF: 49.1% vs 43.9%). In 42.1% of level 2 units water soluble vitamins were added in aqueous PN and fat soluble vitamins in lipid syringe, whereas in 53.7% of level 3 units both vitamins were added in aqueous PN bag. In 64.2% of units lipids were commenced on day 1. The majority (66.7%) of units stop lipids when enteral feeds are 150 ml/kg/day, compared to 18.2% when enteral feeds are 120 ml/kg/day and 11.4% when enteral feeds reach half of total volume. Almost 70% of level 2 units have no policy, compared to 28% of level 3 units. 38% of units use gram/kg/day for lipids (max 3 g/kg/day) and 62% of units use ml/kg/day (max 15 ml/kg/day). There are 14 different ways to start and increase lipids when using g/kg/day, compared to 27 different ways when using ml/kg/day.

### Conclusions

There is wide variability in the use of PN lipids across the UK. In the majority of units intralipid is the preferred lipid infusion and lipids are commenced on day 1. An important finding is also that in the majority of level 2 units there is no policy for performing lipid profile regularly. It is difficult to judge which policy is better or worse, however a national guideline could offer answers and optimise practice across the UK.

Nutrition and gastroenterology / Nutrition of the Very Preterm

## SPLANCHNIC REGIONAL OXYGEN SATURATION IN EXTREMELY PRETERM INFANTS AT INTRODUCTION OF ENTERAL NUTRITION (327)

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### Introduction /Case Report

Near infrared spectroscopy (NIRS) has been recently used to monitor bowel perfusion in newborn infants with different clinical conditions, such as during acute intra-abdominal pathologies or blood transfusion. Nevertheless, there is limited knowledge concerning the bowel oxygenation during the early phases of enteral nutrition in stable extremely low gestational age infants (ELGA). Few and small studies report data on normal splanchnic regional oxygen saturation (SrsO<sub>2</sub>) curves and variability in ELGA infants.

The main aim of this study was to assess the bowel oxygenation and cerebral splanchnic oxygenation ratio (CSOR) at early stages of enteral nutrition in stable ELGA infants.

### Patients and Methods

This study was part of a prospective observational cohort study, approved by the regional ethics review board. All stable extreme infants born below week 28 from September 2014 to March 2015, without major gastrointestinal, cardiac, or chromosomal abnormalities, were eligible for this study. We used INVOS 5100C equipped with neonatal sensors to measure both cerebral and splanchnic oxygen saturation (infra-umbilical region). The registration was 20 minutes long after baseline and done at 48 h to 120 h hours of life. We prospectively collected neonatal and clinical characteristics from patient's charts. All infants were on enteral nutrition during the monitoring. We used cerebral splanchnic oxygen saturation (CrSO<sub>2</sub>) as reference for SrsO<sub>2</sub>. CRSO was calculated as ratio between CrsO<sub>2</sub>/SrsO<sub>2</sub>.

### Results

We included 18 ELBW, mean (SD) weight 798g (213), GA 25,8 ± 1,8 w and postnatal age 95 hours (± 21h) (table 1). One patient needed inotropes during the measurements and was therefore excluded. Splanchnic measurements of three patients were excluded afterwards, due to incorrect sensor placement during more than 70% of the NIRS monitoring or missing NIRS data. Mean CrsO<sub>2</sub> was 74,8 ± 4,0 (range 61,4- 87,9). Mean SrsO<sub>2</sub> was 51,1 ± 12,7 (range 18,6 -93,2) (figure 1). Mean CSOR 1,76 ± 0,89. We noted a considerable individual variability (defined as >10% SD) in SrsO<sub>2</sub> values (average variability 33% SD) compared to CrsO<sub>2</sub> values (average variability 5,5% SD). No statistically significant correlation was noted between CrsO<sub>2</sub> or SrsO<sub>2</sub> and birth weight, gestational age and days at full enteral nutrition. None of the subjects developed necrotizing enterocolitis.

### Conclusions

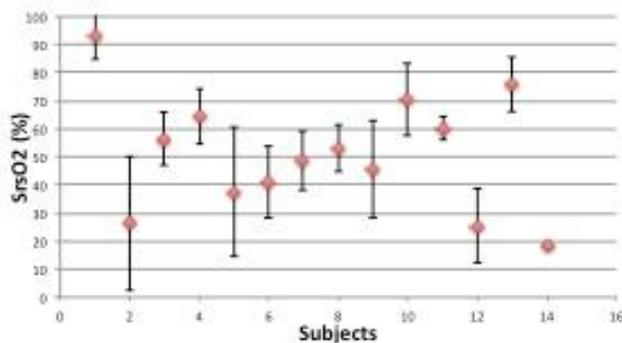
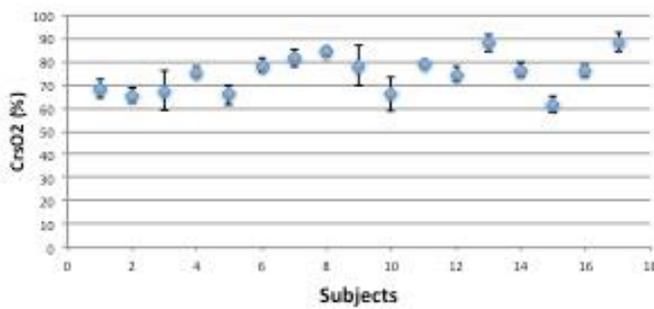
SrsO<sub>2</sub> has lower mean values and a large variability compared to CrsO<sub>2</sub> in ELGA. Despite the high variability and low SrsO<sub>2</sub> none of the subjects developed NEC. The variability of SrsO<sub>2</sub> is mainly due to bowel

movements, intestinal anatomical differences and the presence of patent duct. This intra- and inter-individual variability highlights the difficulty to interpret an absolute value of SrsO2 and define a cut off-value for pathological SrsO2.

Table

PATIENTS CHARACTERISTICS	N (18)
GESTATIONAL AGE (weeks)	25,8 ± 1,8
BIRTH WEIGHT (g)	798 ± 214
MALE (n, %)	11, 61 %
POST NATAL AGE(hours)	95 ± 21
APGAR AT 10' < 5 (n, %)	2, 11%
SGA (n,%)	5, 28 %
RESP SUPPORT:	
nCPAP(n, %)	11, 61 %
MECHANICAL VENITLATION(n, %)	7, 39%
hsPDA (n, %)	5, 28 %
AGE AT FULL ENTERAL NUTRITION (days)	16 ± 15

Picture



## Nutrition and gastroenterology / Necrotising Enterocolitis

Food Protein Induced Enterocolitis Syndrome (FPIES) is an important differential diagnosis of Necrotizing Enterocolitis in preterm infants (781)

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### Introduction /Case Report

GI dysmotility and poor growth are common in preterm infants. Necrotizing enterocolitis (NEC) may develop, when dysmotility, luminal contents and gut bacteria drive mucosal inflammation. Exclusive breast feeding is protective. Food Protein Induced Enterocolitis Syndrome (FPIES) may mimic NEC, including abdominal distension and intramural gas. In contrast to NEC, FPIES manifests increased platelet and neutrophil counts. We have examined whether cases initially diagnosed as NEC were due to FPIES induced by cow's milk (CM) challenge.

### Patients and Methods

9 preterm infants from a single UK tertiary centre (gestation 23-36 weeks, BW 535- 1700g) were identified as having possible FPIES on the basis of close temporal link between introduction of CM and onset of acute GI symptoms. A timeline was obtained of symptoms, feed type including supplementation, and blood parameters.

### Results

3/9 infants showed gastro-oesophageal reflux, improving on milk exclusion and worsening on challenge. All gained weight poorly leading to CM introduction, which worsened symptoms. Symptoms settled on exclusion and returned on challenge, remitting only after transfer to extensively hydrolysed or amino acid formula. Investigations showed thrombocytosis and reduced albumin after CM introduction. 6 infants were diagnosed with NEC (2 recurrent NEC). All had shown dysmotility and poor weight gain on breast milk, and in all cases NEC symptoms began within 48 hours of introduction of cow's milk formula, fortifier or carob thickener. In one case thrombocytopenia and neutropenia was consistent with classic NEC, while in 5/6 the platelet count increased (mean 422, range 310-550) as did the white cell count (mean 17, range 16-25). All eventually settled only on hydrolysate or amino acid formula.

### Conclusions

The NEC-like illness of these cases concords with Powell's classic report of FPIES in low birth weight infants. Almost all documented cases of NEC manifest thrombocytopenia: thrombocytosis is not reported. All infants showed dysmotility & poor weight gain with thrombocytosis on good intake of breast milk: this suggests non-IgE-mediated allergy. A preterm infant with thrombocytosis & dysmotility should be a red-flag sign for non-IgE-mediated food allergy & risk of FPIES on formula introduction

## Nutrition and gastroenterology

Volvulus in term and preterm infants – alike but not the same? (356)

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### Introduction /Case Report

Volvulus is strongly associated with disorders of the intestinal rotation and fixation, but may also occur in infants without anatomic anomaly. Presenting symptoms and underlying causes of volvulus have been hypothesized to be different in term and preterm infants. However, data on volvulus in preterm infants are scarce

### Patients and Methods

We reviewed medical records and imaging data of all infants aged less than 6 months with volvulus treated in a single surgical referral center 2006-2013. Data on basic characteristics, relevant clinical symptoms, laboratory tests, imaging findings prior to surgery, intraoperative findings, treatment, and outcome were retrieved.

### Results

Nineteen infants, 7 term and 12 preterm (mean gestational age 31 weeks, range 24-36), were diagnosed with volvulus. Volvulus without anatomical anomaly was seen in 4 of 19 infants (1/7 term and 3/12 preterm infants). Most cases (14/19) occurred during the first 8 days of life. Later presentations occurred exclusively in preterm infants, only 1 of 5 had no anatomic anomalies. Bilious vomiting was seen in all term infants while symptoms in preterm infants were rather nonspecific. Intestinal necrosis with the need for bowel resection occurred in 1/7 term (14%), as opposed to 9/12 (75%) preterm infants.

### Conclusions

Clinical presentation and outcome of volvulus differs between preterm and term infants. However, the rate and distribution of underlying anomalies did not differ in both groups. Symptoms in preterm infants are often nonspecific and may lead to a detrimental delay in diagnosis. This might contribute to the higher rate of intestinal necrosis and partial bowel resection in preterm infants compared to terms.

Nutrition and gastroenterology

## RANITIDINE USE AND BACTERIAL INFECTION IN LOW BIRTH WEIGHT INFANTS IN THE NEONATAL INTENSIVE CARE UNIT (518)

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### Introduction /Case Report

Low birth weight (LBW) and premature infants are at an increased risk of hospital-acquired infections (HAI) due to an immature immune system, invasive procedures, antibiotic use and prolonged hospitalization in the NICU. Thus infants must rely on mechanisms, such as gastric acidity, for protection against microbial pathogens. The use of ranitidine, an inhibitor of gastric acid secretion, is commonplace in the NICU and may increase the risk of infection secondary to reduced gastric acidity and bacterial overgrowth by opportunistic bacteria. We hypothesized that ranitidine would increase HAI in infants compared to those that did not receive ranitidine.

### Patients and Methods

After IRB approval, we performed a retrospective chart review of our electronic medical record for infants born between 401-2000 grams and admitted within 24 hours of birth between 2009 and 2013. The cumulative rate of infection, including pneumonia, UTI, sepsis, meningitis, and NEC were determined in infants who did, or did not, receive ranitidine. The Fisher exact test was used to compare the number of infections between the two groups and to compare the number of infections among Ranitidine users based on duration of treatment. Classification of significance was based on a significance level of  $p < 0.05$ . Statistical analysis was performed using SPSS V.21.

### Results

Forty three (43) infants met inclusion criteria. Fourteen (14) infants received ranitidine (33%) and 29 infants (67%) did not. Three of the 14 infants who received ranitidine developed infections (21.4%) whereas only one of the 29 (3.4%) who did not receive Ranitidine, developed infection ( $p = 0.09$ ). All of the infections among the infants exposed to ranitidine occurred in those who were exposed to the medication for more than 7 consecutive days ( $p = 0.33$ ).

### Conclusions

The use of ranitidine in low birth weight infants in the NICU was associated with an increase in HAI. The limitations of this study were its small sample size from a single institution. Additional data collection is ongoing to determine the role of concurrent medications and the use of proton pump inhibitors, and the effect of breast milk feeding and iron supplementation, all of which that may further influence microbial colonization and increase risk of infection in this vulnerable population.

Nutrition and gastroenterology / Metabolism

SERUM SCLEROSTIN LEVELS IN NEWBORNS BORN TO MOTHERS WITH VITAMIN D DEFICIENCY (281)

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### Introduction /Case Report

Sclerostin inhibits osteoblast functions, differentiations, and survival rates. The aim of this study was to investigate the association between circulating sclerostin (an emerging biomarker and important regulator of bone formation) and neonatal parameters in vitamin D deficient mothers.

### Patients and Methods

Forty-five mothers and their newborns were recruited the study. The mothers divided two groups as vitamin D deficient group 25-hydroxyvitamin D3 (25(OH)D)20 ng/ml). Their newborns had measurements of weight, height, calcium, phosphate, alkaline phosphatase, sclerostin and 25(OH)D at birth.

### Results

There were no significant differences between vitamin D deficient and sufficient women for sclerostin concentrations ( $205.4 \pm 64.8$  pg/mL vs.  $291.6 \pm 122.9$  pg/mL). However; 25(OH)D ( $10.1 \pm 8.1$  ng/mL vs.  $33.4 \pm 11.6$  ng/mL;  $p < 0.001$ ) and sclerostin concentrations ( $182.9 \pm 15.3$  pg/mL vs  $288.8 \pm 32.3$  pg/mL;  $p: 0.01$ ) were lower in newborns born by vitamin D deficient mothers compared and with newborns of vitamin D sufficient mothers. Circulating sclerostin measurements were not associated with 25(OH)D levels of both mothers and their newborns.

### Conclusions

We found significantly lower sclerostin levels in newborns born by women with vitamin D deficiency compared with newborns of non-deficient mothers.

## Nutrition and gastroenterology / Necrotising Enterocolitis

### DECREASED PHYSICAL ACTIVITY PRECEDES ONSET OF NECROTIZING ENTEROCOLITIS IN PRETERM PIGS (323)

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#### Introduction /Case Report

Necrotizing enterocolitis (NEC) is a serious feeding-related gut inflammatory disease with high mortality. Early clinical markers of NEC are of great importance for preventive interventions. Using preterm pigs as models, we hypothesized that the postnatal onset of NEC could be predicted by decreased physical activity level in the first few days after birth.

#### Patients and Methods

Caesarean-delivered preterm pigs were fed parenteral nutrition (PN) plus enteral milk nutrition for 8 (Exp 1), 5 (Exp 2), or 5 (Exp 3) days after birth by caesarean section. Pigs were scored for macroscopic NEC lesions (score 1-6) in stomach, intestine and colon after euthanasia on day 9 (Exp 1), 5 (Exp 2) or 5 (Exp 3). Physical activity was recorded by continuous camera surveillance for 8 (Exp 1), 5 (Exp 2) or 3 (Exp 3) days after birth with automatic activity detection quantified as total activity counts and proportion of active time during these time periods.

#### Results

The incidence of clear NEC lesions (score 4-6) was 38, 61 and 32%, respectively, in the three experiments. For the mean daily activity values, there was no difference between NEC and control pigs in Exp 1 (7 d recordings,  $P>0.05$ ) while the mean daily activity over the first 3-5 days were reduced in pigs developing NEC lesions on day 5 in Exp.2 and Exp. 3 ( $P<0.05$ ).

#### Conclusions

The early postnatal onset of NEC lesions is associated with decreased physical activity level during the first 3-5 days after birth, maybe due to some initial abdominal discomfort. As NEC develops, activity counts may increase above normal in response to more severe abdominal pain, explaining that activity levels recorded over the entire period from birth to euthanasia failed to show NEC effect (Exp 1). Decreased physical movement may be an clinical sign of NEC.

Nutrition and gastroenterology

## SYMPTOMS OF FEEDING INTOLERANCE IN PRETERM NEONATES WITH EXTREMELY LOW BIRTH WEIGHT (447)

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### Introduction /Case Report

Symptoms of feeding intolerance are common in preterm infants with extremely low birth weight (ELBW). Necrotizing enterocolitis is known for presenting with feeding intolerance, although the presence of these symptoms does not always result in the diagnosis of NEC. Other factors, such as respiratory support and nutrition, may have an influence on the presence of these symptoms as well. However, their exact role in the presence of feeding intolerance remains unclear. The aim of this study was to determine the prevalence of symptoms of feeding intolerance during the first 6 weeks after birth in ELBW infants, and to identify factors that are associated with feeding intolerance.

### Patients and Methods

We included 40 preterm neonates with a birth weight  $\leq 5$  ml before a feed. Furthermore, we collected data regarding respiratory support (CPAP, mechanical ventilation or no breathing support, i.e. low flow by canula) and type and composition of nutrition. We calculated the prevalence of symptoms for each week separately. Next we calculated odds ratios with 95% confidence interval (CI) for clinical factors such as respiratory support, nutrition, and NEC that might be associated with these symptoms.

### Results

In week 1 and 2, 63% and 38% of the preterm infants had bilious residuals while an extended abdomen was present in 13% and 18%. Vomiting and residuals  $>5$  ml were less common, with prevalence decreasing to 0% in week 5. NEC was considered in 16 infants, of which 5 indeed developed NEC. Extended abdomen and bilious residuals occurred more often in the infants suspected of NEC than in those without, OR=9.2, CI 0.9–93.0 and OR=16.5, CI 1.7–157.1 respectively. Mechanical ventilation was associated with residuals  $>5$  ml, vomiting and extended abdomen in week 2, OR=4.7 CI 0.4–50.0, OR=4.7 CI 0.4–49.9 and OR=4.3 CI 0.7–26.1 respectively. Fewer symptoms occurred in the infants without respiratory support, especially during week 1 and 2. Regarding feeding, extra protein fortifier was associated with extended abdomen and bilious residuals in week 4 (OR=10.3 CI 1.1–97.7 OR=7.9 CI 0.8–76.3 respectively).

### Conclusions

The prevalence of bilious residuals and extended abdomen is high during the first weeks after birth, while vomiting and residuals  $>5$  ml are less common. Factors that seem to be associated with feeding intolerance are mechanical ventilation, but not CPAP, and supplementation of extra protein with fortifier. Suspected NEC occurs more than twice as often than proven NEC.

Nutrition and gastroenterology / Breast feeding

## APPLICATION OF FORTIFIER DURING BREASTFEEDING - A NEW PERSPECTIVE FOR THE DISCHARGED PREMATURE INFANT? (021)

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### Introduction /Case Report

To meet the nutritional needs of preterm infants and to establish adequate growth, multicomponent fortifiers are added to expressed human milk until term or in growth restriction up to 52 weeks of gestation according to the ESPGHAN guidelines.

This is in conflict with direct breastfeeding. We established a method of feeding fortifier with finger feeder during breastfeeding and investigated the impact of this new method on weight gain in preterm born infants after discharge. Furthermore, acceptance and practicability of fortification with the finger feeder were evaluated.

### Patients and Methods

Infants born <34 weeks were included in this observational study. Before discharge mothers were trained by lactation consultants to feed fortifier with finger-feeder during breastfeeding. Therefore the fortifier was dissolved in 2-3 ml of warm water. The mixture was drawn up in a syringe attached to a finger-feeder and injected slowly in the mouth corner of the infant during breastfeeding. Primary outcome of the study was weight gain; secondary outcomes were acceptance and practicability of this new method.

### Results

In total, 25 infants were analysed and divided into "fortifier acceptors" (n=17) and "non-fortifier acceptors" (n=8). Demographic parameters were similar between the two groups. Weight gain per day after discharge was higher in the fortifier acceptors (median weight gain: 35,3 g/d vs. 36,4 g/d, p=0,754) without reaching statistical significance. In 52% of the study population, the acceptance was very high; the other half reported feeding problems and irritation of the infant due to finger-feeder use.

### Conclusions

Finger-feeder use for fortifier application in preterm infants enables mothers to exclusively breastfeed their baby. Weight gain of premature infants after discharge was higher in the group where mothers used this new method.

Nutrition and gastroenterology / Necrotising Enterocolitis

Probiotic use in neonatal units in the UK and Ireland (082)

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## Introduction /Case Report

Enteral probiotics have been shown to reduce the incidence of severe necrotizing enterocolitis and mortality in premature infants under 1500g, with typical relative risks of 0.43 and 0.65 respectively.[1] A 2014 Cochrane review strongly suggested a change in practice and recommended comparative studies of preparations, timing and treatment length. We were interested in whether the evidence for the use of probiotics was being translated into practice and how many neonatal units in the UK and Ireland are currently using them. We were also interested in looking at the barriers to their introduction and elucidating the reasons that units may choose not to use probiotics.

## Patients and Methods

An email survey consisting of five questions was sent to 188 of the 207 neonatal units in the UK and Ireland over an eight month period from December 2013 to August 2014.

## Results

92 units (49%) responded, of which just 13% gave probiotics to their neonates. Of the 87% of units who did not use probiotics, 15% had plans to introduce them in the near future and 5% were considering introducing them. The majority of the units that did not use, and were not currently planning on introducing probiotics, were waiting for further information about probiotic strain and timing of introduction (62.5%), or further risk/benefit analysis (53%). Other reasons for not using probiotics included difficulty gaining trust approval, cost, belief that existing studies were flawed, having an inappropriate caseload, and difficulty resourcing probiotics. 10% of the units reported being guided by provisional report of the UK based PiPS trial showing no benefit of single strain probiotic, *Bifidobacterium breve*.

## Conclusions

Probiotics are not widely used in the UK and Ireland, despite evidence for their safety and efficacy in reducing the incidence of severe NEC, mortality, duration of hospitalisation and length of time until full enteral feeds.[1] Guidelines are available for strain, timing of introduction and therapy duration, but further studies focusing on these factors could promote probiotics and improve quality of neonatal care.

Nutrition and gastroenterology

## OUTCOME OF POSTOPERATIVE TREATMENT IN NEWBORNS WITH CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL – ANOTHER 8 YEARS OF EXPERIENCE (744)

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### Introduction /Case Report

Prognosis of newborns with congenital anomalies of digestive system and abdominal wall has improved significantly over the last few decades. This is the largest group of patients with congenital anomalies of digestive system and abdominal wall treated in the single hospital in Croatia

### Patients and Methods

: In the period 2007-2013 in Neonatal Intensive Care Unit were treated 2640 newborns. 145 ( 5.5 %) were postoperatively treated due to abdominal wall and alimentary system anomalies. Duration of their hospital stay was 8198 days, and average duration was 57 days (64 for survivors and 16 for deceased). Healed or recovered were 121 (83%) and 24 (17%) newborns died

### Results

The most important statistical data are presented in the Table. Other anomalies were rare, as follows: anular pancreas (2), duodenal stenosis (2), duodenal membrane (2), ileal stenosis (1), anal membrane (2). All these newborns were well after operations.

### Conclusions

These results of short-term survival ( to discharge from hospital) are encouraging and showing improvement of survival comparing to previous observed period 1991-2006 ( 80% newborns healed , 20% died, average duration of hospital stay was 31) but duration of their treatment is prolonged. Further investigations on prenatal diagnosis of anomalies, the impact of place of birth (level of neonatal care) on final outcomes, long- term survival and quality of life are in process.

Table

Anomaly	Total	%	Live	%	Days treatment	of Died	%	Days treatment	of
Esophageal atresia	38	19	36	95	65	2	5	31	
Gastroshisis	23	15	22	96	109	1	4	85	
Anal atresia	20	13	17	85	37	3	15	58	
Diapharagmatic hernia	34	22	19	56	62	15	44	12	
Omphalocela	10	6	7	70	39	3	30	23	
Intestinal atresia	9	6	9	100	43	0	0	0	
Duodenal atresia	3	2	3	100	51	0	0	0	
Intestinal malrotation	8	5	8	100	26	0	0	0	

## Nutrition and gastroenterology / Necrotising Enterocolitis

### Surgical management of perforated necrotizing enterocolitis in VLBW or ELBW infants (284)

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#### Introduction /Case Report

Necrotizing enterocolitis (NEC) progressing to perforation usually puts VLBW or ELBW infants in a critical condition. Pediatric surgeons are often faced with the dilemma of whether or not to go for aggressive surgical intervention because these infants may not sustain lengthy surgical procedures. This report presents an institutional experience of surgical intervention in these challenging cases.

#### Patients and Methods

Nine preterm newborns of 508~1210gm with pneumoperitoneum were referred for surgical intervention. Three (845~1210gm) were subjected to a bedside drainage and six (508~1200gm) to a laparotomy. The latter had extensive NEC involvement ranging from mid-jejunum to transverse colon. Their management and outcome were reviewed and discussed.

#### Results

Among 3 with bedside drainage, two died and one survived without the need of further surgical intervention. As for 6 cases with laparotomy, their diseased bowels were left un-resected due to either skip NEC involvement or uncertain viability of the lesions. A loop enterostomy was created at the most distal end of healthy bowels with drain placement following peritoneal saline irrigation. The whole operation was finished within 60 minutes. After the 1st operation, one died of pulmonary complication 3 weeks later. The remaining five had second-look operation 2 months later, consisting of extensive enterolysis and resection of stenotic or atretic bowels with anastomoses. Finally, four had stoma closure concurrently. One had delayed restoration of bowel continuity 4 weeks later because of multiple anastomoses up to 8 locations. All of them could be weaned off total parenteral nutrition.

#### Conclusions

Bowel diversion and drainage were simple and effective in helping critically-ill infants get through the most difficult times of NEC. Resection of diseased bowels might not be needed at the first laparotomy considering that critically-ill infants might not endure time-consuming bowel resection and anastomoses, or some of diseased bowels might be reversible. Our approach might potentially preserve more bowels in NEC infants.

## Nutrition and gastroenterology / Breast feeding

EXTREMELY LOW BIRTH WEIGHT INFANT AND BREASTFEEDING: IMPACT OF KANGAROO MOTHER CARE, EXPERIENCE AND RESULTS AT ONE YEAR OF CORRECTED AGE IN A COHORT OF 737 INFANTS DISCHARGED HOME IN KANGAROO POSITION (2001-2015) (253)

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## Introduction /Case Report

Objective: To evaluate the rate of breastfeeding and growth results at one year of corrected age in a cohort of extremely low birth weight preterm (<1000g) treated in our ambulatory KMC program between 2001 and 2015 (3,5% of the total cohort of 20835 LBW or premature infants followed during the same period).

## Patients and Methods

Prospective cohort of 737 ELBWI infants (BW<1000g) discharged home in kangaroo position (KP) with periodical follow-up until 12 months of corrected age. Promotion of breastfeeding is one of the main components of the KMC intervention.

## Results

737 eligible infants were admitted to the ambulatory KMC program. 91,6% were less than 30 weeks of GA at birth; 28% with IUGR; 99,3% were admitted more than one month with 87% UCI graduates (median of hospital stay: 61 days). Nosocomial infection was reported in 41%; 81,4% were receiving oxygen at entry and weight of weaning was 4622 gr in average (150 days of chronological age). Exclusive breastfeeding at 40 weeks of gestational age was reported in 15% and 77,2% received mix feeding. At 12 months of corrected age 20,6% were still breastfeed. Anthropometric data at 40 weeks were for weight 2627 g ;height 45 cm and 33,6 cm for head circumference. At one year the weight was in average 7730 g; height 70 cm and head circumference 44,4 cm. The overall mortality from discharge up to one year of corrected age was 2,7%, 10% were lost to follow up and 11,8% lost their health insurance.

## Conclusions

Considering the beneficial effects of breast milk on digestive tolerance, nutritional quality and protection against infection and these anthropometric results, the argument to stimulate the feeding of the extremely preterm babies with milk from their own mother is valid. Breastfeeding the premature and/or LBWI is the cornerstone of KMC nutrition strategy and go in parallel with the strategy of open unit 24 hours /day to parent and family.

Nutrition and gastroenterology / Nutrition of the Very Preterm

Milk bank sharing: promotion of lactation and breastfeeding in preterm infant mothers (835)

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## Introduction /Case Report

Mother's own milk is protective against NEC in preterm babies. If not available, the best alternative is donor human milk. Comparing centers in the Vermont Oxford Database, the incidence of NEC in infants <30 weeks and <1500g was 10,3% in Bolzano versus 4,7% of NICU type B (2010). Since August 2011 Bolzano has been feeding preterm babies without mother's own milk available with pasteurized donor human milk provided by the milk bank of the nearby NICU of Trento. The incidence of NEC in Bolzano decreased to 3,8%(2012). Surgical NEC dropped from 7,7%(2010) to 0%(2012). Since 2013 Bolzano supports lactation in mothers of preterm babies following an institutional protocol of breast milk pumping.

## Patients and Methods

A retrospective chart review was used to collect information concerning all infants <1500g and <32 weeks born in Bolzano in 2010 (n=68; formula milk or mother milk were used to feed preterm babies), 2012 (after the sharing of the milk bank with Trento: donor human milk or mother milk were used to feed preterm babies: n=53) and 2014(after the introduction of new protocols of breast milk expression and progression of feeds:n=64).

We compared the incidence of NEC, surgical NEC, time to achieve full enteral feeding, days of donor human milk feeding, any mother milk at discharge and exclusive mother milk at discharge, volume of mother milk expressed at day 7 after birth and early breast pumping. Moreover we compared the outcome in the Vermont Oxford Database in Bolzano in the different years.

## Results

In Bolzano the incidence of NEC was 10,%(2010), 3,8% (2012), 0% in 2014. The incidence of surgical NEC was 7,7% (2010), 0% (2012), 0% (2014). Growth was comparable in the 3 years. Full enteral feeding was achieved at day 18,6+/-10 (2010); 18,1+/-25 (2012) and 9+/- 2 (2014). In 2012 babies were fed with donor milk for an average of 7+/-1 days versus 6+/-5 days in 2014. At discharge 82% of ex preterm babies received mother milk of which 60% exclusively (2010). In 2012, at discharge 78% of ex preterm babies received mother milk of which 52% exclusively versus 2014: mother milk in 86% of babies (64% exclusively). Volume of mother milk expressed at day 7 after birth was 298ml +/-221ml(2010) versus 244ml+/-143ml (2012) and 410 ml+/-247ml (2014). Early (<6 hours after birth) pumping was started in 75% of mothers in 2014. Except of increased number of ELBW in 2012 populations were comparable

## Conclusions

After human milk bank sharing,the incidence of NEC in our NICU decreased.Full enteral feeding was achieved earlier (day 9 versus day 18) since the introduction of a new protocol of progression of feeds.The volume of milk produced at day 7 after birth was improved through early breast pumping. The already high

rate of breastfed babies at discharge in our Unit didn't increase. The maintenance of milk production at long term remain to be sustained.

## Nutrition and gastroenterology / Perinatal growth

### CATH-UP GROWTH IN VERY LOW BIRTH WEIGHT IN THE FIRST YEAR OF LIFE IN A NICU OF A UNIVERSITY HOSPITAL IN CANOAS/RS (229)

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#### Introduction /Case Report

About twenty million premature babies are born per year worldwide. The improvement in care quality has increased patient survival. This increase results in associated comorbidities, requiring a multi-disciplinary monitoring of this population. The follow-up clinic of high-risk neonates discharged from the Newborn Intensive Care Unit (NICU) aims to track the growth and development process with early interventions that could improve the process. The assessment of nutritional status is an important factor in the development and growth of premature babies with very low weight.

#### Patients and Methods

The aim of this study was to evaluate the weight and height gain after discharge of very low birth weight preterm babies. A Cohort study was lead in the follow-up clinic of preterm infants discharged from NICU of a University Hospital in southern Brazil. A total of 83 children from January 1, 2011 to August 31, 2014 were followed. All infants had birth weights less than or equal to 1500 g. Data were obtained from medical records and newborn physical examination. The New Ballard score evaluated gestational age at birth and the Alexander's curve was used to reference birth weight for the gestational age. The World Health Organization (WHO) growth curve was used at six and twelve months of corrected age. The catch up point was set when premature reached -2 Z score in the reference population.

#### Results

At 6 months of corrected age, 83.4% of children reached catch-up in relation to weight and length, and 96.3% in relation to head circumference. The catch-up at 12 months of age was reached by 94.3% in relation to weight, 97.2% to length and every child had retrieved head circumference. Of the patients who were small for gestational age (SGA), 26.3% did not achieved catch-up weight at 6 months of corrected age, compared to 11.4% of those born with adequate weight to gestational age (AGA) ( $p = 0.255$ ). At 12 months corrected age, 7.7% of SGA and 4.5% of AIG had not achieved catch-up ( $p = 0.143$ ). The catch-up in the evaluated parameters occurred at 6 months corrected age (83.4%), earlier when compared to a study conducted in 2012 by Groenendaal (68.4%). The chronology of the catch-up in this study, which first occurred in head circumference, is similar to that found in the same studies.

#### Conclusions

The number of premature reaching the catch-up with one year corrected age is high in patients born and followed at University Hospital Ulbra / Mãe de Deus. A larger population of premature infants is needed to validate these results

Epidemiology / Nosocomial infection and colonization

## NOSOCOMIAL INFECTION IN A NEONATAL INTENSIVE CARE UNIT (290)

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### Introduction /Case Report

Nosocomial Infections (NI) persist as a major problem in most Neonatal Intensive Care Units (NICUs), being among the main causes of patient morbidity and mortality in the hospital setting. NI in the NICU are commonly related to device use, especially in Very Low Birth Weight (VLBW) and premature infants who are at high risk for NI due to multiple factors, such as immunological immaturity, frequent use of invasive procedures and prolonged hospitalization. Programs for prevention and control of these infections require a multidisciplinary approach. The aim of our study was to characterize NI and its associated risk factors.

### Patients and Methods

Retrospective review of all newborns admitted to a Portuguese level III NICU from January to December 2014. Nosocomial infections were defined as those that occur beyond 48 hours after hospitalization and caused by a microorganism not associated with maternal transmission, according to the National Program of Infection Control in level III NICUs.

Several parameters were analyzed: gestational age, gender, birth weight, length of stay, invasive device use, NI incidence, isolated microorganisms, antibiotic resistance and mortality.

Statistical analysis was performed by  $\chi^2$  and t Student tests. A p value of  $<0,05$  was considered statistically significant.

### Results

We analyzed 216 clinical records; 29,6% were VLBW infants. NI incidence was 18% (39/216). Neonates with NI had a lower mean gestational age (30 vs 35 weeks,  $p<0,001$ ) and mean birth weight (1297 vs 2389g,  $p<0,001$ ). This group had a higher mean length of stay (32 vs 12 days,  $p<0,05$ ), central venous catheters use (48,4% vs 7,0%,  $p<0,001$ ), intubation rate (51,6% vs 10,3%,  $p<0,001$ ) and parenteral nutrition support (87,1% vs 29,2%,  $p<0,001$ ). Sepsis was the most common infection (89,7%). The incidence of central line-associated bloodstream infections (CLABSI) was 64 infections per 1000 catheter-days.

The most frequently isolated microorganisms were *S. epidermidis*, other coagulase-negative Staphylococci (CoNS) and *S. aureus*, with high resistance rates to penicillin (100% for all) and ampicillin (66,7%, 100% and 100%, respectively) and no resistance to vancomycin.

Two newborns died from NI.

## Conclusions

Similar to other centers, we found that preterm and VLBW newborns have an increased risk of NI. Infection prevention requires a multimodal strategy: multicentric infection control programs, education and training of health care providers, adequate numbers of nursing staff, proper hand hygiene and appropriate laboratory support. There is urgent need to improve efforts to reduce CLABSI by implementing protocols for line-care maintenance and access.

THE PROGNOSTIC VALUE OF GENE POLYMORPHISM ANALYSES IN UKRAINIAN NEONATES WITH PERIVENTRICULAR LEUCOMALACIA (392)

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Introduction /Case Report

Performed studies indicate that periventricular leukomalacia (PVL) is often indicated in the neonatal intensive care unit (NICU). The head ultrasonography usually demonstrated increased periventricular white matter echogenicity with or without cystic abnormalities. Identify changes characterize also the degree of brain maturity of the newborn and can be detected throughout the first month of life. Long-term follow up children with PVL are shown different neurodevelopmental according to impaired grade. Analysis of different genes polymorphism is needed to determine the leading pathogenetic components of the pathological process contributing to brain damage in children with neonatal PVL.

Patients and Methods

32 neonates (group I) with PVL (7 terms and 25 preterm) were treated in NICU of Poltava region in 2010-2014 years. All neonates had full clinical examination. The case-control study included also 110 term healthy newborns (group II). Informed consent was obtained from parents of all children. Investigation was approved by the Ethics Committee. We analyzed the medical history and perinatal period course. The polymorphic variants of GSTT1 (deletion/allele), GSTM1 (deletion/allele), ACE (insertion/deletion), AT2R1 (A1166C), MTHFR (C677T), TNF $\alpha$  (G308A) genes were investigated in both groups. Statistical analysis was determined using binary logistic regression (SPSS 17.0). To visualize the obtained results we used classification and regression trees and ID3 algorithm (R-program).

Results

Reliable prognostic markers in statistical model ( $p < 0,001$ ) of the PVL risk was premature birth, low birth weight in relation to gestational age, Apgar score, ACE gene polymorphism. The significantly differences in ACE genotype was determined (Table). Akaike index calculation showed that the dominant model was accurate, i.e. for neonates with ID and DD genotypes was increased PVL risk ( $\chi^2 = 18,15; p = 0,001; OR = 26,80$  95%CI: (3,53-23,27)). Genetic statistical model had prognostic value 80,3%. Less than 6 Apgar score in neonates (Picture) by 1 minute, significantly contributed to the PVL development. A studied genes polymorphism influenced on the PVL development if Apgar was above 6 score. AT2R1 (1166AC, 1166CC) and ACE (ID, DD) genotypes significantly better predicted PVL in neonates with higher Apgar score. Obtained algorithm shown when must genetic markers determine for PVL prognosis.

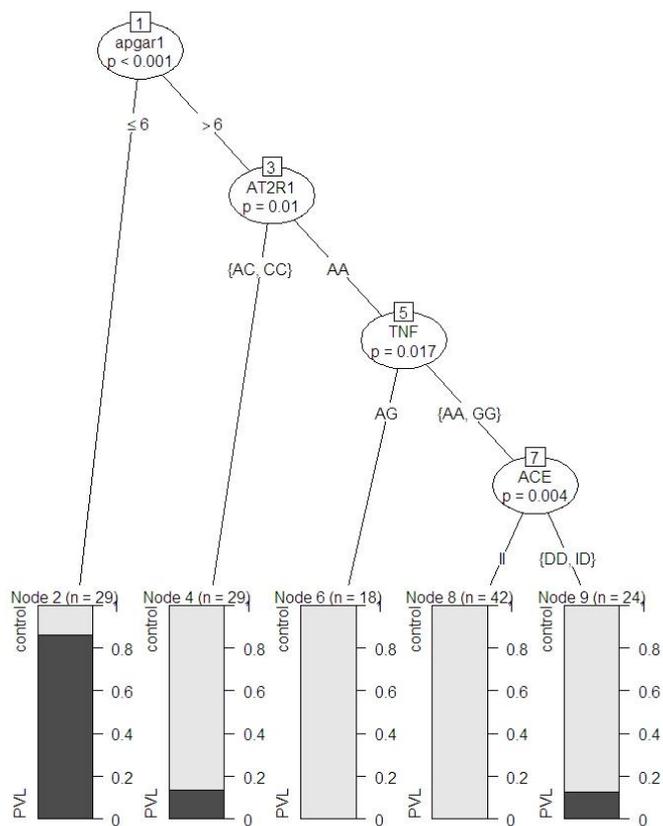
## Conclusions

These results indicated that the most significant influence on the PVL risk development had renin angiotensin system genes polymorphism responsible for neonatal cardiovascular homeostasis. ACE and AT2R1 genetic variants may be analyze in clinical practice for new diagnosis strategies. Future studies are needed to propose new approaches to therapeutic and preventive measures, taking into account genetic polymorphism associated with PVL.

Table

Gene / genotypes	Group I (n=32)		Group II (n=110)	
	n	%	n	%
<i>ACE_II</i>	1	3,12	51	46,36
<i>ACE_ID</i>	21	65,63	44	40,00
<i>ACE_DD</i>	10	31,25	15	13,64

Picture



## Pulmonology / Surfactant

### SEDATION INCREASES COMFORT OF PRETERM INFANTS DURING MINIMAL INVASIVE SURFACTANT THERAPY (459)

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#### Introduction /Case Report

Although infants are routinely sedated for endotracheal intubation, it is unclear whether during a minimally invasive surfactant therapy (MIST) procedure sedation should be given. The aim of this study was to compare the level of comfort when preterm infants receive MIST with or without sedation with propofol (1 mg/kg).

#### Patients and Methods

A case-control study was performed of preterm infants with a gestational age of 26-37 weeks receiving sedation or no sedation during MIST in the neonatal intensive care unit of the Leiden University Medical Center in 2014. Sedation during MIST was optional and left to the discretion of the caregiver. A standardized comfort score (COMFORTneo) was taken before, during and after MIST. Basic characteristics, success of MIST and complications were noted.

#### Results

In 25/40 infants receiving MIST the COMFORTneo scores were complete, 17 received sedation and 8 no sedation. Mean (sd) gestational age (29.1(2.5) vs 29.6(2.8)) and birth weight (1220(492) vs 1451(523) grams) were not statistically different. COMFORTneo <14 during MIST occurred more often in the sedated group (59% vs 13%;  $p < 0.05$ ). COMFORTneo was not statistically different between the groups before (12.3(4.8) vs 10.6(1.3)) and after MIST (10.5(4.3) vs 10.3(3.2)), but during MIST the sedated group had lower scores (12.6(3.9) vs 20.1(6.0);  $p < 0.05$ ). Duration of MIST (2.7(1.1) vs 2.5(0.7) minutes), oxygen desaturation (<80%; 2.9(2.5) vs 1.0(1.2) minutes), occurrence of bradycardia (<80bpm; 19% vs 29%) and hypotension (<30 mmHg; 50% vs 50%) were not statistically different. No infants were intubated during or within 3 hours after MIST.

#### Conclusions

Preterm infants receiving sedation during MIST seem to be more comfortable, without leading to more haemodynamic complications. A RCT is warranted to confirm this.

Circulation, O2 Transport and Haematology / Organ blood flow and autoregulation

## CHANGES IN CEREBRAL & RENAL PERFUSION AFTER SURGICAL LIGATION OF THE PATENT DUCTUS ARTERIOSUS (607)

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### Introduction /Case Report

Research into the effect of surgical ligation of the ductus arteriosus (DA) on regional tissue perfusion is limited. Data suggests that surgery is detrimental to cerebral and systemic perfusion. Near-infra red spectroscopy (NIRS) is a non-invasive means of monitoring regional perfusion. Probes placed on the head allow estimation of regional venous saturations and calculation of free tissue oxygen extraction (FTOE). We work in a regional NICU which performs around 20 DA ligations per year. We monitor cerebral NIRS on babies undergoing the procedure. This retrospective pilot study aimed to compare cerebral and renal function pre and post-operatively as indicators of end organ perfusion.

### Patients and Methods

All babies who underwent surgical DA ligation and had cerebral NIRS monitoring attached were eligible for the study. NIRS monitoring was carried out using the INVOS 5100 near-infrared spectrometer (Covidien, Ireland). We retrospectively examined hourly readings from the NIRS monitors documented on patient observation charts from 4 hours pre-operatively until 24 hours post-operatively. We compared plasma creatinine levels pre-operatively and then 24 and 48 hours post-operatively. Statistical analysis was carried out using SPSS. Cerebral NIRS and FTOE were analysed using a repeated measures design with a main effects plot. Creatinine concentrations were analysed using a paired student t-test.

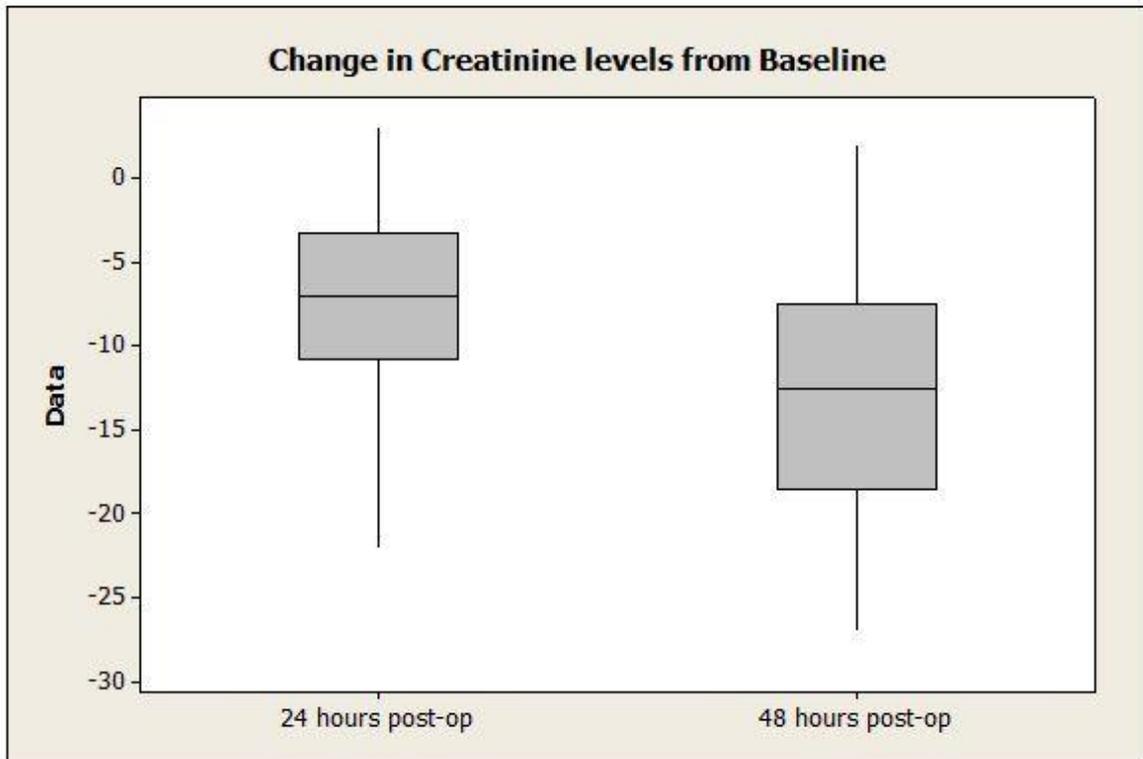
### Results

Eleven babies were included with a mean age at surgery of 29 days. The median gestational age at the time of surgery was 28+0 weeks (IQR: 27+2, 29+4 weeks) and mean weight was 1022g. Overall mean cerebral NIRS was 69% pre- and 71% post-operatively. The difference was not statistically significant ( $p = 0.245$ ). Overall cerebral FTOE was not significantly different pre- and post-operatively (pre-op: 26%, post-op: 24%,  $p = 0.292$ ). When analysed hourly, there was no significant difference in cerebral NIRS or FTOE from 4 hours pre-operatively until 24 hours post-operatively ( $p = 0.326$ ,  $p = 0.525$  respectively). Creatinine concentrations were significantly reduced post-operatively (Fig 1). Creatinine concentrations decreased by a mean of 7.7 mmol/l at 24 hours (95% CI - 2.6, 12.8 mmol/l,  $p = 0.008$ ) and by a mean of 13 mmol/l at 48 hours (95% CI - 7.0, 19.0 mmol/l,  $p = 0.001$ ).

### Conclusions

Our pilot data indicates that surgical ligation of the DA does not adversely affect cerebral tissue oxygenation. Furthermore, surgical ligation appears to increase renal perfusion as shown by a significant decrease in creatinine concentrations.

Picture



Epidemiology / Early origins of adult disease

## PREVALENCE OF NEONATAL DEAFNESS AND ASSOCIATED RISK FACTORS IN A UNIVERSITY HOSPITAL IN SOUTHERN BRAZIL (117)

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### Introduction /Case Report

The Newborn Hearing Screening (NHS) routine is the only strategy to detect early hearing loss that may affect the quality of life of the individual. It is essential in the first 28 days of the newborn, seeking early diagnosis, prognosis improvement and harm reduction in child development. The present study aimed to evaluate in the studied population, hearing disorder through newborn hearing screening (NHS), based on the achievement of behavioral procedures, electroacoustic and/or electrophysiological identification of hearing impairment.

### Patients and Methods

In a prospective study, we evaluated the population of newborns in University Hospital of ULBRA/HMD in Canoas-RS, admitted in rooming in and Newborn Intensive Care Unit, during one year. The population consisted of 2418 newborns undergoing evoked otoacoustic emissions (OAE). We evaluated the risk factors for neonatal hearing loss and specificity of screening method.

### Results

A total of 2418 newborns were studied, two had hearing impairment requiring referral to placement of the hearing aid (0.84: 1000 births). Of the risk factors evaluated, only the association of group STORCH infections during pregnancy was significant for positive screening (RR = 2.57, 95% CI [1.3-5.05]). The OAE test showed a high rate of false positives (10.6%) and increased specificity (99.1%) were performed with 14-day-old newborn.

### Conclusions

The incidence of neonatal deafness was according data from national and international literature. The OAE test showed a high rate of false positives than previously described in literature.

EVALUATION OF SIGMA-1 RECEPTOR LIGANDS TO PROTECT AGAINST GLUTAMATE-INDUCED NEONATAL BRAIN INJURY (093)

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Introduction /Case Report

Newborn brain injury is a relevant problem. We focus on therapeutic strategies, which after sufficient data acquisition in the experimental setting, could be rapidly transferred to a clinical study. Substances acting as sigma-1 receptor ligands were shown to be protective in adult models of brain injury and are already undergoing clinical trials in adult neurological diseases. Thus they might also be considered a promising therapeutic option in neonatal brain injury. We previously showed that the selective sigma-1 receptor agonist PRE-084 (2-(4-morpholinethyl)1-phenylcyclohexane-carboxylate) protects against excitotoxic newborn brain injury in vivo.

Patients and Methods

The aim of this study is to further evaluate the effect of PRE-084 in neonatal brain injury, with special focus on the potential of neuroprotection in in vitro analyses, in order to increase our knowledge on this promising and cost-effective therapeutic strategy. Primarily we used neuronal cell types (HT-22) and oligodendroglial cell types (OLN-93), after induction of a more immature phenotype corresponding to pre-oligodendrocytes (pre-OL), as model systems for neonatal brain injury. Cells were pretreated with PRE-084 in three dosages (1, 10 and 100  $\mu$ M) before glutamate was applied and subsequently analysed for metabolic activity assessed by means of a cell viability assay (CCK-8, Dojindo).

Results

Pre-treatment with PRE-084 did not affect cell viability after glutamate exposure, neither in pre-myelinating oligodendroglial (pre-OL cell viability: glutamate control 21.2% versus PRE-084 1 $\mu$ M 18.8%, PRE-084 10 $\mu$ M 21.0%, PRE-084 100 $\mu$ M 19.6%, n=5, p>0.05) nor in neuronal cell types (HT-22 cell viability: glutamate control 30.5% versus PRE-084 1 $\mu$ M 27.2%, PRE-084 10 $\mu$ M 32.0%, PRE-084 100 $\mu$ M 28.3%, n=3, p>0.05). Ongoing analyses are focusing on different application regimens (concomitantly to [co-treatment] and after injury induction [post-treatment]) in order to determine alternative treatment options affecting the effect of PRE-084 in this in vitro model.

Conclusions

Our preliminary data show that pre-treatment with PRE-084 does not reduce cell death after glutamate-induced injury in immature oligodendroglial and neuronal cell types. Based on our previous studies, we think that sigma-1 receptor agonists show considerable promise of playing a role as therapeutic strategy in neonatal brain injury and thus warrant further investigation.

Epidemiology / Nosocomial infection and colonization

## ETIOLOGIC AGENTS ISOLATED IN NEWBORNS WITH NEONATAL SEPSIS AT THE NEONATAL INTENSIVE CARE UNIT OF BRAGA HOSPITAL DURING 2012 AND 2013 AND THEIR ANTIMICROBIAL SUSCEPTIBILITY PROFILE (826)

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### Introduction /Case Report

Newborn infections are an important cause of neonatal death. Neonatal sepsis is a systemic infection with bacteriemia that occurs during the first 28 days of life. It can be classified as early-onset sepsis, with onset during the first 72h of life or late-onset sepsis, after 72h of life. The profile of the microorganisms causing sepsis has changed over the years, influenced by the emergence of new classes of antibiotics and by the institution of prophylactic antibiotics in certain cases. This work aims to evaluate the incidence of neonatal sepsis at the Neonatal Intensive Care Unit (NICU) of Braga Hospital in 2012 and 2013 and to identify the etiologic agents involved.

### Patients and Methods

We have analysed bacterial isolates data collected from blood, urine and cerebrospinal fluid of the newborns with clinical signs of infection.

### Results

The incidence of neonatal sepsis was 0,95% in 2012 and 0,96% in 2013 and there were respectively 27 and 25 cases of laboratory-confirmed bacteriemia. From these, 23 were admitted at NICU in 2012 and 20 in 2013. There were 7 cases of early-onset sepsis and 16 cases of late-onset sepsis in 2012. In 2013 there were 2 cases of early-onset sepsis and 18 cases of late-onset sepsis. *S. epidermidis* was the most commonly isolated agent in 66,7% of isolates in 2012 and 50% in 2013. Other microorganisms isolated were *S. aureus* in 9,1% of 2012 cases and *K. pneumoniae* and *S. haemolyticus* each in 11,1% of 2013 cases. An antimicrobial susceptibility profile was inferred from the data concerning the total isolates from NICU for both years of 2012 and 2013.

### Conclusions

Neonatal sepsis has important consequences for motor, cognitive and neurosensory development. It is important to improve antibiotic protocols for prophylactic treatment or to treat bacterial agents after identification, being necessary to know the bacterial flora and antimicrobial susceptibility profile of the NICU. Our study is a contribution to know the bacterial flora and antimicrobial susceptibility profile of Braga Hospital NICU.

Brain & Development / Early developmental care

## THE ROLE OF THE SEROTONERGIC SYSTEM IN THE DEVELOPMENT OF POOR NEONATAL ADAPTATION IN INFANTS EXPOSED TO ANTIDEPRESSANTS IN UTERO (074)

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### Introduction /Case Report

Infants exposed to selective antidepressants (SADs) in utero are at risk to develop Poor Neonatal Adaptation (PNA) after birth. The pathophysiology of PNA is yet unknown which hampers the diagnostic process of PNA. The purpose of this study was to determine if the serotonin metabolism, reflected by neonatal urinary 5-HIAA levels, plays a role in the development of PNA in infants exposed to SADs in utero.

### Patients and Methods

In this non-randomised controlled study in the Sint Lucas Andreas Hospital, infants who were admitted to the maternity ward or Neonatal Care Unit after birth between February 2012 till August 2013 were included. Infants exposed to SADs during pregnancy were included in the patient group (n=63). Infants not exposed to psychotropic drugs who were admitted for another indication with an expected hospital stay  $\geq 72$  hours were included in the control group (n=126). During the first 3 days after birth, urine was collected by a validated filter placed in the diaper. The course of urinary 5-HIAA levels (the main serotonin metabolite) during the first 3 days after birth was compared between the groups. Within the patient group, infants who did and did not develop PNA were compared.

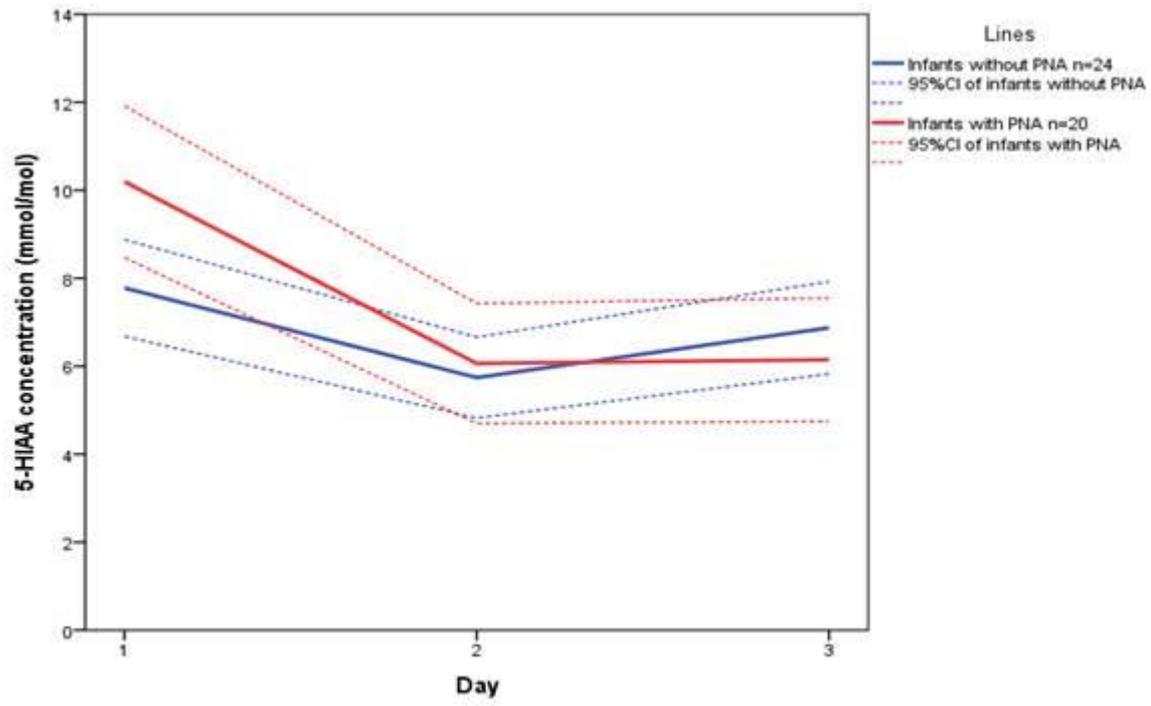
### Results

The course of 5-HIAA over the first three days after birth did not differ between the patient and control group ( $p=0.227$ ), however did differ between infants with and without PNA ( $p<0.001$ ) with the 5-HIAA level of infants with PNA on day one being increased (2.42 mmol/mol,  $p=0.001$ ) (Figure 1). Maternal stress after delivery modified this relationship.

### Conclusions

Based on our results, a transient disturbance of the serotonergic system seems to play a role in the pathophysiology of PNA. Other factors, such as maternal stress, also seem to play a role in the development of PNA. Further studies are needed in order to further unravel the pathophysiology of PNA.

Picture



Circulation, O2 Transport and Haematology

LOW INCIDENCE OF HYPERBILIRUBINEMIA IN SWITZERLAND: BUT IT COULD EVEN BE BETTER! (297)

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## Introduction /Case Report

Severe hyperbilirubinemia is the most common cause of neonatal hospital readmissions. It can lead to an acute encephalopathy and potentially to kernicterus with persistent neurodevelopmental sequelae. Early discharge from nurseries and a lack of follow-up of the jaundiced infants seem to be the major causes for a surge in recent years. In Switzerland, duration of postnatal hospitalization of mother and newborn infant with a mean of 6.5 days is longer than in other countries. This nationwide, population based, prospective study aimed to determine incidence and aetiology of severe hyperbilirubinemia in term and late preterm infants in Switzerland.

## Patients and Methods

The study was conducted prospectively over 5 years (2007 -2011) in collaboration with all 33 paediatric hospitals in Switzerland, the Swiss Paediatric Surveillance Unit and the Swiss Federal Offices of Statistics and of Public Health. An anonymous, two step reporting system was used with a check-off form and a secondarily sent detailed questionnaire. All newborn infants with gestational age (GA)  $\geq 35$  weeks with at least one value of total serum bilirubin (TSB) exceeding the age specific exchange transfusion limit (ETL) were included. ETL was defined as TSB  $\geq 430$   $\mu\text{mol/L}$  in healthy term infants,  $\geq 370$   $\mu\text{mol/L}$  in sick term infants or with hemolysis, and  $\geq 320$   $\mu\text{mol/L}$  in term infants with birth weight  $< 2500\text{g}$  or in premature infants.

## Results

During the study period, 379'280 live births (LB) with GA  $\geq 35$  weeks were recorded in Switzerland of which 129 developed severe hyperbilirubinemia (incidence: 34.0/100'000 LB). Preterm infants ( $> 200/100'000$  preterm LB) and boys (65.9%) were overrepresented. Incidence of very high TSB peaks ( $> 514$   $\mu\text{mol/L}$ ;  $> 30$  mg/dL) was 1.8/100'000 LB. The aetiology was identified in 63 cases (58.8%) of which 58 were related to blood group incompatibility (ABO: 63.6%; Rhesus and subgroups: 24.3%) and 3 cases to severe hematoma (4.5%). The first TSB measurement was performed within the first 12h only in 9.6%, although the risk factors (mother's blood group and hematoma) were known at birth. In 54 (43.2%) of the 125 patients with available data, the first bilirubin measurement was already above the ETL. In 16 (29.6%) of these cases, the first TSB was measured only  $> 12\text{h}$  after first notice of jaundice.

## Conclusions

The incidence of severe hyperbilirubinemia in Switzerland is lower than those reported in other countries. However, many of the recorded cases could have been avoided by a better recognition of the risk factors (mother's blood group potentially leading to incompatibility, hematoma and prematurity) and an earlier

measurement of TSB. In many cases, there is a delay between recognized clinical jaundice and first TSB measurement.

Nutrition and gastroenterology / Necrotising Enterocolitis

## FECAL LACTOFERRIN AND FECAL CALPROTECTIN LEVELS IN DIFFERENT STAGES OF NECROTIZING ENTEROCOLITIS IN A RAT MODEL (067)

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### Introduction /Case Report

Background and aim: Necrotizing enterocolitis (NEC) is a severe disease of mostly premature infants with high morbidity and mortality rates. There is no reliable biomarker for detecting newborns at risk for NEC development. We aimed to investigate fecal lactoferrin (FLF) and fecal calprotectin (FCAL) levels as predictors and indicators of disease severity in an experimental newborn rat model.

### Patients and Methods

Newborn pups were randomly divided into two groups, NEC and control. The NEC group pups were decapitated on the second, third and fourth days of the experiment for an assessment of the different stages of NEC. In the study group, hypoxia-reoxygenation model used to induce NEC. As biochemical parameters, FLF and FCAL levels were measured with an enzyme-linked immunosorbent assay technique and intestinal injury scoring was evaluated as a pathologic parameter.

### Results

The levels of both FLF and FCAL increased in the second and the third day groups, but began to decrease by the fourth day. The first, second and third day levels of FLF and FCAL were higher than controls. The intestinal injury scores of all NEC groups were significantly higher than the control group.

### Conclusions

Fecal lactoferrin and fecal calprotectin were good markers for demonstrating NEC. However, instead of spot testing, monitoring the levels of these markers may be more informative.

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

Plasma B-type Natriuretic Peptide Levels on Echocardiographic Flow Pattern of Patent Ductus Arteriosus in Preterm Infants with Respiratory Distress (773)

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### Introduction /Case Report

The shunt flow of patent ductus arteriosus (PDA) in preterm infants is associated with severity of respiratory distress and an increased risk of adverse outcomes. It has been suggested that the different patterns of patent ductus arteriosus (PDA) shunt flow are useful for the prediction of risk of hemodynamically significant PDA (hsPDA), especially growing or pulsatile patterns. The plasma B-type natriuretic peptide (BNP) is emerging as a diagnostic biomarker of PDA. We investigated the relations between the PDA shunt flow patterns and plasma BNP level along with echocardiographic parameters.

### Patients and Methods

Preterm infants with gestational age < 34 weeks who required respiratory supports and had patency of ductus arteriosus were studied prospectively during February 2014-March 2015. Echocardiographic evaluation and plasma BNP level measurement were performed within the first 96 hours after birth, and serial observations were made until ductal closure. The flow patterns of PDA shunt were identified using the pulsed Doppler echocardiography and total 13 echocardiographic parameters were evaluated simultaneously.

### Results

30 preterm infants with  $29.0 \pm 2.5$  weeks of gestational age and  $1,287 \pm 525$  gram of birth weight were enrolled and 138 simultaneous exams were done. Five of thirteen echocardiographic parameters, such as transductal diameter ( $p=0.002$ ), ductal velocity ( $p<0.001$ ), the ratio of ductal to left pulmonary arterial diameter (PDA/LPA ratio) ( $p=0.006$ ), the left atrial to aortic root ratio (LA/AO ratio) ( $p=0.007$ ) and isovolumic relaxation time ( $p=0.002$ ) were significantly different between the flow pattern groups. The BNP values were significantly different among the flow pattern groups ( $p<0.001$ ). The BNP levels of the growing and pulsatile pattern groups were higher than those of other groups. (Table 1)

### Conclusions

The PDA shunt flow patterns which reflect the magnitude of ductal shunt are associated with the plasma BNP level. In preterm infants with PDA, plasma BNP level measurement as well as the echocardiographic assessment of PDA flow pattern may useful to predict the development of hsPDA.

Table

**Table 1. Echocardiographic parameters and plasma BNP levels in relation of PDA flow pattern**

PDA flow pattern group	Pulmonary HTN (N=2)	Growing (N=10)	Pulsatile (N=47)	Closing (N=78)	Unknown (N=1)	p-value
Transductal diameter (mm)	1.11±0.21	1.58±0.41	1.56±0.46	1.24±0.45	1.13	0.002
Ductal velocity (cm/s)	0.61±0.01	0.91±0.28	1.40±0.33	2.20±0.60	1.48	<0.001
PDA : LPA diameter	0.58±0.11	0.61±0.13	0.59±0.11	0.50±0.16	0.43	0.006
Left atrial : aortic ratio	1.16±0.02	1.35±0.12	1.43±0.20	1.33±0.14	1.24	0.007
IVRT (ms)	48.06±5.23	63.22±14.10	50.60±10.46	57.44±11.12	59.15	0.002
BNP (pg/ml)	314.5±260.9	2930.9±1804.8	1908.2±1519.6	802.2±982.3	82.0	<0.001

Brain & Development / Early developmental care

## THE EFFECT OF CYCLED LIGHTING VERSUS NEAR DARKNESS LIGHTING ON PHYSIOLOGICAL STABILITY AND MOTOR ACTIVITY LEVEL OF PRETERM INFANTS (320)

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### Introduction /Case Report

After birth, preterm infants develop in the neonatal intensive care unit (NICU) characterized by a high and variable lighting, in contrast to the dark intra-uterine environment. Exposure to a high or variable NICU lighting can create physiological instability in preterm infants and increase their motor activity level. Two methods of lighting control in the NICU have been proposed and studied in the literature: near darkness lighting and cycled lighting. However, findings of these studies are contradictory. Therefore, the optimal control of NICU lighting remains unknown.

### Patients and Methods

The purpose of this study was to evaluate the effects of cycled lighting versus near darkness lighting on the physiological stability and motor activity level of preterm infants. A randomized controlled trial comparing preterm infants' physiological stability and motor activity level was conducted. 38 preterm infants born between 28 to 32 weeks of gestational age were recruited from a level III NICU. Infants were randomly allocated to either cycled lighting or near darkness lighting for 24 hours. Physiological stability was assessed with the Stability of the Cardio Respiratory System in Premature Infants (SCRIP) score, while the motor activity level was evaluated by an accelerometer.

### Results

There were no significant difference between the two intervention groups (P value = 0.21 to 0.97). There were no significant differences between the two intervention groups in regard to physiological stability (SCRIP score) (P value = 0.54 to 0.963) and motor activity level (P value = 0.0975 to 0.882). Premature infants were physiologically stable and their motor activity was similar under both lighting conditions (cycled lighting vs near dark lighting). Light intensity measured with a light meter indicated that participants were exposed to assigned lighting mode with fidelity.

### Conclusions

Guidelines to decrease bright light, either near darkness lighting or cycled lighting should be adopted in NICUs to control preterm infant's exposure to light. Further research is needed to identify if there is an optimal NICU lighting control.

## Epidemiology

### EVALUATION OF THE MORBIDITIES OF EARLY TERM INFANTS IN NEONATAL INTENSIVE CARE UNIT: A PILOT STUDY OF SINGLE CENTER (730)

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#### Introduction /Case Report

Pregnancy is classified as term between 37 and 41 6/7 gestational weeks according to the last menstrual date and defined as postmenstrual age. The infants in this 5-week period are usually evaluated in a homogeneous group. After the classification of preterm infants according to the gestational week in 2005 and determining differences in morbidities and mortalities between the groups, similar approach was performed in order to evaluate morbidity and mortality for term infants. Infants are classified as early term (37-38 6/7 weeks) and full term (39-41 6/7 weeks). Our aim is to evaluate the morbidities and determine the differences between early term and full term infants.

#### Patients and Methods

Term infants who were born and hospitalized between January 2013 and April 2013 in Zekai Tahir Burak Maternity Teaching Hospital were enrolled. Infants were classified as early term and full term. The primary outcome was the hospitalization in neonatal intensive care unit (NICU). The secondary outcomes were respiratory problems, length of stay in hospital, need of intravenous fluid and iv antibiotic treatment. Respiratory problem is defined as the hospitalization in NICU for respiratory distress for any reason. Indications of the iv fluid treatments were feeding intolerance and hypoglycemia. Demographic characteristics, mothers' age and comorbidities, type of the delivery and early morbidities were recorded retrospectively.

#### Results

Between January 2013 and April 2013, 5298 infants were born in our hospital, 341 of term infants were recruited in the study. Hospitalized infants of 179 (52%) were early term and 162 (48%) of them were full term infants. There were no significant difference in gender, birth weight, mothers' age, type of delivery, length of hospital stay and Apgar scores in 1. and 5. minutes between the two groups. Infants were classified according to the birth weight and gestational week, 31 (18%) of the early term infants were small for gestational age (SGA) and 4 (2%) of the full term infants were SGA ( $p < 0.05$ ). There was no significant difference in early morbidities between the two groups.

#### Conclusions

Early morbidities of the early term and term infants were found similar in our neonatal intensive care unit. This result can be attributed to the small sample size of our pilot study. Further multiple center and large sample size studies are needed to evaluate the early morbidities of early and full term infants.

## Epidemiology / Early origins of adult disease

Population-based study on the incidence of alcohol consumption in pregnancy in easter pommerania: The SNIp birth cohort. (263)

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## Introduction /Case Report

Introduction: The incidence of the entire spectrum of alcohol associated disease in newborns is 4-6/1000 births. The potentially avoidable sequelae are of social, medical and socioeconomic relevance.

## Patients and Methods

Alcohol consumption in pregnancy was investigated in 5402 pregnant women between 2002-2008 as part of the population-based Survey of Neonates in Pommerania (SNIp). The women filled in an anonymous questionnaire (AUDIT-C, incl. index of dependence). Neonatal outcome parameters were recorded: size, weight, head circumference, APGAR and possible symptoms of a fetal alcohol syndrome (FAS) like stigmata, muscular hypotonia and being small for gestational age. Statistical analysis was performed using SPSS and Stata-Statistic.

## Results

4785 (88.6%) questionnaires were completed. 1077 mothers (22.5%) stated alcohol consumption in pregnancy. Of these, 16.4% drank alcohol on average once a month, 3.3% 2 to 4 times per month, and 0.2% 2 to 3 times per week. 54% of pregnant women with alcohol consumption > 2 times per month passed the final secondary school examination (Abitur, no alcohol 29%), 38% had the general certificate of secondary school education (Realschulabschluss, no alcohol 53%) and 6% the certificate of secondary education (Hauptschulabschluss, no alcohol 15%). Mothers with alcohol consumption in pregnancy were more likely to deliver prematurely (<37 weeks of gestation). Mothers who did not fill in the questionnaire were less likely to deliver prematurely but possible symptoms of FAS were found in their offspring (Table).

## Conclusions

The rate of alcohol consumption in pregnancy was high and associated with higher school education and higher risk of premature delivery. An association between symptoms of FAS and alcohol consumption was only found in the offspring of mothers who did not fill in the questionnaire. These women should be regarded as a group at risk. These findings underline the difficulties in identifying newborns with alcohol exposure in pregnancy.

Table

	symptoms of FAS	premature birth
OR (CI 95%): no alcohol/alcohol	1.21 [0.84;1.75]	1.42 [1.14;1.78] p < 0.05
OR (CI 95%): no alcohol/no information)	1.61 [1.07;2.44] p < 0.06	0.71 [0.56;0.89] p < 0.05

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

Selective prophylactic Ibuprofen treatment in extrem preterm newborns (848)

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## Introduction /Case Report

Despite of growing data regarding potential role of PDA in prematurity related adverse outcome, timing of treatment is still controversial. Prophylactic approach is the only strategy which has shown any short term positive effect in terms of lower severe IVH rate, even if it is not translated into any long term benefit. When drug is given prophylactically, many newborns receives a potentially toxic drug unnecessarily and this may limit long term positive effects. We introduced a selective prophylactic treatment protocol in <26+6 wks preterms in January 2013. Aim of our study was to investigate the impact of selective profilactic Ibuprofen (IBU) treatment on IVH and BPD rate.

## Patients and Methods

Newborns less than 26+6 gestation age, delivered at our hospital from Jan 2013 through Sept 2014 were studied. Those with heart defects or death within 24 hrs postnatally were excluded. Echocardiography was performed at 6-12 hrs of age and 10 mg/kg Ibuprofen was commenced if DA revealed patent. After 24 hrs PDA was reassessed and treatment discontinued if DA was closed or showed significant constriction. Otherwise 2nd and 3rd dose of Ibuprofen (5-5 mg/kg, 24 hourly) was given. We prospectively collected the following data: ductal patency on day1 and 2, need for first IBU dose, need for complete (3 doses) treatment, need for late PDA treatment, BPD and PDA incidence, rate of renal complications. A matching group of patients were used as historical control from VON year 2012 database.

## Results

54 preterm newborn (652g, 24,5 wks) met the inclusion criteria. In 7 cases DA was closed at 6-12 hrs of age (group1- no treatment). 14 babies required only one dose of IBU (group2) and 33 pts were given complete treatment (group3.). BPD and severe IVH rate were either 1/7 (14,3%) in group1, 9/33 (27,3%), and 3/14 (21,4%) in group2, 4/14 (28,6%), and 6/33 (18,2%) in group3 respectively. Oliguria was more common in group3 (7/33 - 21,2%), than in group2 (1/14 - 7,1%) and revealed reversible in all cases. Need for late PDA treatment was 1/7 (14,3%) in group1, 3/14 (21,4%) in group2. and 6/33 (18,2%) in group3. Compared to year 2012 data BPD rate decreased moderately (5/15 - 33.3%) vs. 14/54 - 25.9%) and severe IVH rate decreased markedly (5/16 - 31.2%) vs. 10/54 - 18.5%).

## Conclusions

Selective prophylactic IBU treatment may decrease the risk of severe IVH and BPD in <26+6 wks preterm newborns and not associated with severe renal complications.

## Brain & Development / Neonatal Brain Injury and Neuroprotection

PROSPECTIVE STUDY OF THE CEREBRAL HAEMODYNAMIC CORRELATE OF BURST SUPPRESSED OR DISCONTINUOUS ELECTROENCEPHALOGRAPHIC ACTIVITY IN HYPOXIC ISCHAEMIC ENCEPHALOPATHIC INFANTS. (386)

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### Introduction /Case Report

Despite recent advances in the management of neonates with hypoxic ischaemic encephalopathy (HIE), uncertainty remains as to the pathophysiological significance of certain neurophysiological states. Burst suppression is described by bursts of high frequency activity or sharp and slow wave activity interrupted by periods of silence [1]. The discontinuous trace is characterized by bursts with non-silent interburst intervals that are not associated with normal preterm or term non-REM sleep EEG. Here, we present data from an ongoing prospective study of neurovascular coupling in neonates with HIE, which focuses on two forms of abnormal electroencephalogram (EEG) trace.

### Patients and Methods

Twenty term newborns with suspected or confirmed HIE, following informed parental consent, were recruited from the Neonatal Intensive Care Unit of the Rosie Hospital, Cambridge. The NTS optical imaging system (Gowerlabs Ltd, London), coupled to a video EEG was used to scan each infant between 1 to 4 hours during therapeutic hypothermia. Spectral analysis of the raw and filtered (high and low pass) EEG data was conducted and reviewed independently by a Clinical Neurophysiologist. The data were analysed using MatLab and the Fieldtrip and HOMER2 packages. Pre-processing of the data for artefact rejection and synchronization was performed. Changes in optical density were converted to those of total, oxy- and deoxy-haemoglobin using the modified Beer-Lambert law.

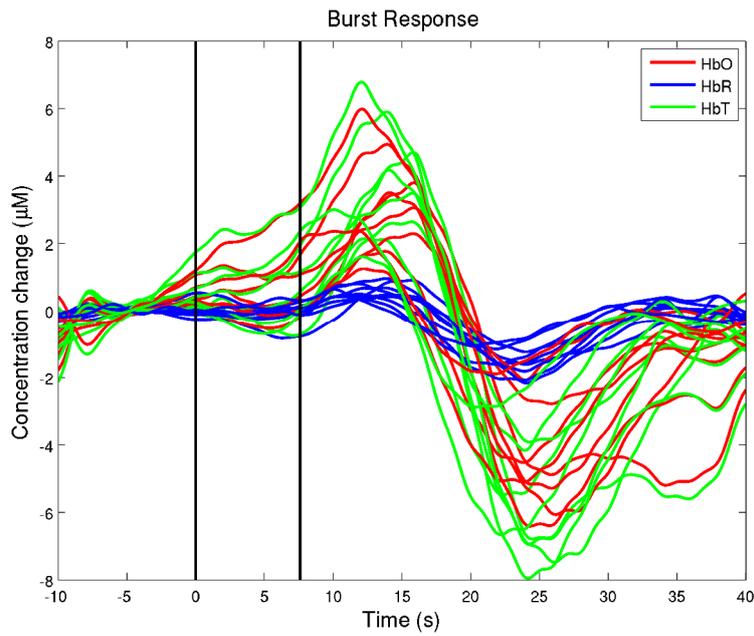
### Results

We present preliminary findings from 5 patients who demonstrated burst suppression or a discontinuous trace. All these infants had initially had seizure activity and had received anticonvulsant medication. By using a deconvolution approach, the haemodynamic response to electrographic bursts could be isolated. Figure 1 shows an example of this cortical haemodynamic response in 9 randomly selected optical channels, positioned across the head (Fig 2) in an infant with bursts and discontinuous activity during recording. The median (range) duration of the bursts was 7.6 (5.0-11.0) s. At the onset of a burst there is a gradual increase in the total and oxy-haemoglobin concentration followed by a rapid increase and subsequent dramatic decrease in both components until recovery back to the baseline concentrations. This lasts up to 35 seconds and the response is apparent across the cortex.

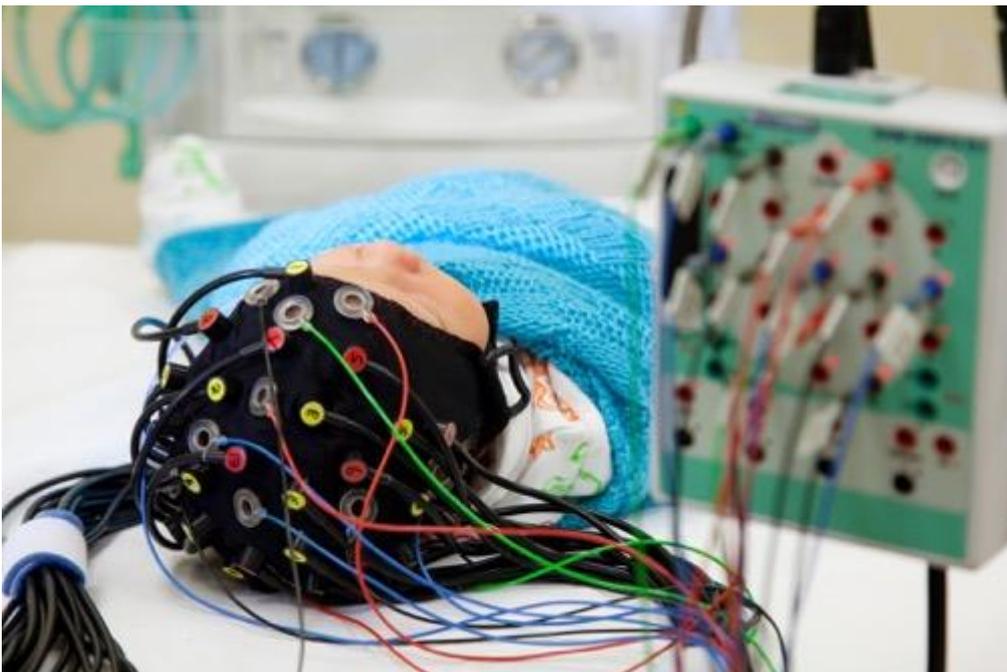
## Conclusions

We have previously described similar dramatic haemodynamic alterations occurring simultaneously with electrical seizure activity [2]. The extent and duration of the fall in cerebral oxygenation may put the brain at risk of further hypoxic injury. Combining optical imaging with EEG is a powerful, safe and non-invasive tool for monitoring infants with HIE.

## Table



## Picture



Brain & Development / Placenta and prenatal factors

## STUDY OF HISTOLOGICAL CHORIOAMNIONITIS ASSOCIATION AS A MODULATOR OF BRAIN INJURY IN PREMATURE INFANTS (033)

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### Introduction /Case Report

The study of histological chorioamnionitis association as a modulator of brain injury in premature brain in premature shows inconsistent results. Prematurity is often associated with chorioamnionitis. The transfontanellar ultrasound is a noninvasive diagnostic method to diagnose brain injury in newborns. The main objective of this work is to investigate the association between chorioamnionitis defined by histological examination and changes in premature transfontanellar ultrasound of newborns at Hospital Regional da Asa Sul (HRAS), Brasilia, DF, Brazil.

### Patients and Methods

Retrospective study in newborns between 26 and 32 weeks gestational age at birth were born in HRAS maternity April 2011 to November 2011. The neonatal variables studied included: gestational age at birth, patent ductus arteriosus, sepsis, intraventricular hemorrhage and periventricular echogenicity. All newborns underwent ultrasound transfontanellar between 4 and 15 days old. Statistical analysis was performed using SPSS software version 16.0. The analysis of continuous variables and mean comparison was applied Student's t test. For analysis of categorical variables we used the chi-square test, obtained relative risk values and confidence intervals. The p value was established as statistically significant  $p < 0.05$ .

### Results

We selected 51 patients who met all inclusion criteria. In this study, 55% of placentas had histological diagnosis of chorioamnionitis. The intraventricular hemorrhage (IVH) was described in 20% of the selected who had histological chorioamnionitis and 14.3% in those who did not have, OR: 1.5; CI (0.29 -7.7), P: 0.66. However, after statistical analysis it was found that chorioamnionitis was not associated with higher incidence of IVH. Regarding hyperechogenicity this was described in the 25% who had selected chorioamnionitis and 47.6% in those who had no RR: 0.36 (0.09 to 1.3); Q: 0.13. Just as in IVH, this study also showed no statistically significant relationship between hyperechogenicity observed in transfontanellar ultrasound and the presence or absence of chorioamnionitis.

### Conclusions

This study highlights the importance of the study of comorbidities affected by premature infants related to chorioamnionitis. Although the study failed to achieve results with statistical significance, the literature data emphasize this condition. An initial database is in HRAS and can be added to many other studies that will trace the profile of the newborn, as well as an analysis provided assistance to him and to pregnant women over time.

## Epidemiology

### COMPARISON OF NEONATAL COMPLICATIONS BETWEEN CESAREAN DELIVERY AND NORMAL VAGINAL DELIVERY (120)

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## Introduction /Case Report

The appropriateness of the rising rate of cesarean delivery worldwide has been debated widely. U.S. cesareans have risen 40% since 1996. IRAN cesareans section rate is 40 % nowadays. However, the high rate of cesareans in the United States has not resulted in improved outcomes for babies or mothers. So must make a decision to lowered rate of SC with out risen of neonatal complications. The aim of this study is to evaluate neonatal complications in caesarian section and vaginal delivery.

## Patients and Methods

We conducted observational study of all women with a singleton gestation and a prior cesarean delivery at 2 academic medical centers in Masshad medical university. Perinatal outcomes were compared between 770 neonates who had born with a normal vaginaly delivery and neonates who had born with an elective cesarean delivery without labor.

## Results

Vaginal delivery was attempted by 344 women, and 426 women underwent elective cesarean delivery without labor. Asphyxia occurred in 30 infants whose mothers underwent elective cesarean delivery and in 11 infants born at term whose mothers underwent a trial of labor ( $P < 0.001$ ). Planned cesarean delivery decreased rates of low up gar score from 11.2% to 17.8% ( $P < .001$ ). The risk for pulmonary disorders (transient tachypnea of the newborn infant and respiratory distress syndrome) rose from 9% to 4.6% ( $P = 0.001$ ) in elective cesarean delivery.

## Conclusions

fetal complications like RDS were significantly higher in cesarean section versus vaginal delivery.

Keywords: neonate, cesarean delivery, normal vaginal delivery

Circulation, O<sub>2</sub> Transport and Haematology / Systemic circulation and cardiac output

THE NEOADAPT PROJECT: NOVEL NON-INVASIVE MEASUREMENTS IN THE ASSESSMENT & TREATMENT OF CARDIOVASCULAR COMPROMISE IN SEVERELY UNWELL TERM & NEAR TERM INFANTS (511)

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### Introduction /Case Report

Up to 50% of all neonates admitted to NICU develop hypotension. The acute consequences of this can lead to poor long-term development that impacts patient, families and society. Treatment involves the use of fluids and drugs such as dobutamine. However there is no agreed definition of hypotension, its treatment lacks evidence and there is a wide variation in its management. Research is also confined to very premature infants despite outcomes for more mature infants with cardiovascular problems being similar to very preterm infants. This study explores the use, relationships and role of non-invasive techniques in the management of term and near term infants with haemodynamic insufficiency.

### Patients and Methods

Data are reported from three ongoing observational cohort studies including infants 33 weeks gestational age who were receiving special care, intensive care or total body cooling admitted to one NICU. For the first 3 days of life infants had routine clinical assessments (e.g. blood pressure) and daily echos, including superior vena cava flow and right ventricular outflow. Concurrent plethysmographic measurements derived from oxygen saturation probes were also calculated (modified pleth variability index and pulse transit time). Treatment strategies used for circulatory compromise and clinical outcomes were recorded. Data are displayed as median and interquartile range (IQR); statistical analysis was by Kruskal Wallis and Chi-squared test (p value <0.05= significant).

### Results

64 infants with median gestational age 35 weeks (IQR 34-40 weeks) and birth weight 2581g (2063-3413g) were included. 40 infants were healthy controls, 24 were sick, requiring intensive care (IC=19) or total body cooling (TBC=5). No significant differences in gestational age or birth weight were found between controls and IC or TBC infants. Significant differences were found between TBC infants and controls, with lower superior vena cava flow (83 vs 125.8 mls/kg/min, p= 0.0004), lower right ventricular outflow (175.3 vs 306.4 mls/kg/min, p= 0.0006) and higher modified pulse time transit time (0.35 vs 0.28 seconds, p= 0.005). No differences were found between groups with regards to modified pleth variability index, or between IC and control infants for any research parameter (see table).

### Conclusions

We found reduced superior vena cava flow and right ventricular outflow in babies undergoing TBC, which is likely to be due to the combined effect of hypoxic injury and cooling on cardiac output, cerebral perfusion

and pulmonary vascular tone. We also found increased pulse transit time in TBC babies, which is likely to reflect peripheral vasoconstriction. These non-invasive biomarkers may have a role in the management of cardiovascular compromise.

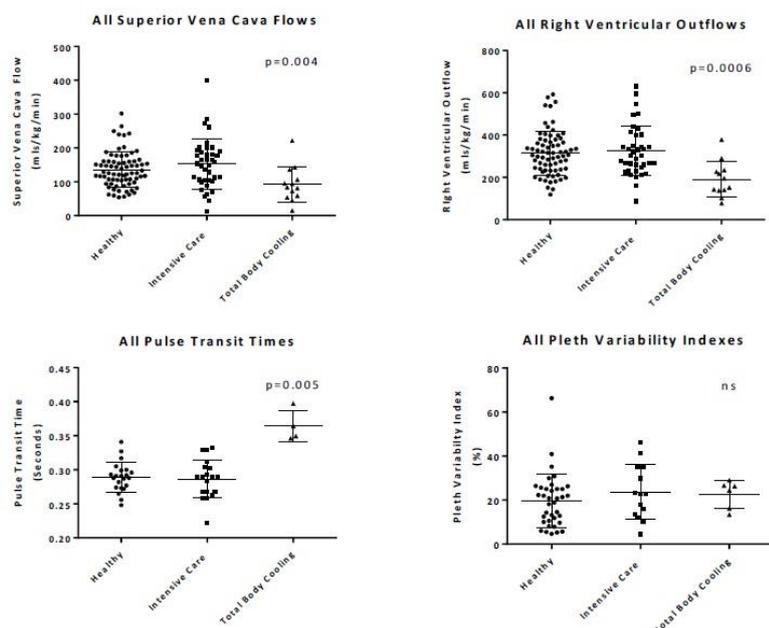
Table

Table 1: Showing Cohort Characteristics & Daily Research Measurement Values

	Cohort			P Value*	Pairwise Comparison (adjusted p value)			
	Healthy Infants (n=40)	Intensive Care (n=19)	Total Body Cooling (n=5)		a vs b	a vs c	b vs c	
Gestational Age (weeks)	35 (34 - 40)	34 (34 - 38)	40 (38 - 41)	0.03	ns	ns	0.03	
Birth weight (grams)	2065 (1550 - 3373)	1960 (1600 - 3176)	3740 (3098 - 4180)	0.03	ns	ns	0.03	
Antenatal Steroids	Yes	16	10	0	ns			
	No	24	9	5	ns			
Multiplicity	Singleton	26	16	0	ns			
	Twin	11	3	5	ns			
	Triplets	3	0	0	ns			
Type of Delivery	Vaginal	24	11	3	ns			
	C-Section	16	8	2	ns			
Superior Vena Cava Flow (mls/kg/min)	Day 1	158.4 (115.8 - 187.8)	159.2 (105.8 - 191.3)	77.5 (28.5 - 91.4)	0.03	ns	0.03	0.04
	Day 2	138.6 (117.3 - 150.5)	159.1 (105.4 - 216.7)	80.6 (50.9 - 123.6)	0.03	ns	ns	0.03
	Day 3	107.2 (86.3 - 151.1)	137.5 (84.5 - 182.8)	103.4 (59.2 - 200.4)	0.7	ns	ns	ns
	Overall	125.8 (101.1 - 160.5)	153.4 (105.4 - 190.1)	83 (55.3 - 120.2)	0.004	ns	0.01	0.002
Right Ventricular Outflow (mls/kg/min)	Day 1	321.9 (267.5 - 366.3)	265.1 (221.8 - 424.1)	102.4 (77.8 - 151.8)	0.01	ns	0.01	0.11
	Day 2	316.4 (241.6 - 385.2)	302.4 (247.5 - 344.1)	195.2 (138.6 - 261.4)	0.03	ns	0.02	0.06
	Day 3	280.3 (202.8 - 369.8)	332 (249.5 - 443.8)	220.9 (161 - 339.7)	0.17	ns	ns	ns
	Overall	306.4 (236.9 - 374.9)	303.6 (243.3 - 399.3)	175.3 (138 - 231.8)	0.0006	ns	0.0007	0.0009
Pleth Variability Index (%)	Day 1	21.9 (11.2 - 28.1)	23.1 (17.6 - 32.4)	19.8 (13.3 - 26.2)	0.81	ns	ns	ns
	Day 2	20.8 (10.2 - 26.7)	19.5 (12.7 - 37.9)	22.5 (16.1 - 28.9)	0.3	ns	ns	ns
	Day 3	14.2 (8.1 - 21.9)	17.9 (4.4 - 41.3)	24.5 (24.3 - 26.6)	0.3	ns	ns	ns
	Overall	20.8(10.3 - 25.3)	22.9 (13.3 - 35.1)	25.3 (15.4 - 27.2)	0.3	ns	ns	ns
Pulse transit Time (sec)	Day 1	0.29 (0.27 - 0.29)	0.30 (0.26 - 0.32)	0.37 (0.35 - 0.39)	0.06	ns	ns	ns
	Day 2	0.28 (0.26 - 0.31)	0.27 (0.25 - 0.29)	0.35 (0.34 - 0.35)	0.7	ns	ns	ns
	Day 3	0.28 (0.26 - 0.29)	0.28 (0.27 - 0.29)	0.35 (0.34 - 0.35)	0.9	ns	ns	ns
	Overall	0.28 (0.27 - 0.29)	0.29 (0.27 - 0.3)	0.35 (0.34 - 0.39)	0.005	ns	0.005	0.004

\*From Kruskal Wallis Test  
ns= not significant

Picture



Circulation, O2 Transport and Haematology

An All-Consuming Lump in the Neck (761)

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### Introduction /Case Report

We present an infant with a very large vascular neck mass, present from birth. Rapid expansion of the infants' vascular lesion was associated with aggressive platelet consumption, requiring multiple platelet and fibrinogen transfusions. Transfer to a specialist quaternary centre resulted in early diagnosis but he remained an inpatient for three months, undergoing multiple invasive and unsuccessful treatments. A multispecialist team including paediatric haematologists, dermatologists, oncologists and radiologists, strove to control his condition and finally he had an excellent response to sirolimus, a therapy previously only used in isolated case reports.

### Case Report

Patient K, a male term infant, was noted at birth to have a massive vascular, discoloured lesion on his neck. He developed widespread petechiae and thrombocytopenia with platelets of  $17 \times 10^9/L$  on the first day of life, requiring platelet transfusion. Severe thrombocytopenia with normal coagulation screen and negative neonatal alloimmune thrombocytopenia screen suggested a diagnosis of Kasabach-Merritt Syndrome, (profound thrombocytopenia, microangiopathic haemolytic anaemia and consumptive coagulopathy in the presence of an enlarging vascular lesion).

The lesion steadily increased in size over days, becoming markedly raised and bulky, resulting in forced right sided neck flexion. The bruised appearance extended dramatically across his face, neck and back. Ultrasound scan demonstrated a well-defined echoic lesion with marked increased vascularity consistent with a large vascular malformation, such as a haemangioma. Dramatic lesion growth and platelet consumption necessitated urgent transfer to Great Ormond Street Hospital (GOSH) for quaternary specialist management.

Ultrasound guided biopsy of the lesion diagnosed a Kaposiform Haemangioendothelioma (KHE), a rare, locally recurrent and aggressive vascular tumour of the skin and soft tissue, mostly seen in infants. It has low metastatic potential but the association of Kasabach-Merritt Syndrome is an important cause of mortality.

Haematologists were consulted due to his need ongoing need for platelet and fibrinogen transfusion. A hickman line was sited and the oncologists commenced weekly intravenous vincristine therapy with daily high dose oral prednisolone. After four weeks, due to poor response, chemotherapy was discontinued and the radiologists performed angiography with embolization. Embolization was performed on three separate occasions over a three week period, resulting in some improvement in lesion size but did not reduce his relentless platelet and fibrinogen consumption. The haematology, oncology and dermatology teams agreed on a trial of oral sirolimus therapy, based on reported success in published isolated case reports. Prednisolone dose was simultaneously weaned.

Patient K demonstrated an excellent response to sirolimus, with lesion regression and significant reduction in transfusion requirement. After three months he was discharged from GOSH inpatient care, to continue sirolimus, with frequent serum level monitoring and measurement of platelets and fibrinogen.

At eight months old, the lesion has continued to reduce in size and patient K has not required further transfusion. Although systemically well, he remains significantly immunocompromised on maintenance dose of sirolimus, requiring additional palivizumab immunisation and parental awareness of early signs of infection. The skin overlying the lesion has broken down on two occasions, requiring ongoing dermatology input. He has required hospital admission for two hickman line infections since discharge from GOSH, with purulent line discharge necessitating removal of the line under general anaesthetic on the second occasion. However, we remain optimistic that as the lesion continues to regress, his need for treatment and thus associated complications should resolve.

### Conclusions

Differential diagnosis of congenital cutaneous vascular lesions include common infantile haemangioma, rapidly involuting congenital haematoma, non-involuting congenital haematoma and rare vascular tumours such as KHE. Awareness of associations such as Kasabach-Merritt and early specialist referral for diagnosis is crucial, as management is aggressive and challenging. Cautious sirolimus therapy was effective in this treatment-refractive KHE case.

### Picture



Nutrition and gastroenterology / Breast feeding

EFFECT OF EARLY ROOMING-IN ON EXCLUSIVE BREASTFEEDING OF HEALTHY LATE PREMATURES (026)

L..Blaga

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#### Introduction /Case Report

There is a misconception based on that prematures needs some maturation to be exclusively breastfed . Old protocols, still used in some hospitals, provides breastfeeding initiation at a certain weight (2200g) or if prematures were able to feed well with bottle. So many healthy preterm babies were breastfed by schedule, taken near mother briefly, reaching or not rooming-in before discharge, increasing the risk of not being exclusively breastfed at home.

Purpose: To study the impact of early rooming-in in healthy "late prematures",on exclusive breastfeeding, during their hospitalization

#### Patients and Methods

We studied healthy "late preterm infants" (34-36 wks gestation) or "late prematures" showing minor problems of adjusting to extrauterine life born in the last 5 months in our Clinic.

The cases were divided into 2 groups: Group 1, prematures hospitalized at our compartment for prematures (n: 20) and group 2, premature infants hospitalized at our compartment for healthy term infants (n: 50) .The average GA of group 1 was 35.6, the mean weight 2336g.The average GA in the second group was 35.54 weeks and the average weight 2565g.

We followed the average for initiating breastfeeding, average day of commencement of rooming-in, average day of hospitalization and feeding methods at discharge. Infants requiring long term phototherapy were excluded from the study

#### Results

Group 1: premature hospitalized at prematures compartment:

Day of breastfeeding initiation (mean): 2.4 days

Day rooming-in initiation (average): 6.3 days

Day of hospitalization (average): 11.6 days

Percentage of exclusively breastfed at discharge: 20%

Percentage of breastfed + fed with pumped breast milk at discharge: 20%

The percentage of mixed fed (breast milk+formula) at discharge: 60%

Group 2: prematures hospitalized at term infant department:

Day of breastfeeding initiation (mean): 2.3 days

Day rooming-in initiation (average): 2.7 days

Day of hospitalization (average): 5.26 days

Percentage of exclusively breastfed at discharge: 72%

Percentage of breastfed + fed with pumped breast milk at discharge: 18%

The percentage of mixed fed at discharge: 10%

### Conclusions

Early rooming-in has a beneficial effect on breastfeeding of the healthy “late premature infant” or “late prematures” with minor adjustment problems, increasing 3 times the rate of exclusive breastfeeding at discharge and shortening hospitalization versus the later initiation of rooming-in although the time of initiation of breastfeeding was the same (2.5 days).

### Picture



Brain & Development / Early developmental care

QUALITY OF CARE OF KANGAROO MOTHER CARE PROGRAMS EVALUATED IN 20835 INFANTS IN COLOMBIA.  
(255)

E. Rodriguez 1; A Montealegre 2; N. Charpak 3; S. Fernandez 4.

#1,4: Kangaroo Mother Care Program, Bogotá, Colombia. #2,3: Kangaroo Foundation, Bogotá, Colombia.

### Introduction /Case Report

Rational: Low birth weight (LBW) deliveries are highly prevalent, particularly in middle and low income countries (12% in Colombia). Since 2001 The Kangaroo Foundation is monitoring around 1000 LBW infants per year in the outpatient Kangaroo Mother Care Programs.

Objective: To evaluate the performance of a Kangaroo Mother Care Program (KMCP) in terms of selected health outcomes achieved and compliance with evidence-based processes.

### Patients and Methods

Design: Cohort of 20835 NB less than 37 weeks and/or less <2500 g, followed up to one year of corrected age in the outpatient KMCP at Bogota and Medellin, Colombia between 2001 and 2014.

Neonatal Outcomes: NCIU stay; any grade of intraventricular hemorrhage; mechanical ventilation; seizures; bronchopulmonary dysplasia; nosocomial infection; days of hospital stay; neurologic exam at 3, 6, 9 and 12 months of corrected age; somatic growth at 40 weeks and 1 years of CA; psychomotor development at 6 and 12 months of corrected age; neurosensory sequel and high risk of cerebral palsy and mortality rate at one year of corrected age.

### Results

20835 eligible infants were admitted. GA<30w 11,3%; 31-34w 39,2%; 35 to 37w 16,3%. 11,3% of mothers was adolescents and 13,5% had more than 35 years old; 28,6% were toxemic, 32,9% had IVU, 10,3 % gynecologic infection and 39,5% bleeding. Of the infants of GA <34 weeks, 71,1% had lung maturation. 70,4% of deliveries was by cesarean section. 51,7% had between 1-15 days at entry. 44,5 % was NICU graduates; 47% of them had been ventilated. 30% were oxygen-dependent at entry and 9,3% had any grade of intraventricular hemorrhage. 12,7% had history of nosocomial infection. At 12 months, lost to follow up was 13,8 %, overall mortality was 0,9. 0,6% of patients were readmitted at least once. Retinopathy was detected in 6 %, ophthalmic surgery with laser in 1,1%, and blindness in 0,1%. Diagnosis of high risk of cerebral palsy was 4% and mean developmental coefficient was 100,0.

### Conclusions

The KMCP is a good strategy and unique opportunity for the follow up of high-risk infants as the premature or low birth weight newborn in Colombia. One year of corrected age is the minimum acceptable follow up for these children, taking into account the data obtained from this 20 years quality monitoring. The opportunity for close monitoring and intervention is essential to detect and reduce reversible alterations in growth and development.

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

## AORTIC COARCTATION OR SPONTANEOUS NEONATAL AORTIC THROMBOSIS (749)

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### Introduction /Case Report

Arterial thrombosis is rare in neonatal period and mostly connected with use of umbilical arterial catheters. Spontaneous arterial, especially aortic, thrombosis occurs sporadically and mortality is over 40% despite treatment

### Case Report

We report three cases during 3-year period, all presented in first days of life with absent pulses, immeasurable pressures on legs and leg's cyanosis and sent in our Unit because of suspicion of aortic coarctation. Doppler ultrasound of the abdominal aorta and its branches was performed after heart echocardiography showed no pathology. Complete occlusion of abdominal aorta has been found in all three cases. Screening for thrombophilia was performed and showed that first patient has PAI-1 mutation, second is homozygote for MTHFR T677T mutation with slightly elevated homocysteine and also has prothrombin G20210A mutation. Thrombophilic screening didn't reveal any pathology in our third patient. First two patients were treated with continuous intravenous heparin and later with subcutaneous LMWH until resolution of thrombus were completed. In third patient demanded thrombectomy and use of tissue plasminogen activator after diagnose was made. After that he was also on continuous intravenous heparin and later on subcutaneous LMWH. All of them are now stabile, but still under the supervision of hematologist, neonatologist and nephrologist.

### Conclusions

Newborn infants with arterial thrombosis may be presented as congenital heart disease and it's necessary to distinguish those two pathologies because of totally different therapeutic approach

ADRENOMEDULLIN HAS A DUAL EFFECT IN THE PROLIFERATION OF HUMAN FETAL PULMONARY ARTERY SMOOTH MUSCLE CELLS VIA THE CAMP/PKA/CREB PATHWAY. (349)

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Introduction /Case Report

Adrenomedullin (AM) is a peptide hormone belonging to the calcitonin/calcitonin gene-related peptide family that has multiple effects in the vasculature: vasodilatation, proliferation, anti-apoptosis, differentiation, migration and angiogenesis. AM is used in humans as a rescue treatment for pulmonary arterial hypertension. AM might promote proliferation via the mitogen-activated protein kinase (MAPK)/Extracellular signal-regulated kinase (Erk) pathway, and it might inhibit proliferation via a mechanism mediated by cyclic adenosine monophosphate (cAMP)/protein kinase A (PKA) pathway. AM is expressed in fetal lung tissue, but the role of AM in fetal pulmonary vascular development is unknown.

Patients and Methods

Fetal PASMC isolated from 15 weeks of gestation fetus were identified based on immunoreactivity against smooth muscle-myosin heavy chain and smooth muscle 22- $\alpha$  staining. The cells were cultured in Dulbecco's modified eagle media + 10% fetal bovine serum or in serum-free conditions. The cells were treated for 48 h with 100 nM AM. After treatment proliferation was measured by bromodeoxyuridine incorporation and by metabolic activity. Intracellular cAMP levels were measured by cAMP chemiluminescent assay kit. cAMP responsive element binding protein (CREB) and Erk phosphorylation were detected via Western blot analysis. To further evaluate the signaling pathways involved, a PKA activity inhibitor (KT5720) was used.

Results

In standard growing conditions, AM inhibited the serum-stimulated proliferation of human fetal PASMC ( $p < 0.05$ ) and increased the levels of cAMP ( $p < 0.01$ ). AM decreased the expression of p-Erk and p-CREB as measured by Western blot ( $p < 0.01$ ), suggesting a mechanism mediated by the cAMP/PKA/CREB pathway. To support this speculation, the inhibition of PKA activity by KT5720 abolished the AM effect. In quiescent human fetal PASMCs, AM increased proliferation ( $p < 0.05$ ) and phosphorylation of Erk ( $p < 0.05$ ), inhibition of PKA activity abolished this effect, suggesting a crosstalk mechanism between the cAMP/PKA/CREB and the MAPK pathways.

Conclusions

AM has a dual role in the proliferation of human fetal PASMC: it promotes proliferation in quiescent cells and decreases proliferation in actively growing cells. The AM effects were abolished by a PKA inhibitor, suggesting that AM effects on fetal PASMC are mediated by the cAMP/PKA/CREB pathway and its crosstalk with the MAPK/Erk pathway.

Circulation, O2 Transport and Haematology

## HOW DO DIFFERENT MODALITIES OF TREATMENT FOR PATENT DUCTUS ARTERIOSUS AFFECT NEONATAL MORTALITY/MORBIDITIES IN VLBW INFANTS? (620)

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### Introduction /Case Report

Patent ductus arteriosus (PDA) in preterm infants is associated with necrotizing enterocolitis (NEC), chronic lung disease, severe intraventricular hemorrhage (IVH), and mortality. There are different strategies for the management of PDA in preterm infants. Although the consensus of optimal treatment has not been reached, there are results from recent investigations that caution adverse neonatal outcome associated with surgery for PDA ligation. The aim of this study was to determine if there's an association between different modalities of treatment for PDA and neonatal outcomes in VLBW infants.

### Patients and Methods

This is a retrospective study by reviewing medical records of infants admitted to NICU of Chang Gung Memorial Hospital during the 24-months period between Jan. 2012-Dec. 2013. VLBW (BW<1500 gm) infants who survived the first 12 hours and developed PDA were included. Patients' demographic data, modes of treatment for PDA: Ibuprofen (I), Surgery (S), Ibuprofen followed by surgery (I+S), and conservative treatment (None), and patient outcome: mortality rate, NEC, IVH $\geq$ Gr. 3, duration of oxygen/ventilator use and hospital stay, were analyzed.

### Results

The overall incidence of PDA in this cohort was 36.2% (161/445). Of those 161 infants with PDA, their treatment modalities were: I+S, 21 (13%), I, 16 (10%), S, 95 (59%) and None, 29 (18%). The mortality rate, incidence of NEC, IVH, O2/ventilator days, and hospital stay were 14.3%, 4.8%, 0%, 78.7 $\pm$ 39.2 days and 91.8 $\pm$ 44.3days; 0%, 5.9%, 5.9%, 74.2 $\pm$ 42.2 days and 83.8 $\pm$ 41.7 days; 11.7%, 8.5%, 12.8%, 80.0 $\pm$ 40.0 days and 90.4 $\pm$ 38.9 days; 26.7%, 6.7%, 23.3%, 69.9 $\pm$ 56.3 days and 78.4 $\pm$ 55.3 days; in I+S, I, S, and None groups, respectively. When segregated into different gestational age, those infants with less maturity (GA<30 weeks) and received surgical ligation for PDA had lower mortality rate, shorter ventilator use and hospital stay, as compared to the other 3 treatment groups.

### Conclusions

In this population with high (PDA) surgical ligation rate, the association of treatment modalities for PDA and neonatal outcome seem to be maturity dependent. Our study result did not show significant deleterious effects of surgery over more conservative management.

Circulation, O2 Transport and Haematology / Transfusion and volume therapy

Use of blood warmers for red cell exchange transfusion in neonates : A nationwide survey of its use (437)

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1. Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, United Kingdom.

### Introduction /Case Report

Neonatal red cell exchange transfusion is mainly performed to manage hyperbilirubinaemia or anaemia due to severe haemolytic disease of the newborn. As Severe Rh haemolytic disease of the newborn becomes increasingly rare neonatal exchange transfusion is also becoming an increasingly rare procedure. Though BCSH and JPAC recommends warming of blood and suggests the temperature of blood to be 37°C immediately prior to transfusion respectively, there is no published evidence for this recommendation or for its safety of use. In our unit we had 2 incidences during exchange transfusion with warmer borrowed from theaters, highlighting unfamiliarity of the team to use the equipment and its safety.

### Patients and Methods

We conducted a telephone survey of all tertiary-level neonatal intensive care units (NICUs) in the UK on current practices of use of blood warmers during exchange transfusion. Data were obtained from the nurse manager or nurse in charge at a unit or the registrar. Data were obtained from all the 56 units approached. The data were stored in a password protected hospital computer and results analysed using ME-2007. Questions included 1) use of warmer for exchange transfusion 2) model and make 3) own or borrowed from theaters 4) any untoward incidences.

### Results

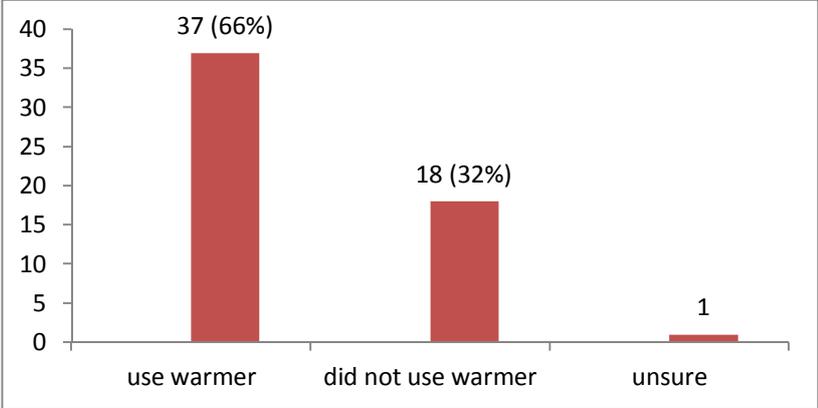
All the surveyed units performed at least 1 to 2 exchange transfusions per year. 37/56 (66%) units confirmed the use of blood warmers for exchange transfusion and 1 unit used specialist service to perform the procedure and were unsure (Figure 1). Out of the 37 units, 29 (78%) used their own warmers whereas 8 (22%) units borrowed from theatres. Different types of warmers were used in 22 units: Ranger, Astoflo, Enflow, Smith hotline, Beigler were some of them with no clear majority for any and around 15% were unable to confirm the make. Regional distribution demonstrated the use of blood warmers 100% in Scotland 50% in Wales, 50% in London, 90% in Midlands and East, 63% in North and 60% in south. One unit reported adverse incident with use of warmer in the form of sudden collapse and hence discontinued its use. Our unit uses Hotline warmer borrowed from theaters for its use.

### Conclusions

Our survey demonstrates that blood warmer is used by many but not all units. Nearly a quarter borrow them hence maintaining the competency and training of staff in its use is difficult. An updated transfusion guideline for neonates and older children with consensus statement on use of blood warmers is warranted and a report on its use, safety, further recommendations could be part of the ongoing BPSU surveillance on exchange transfusion.

Table

Distribution of use of warmers in 56 tertiary units across the U.K (figure: 1)



Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

PILOT DATA FROM THE FIRST PATIENT TRIALS OF A NEW DEVICE TO RECOGNISE CARDIOVASCULAR COMPROMISE IN CHILDREN: PREFILL STUDY (591)

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## Introduction /Case Report

Earlier recognition of clinical deterioration in neonatal and paediatric populations could significantly reduce morbidity and mortality and avoid the need for prolonged intensive care (Sharek 2007). Capillary refill time (CRT) is widely used in neonatal cardiovascular assessments and in paediatric early warning scores to identify and quantify severity of illness and effectiveness of resuscitation efforts (Surviving Sepsis Campaign). The automation of CRT may improve its usefulness (Lima 2005, Shavit 2006). Aim: establish if an automated CRT device detect clinical changes in cutaneous perfusion.

## Patients and Methods

Children admitted to the paediatric intensive care unit (PICU) were monitored during periods of cardiovascular instability through to recovery/stabilisation using a new automated CRT device. The device algorithm filters the data based on quality indices to produce a CRT value every 23 seconds and allow averaging over defined periods of time. The automated optical CRT device uses green photoplethysmography (wavelength 520nm) and applies blanching pressure similar to that clinicians and nurses use. It can be sited on a periphery or centrally. CRT values were compared between the initial phase of illness and subsequent recovery/stabilisation. Area under the curve (AUC) from ROC analysis was used to test this. Ethical approval was given.

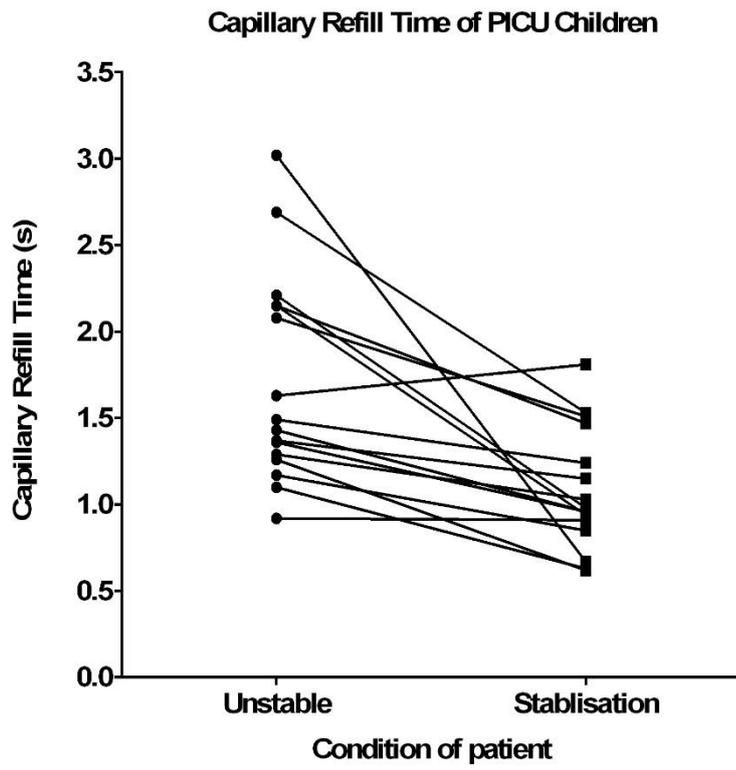
## Results

A total of 16 PICU patients, aged 1 to 15 years, were recruited. The mean CRT time significantly decreased by 32% ( $P=0.0009$ ) as their condition stabilised (see Figure). ROC analysis with AUC = 0.82 (95% CI 0.67-0.97) to detect changes during the initial phase of being unwell compared to the recovery phase.

## Conclusions

Our novel automated CRT device is able to detect changes in perfusion as clinical condition stabilises in critically ill children. Normative values for age and temperature will allow calibration of the device, tailoring it to the individual patient. We are in the process of refining the design and miniaturising it to improve its reliability and accuracy and allow use in the newborn population.

Picture



## Epidemiology

### OUTCOMES OF INFANTS BORN TO MOTHERS WITH HYPERTENSIVE DISEASE OF PREGNANCY (750)

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## Introduction /Case Report

Hypertensive disease of pregnancy is associated with significant maternal and neonatal morbidity and mortality.

There are few studies on neonatal outcomes in hypertensive diseases of pregnancy and the results have shown a wide range of variability.

## Patients and Methods

The objective of the study was to evaluate neonatal outcomes of infants delivered to mothers with hypertensive disorders of pregnancy.

Retrospective analysis of 219 infants delivered between 24 weeks and 36 weeks and 6 days of gestation, between January 2008 and December 2012.

## Results

The median maternal age was 31 years (5,6% were more than 40 years old); 67,9% nulliparous.

Distribution of hypertensive disorders: severe preeclampsia 56,7%; HELLP 18%; chronic hypertension 7,2% and mild preeclampsia 18%. 50% had fetal growth restriction. Fetal mortality was 1,2%.

The median gestational age was 33 weeks (24 weeks - 36 weeks and 6 days) and median weight was 1640g (470g - 3580g). 95,6% had prenatal corticoids.

Hyaline membrane disease developed in 39,4% of infants and bronchopulmonary dysplasia in 10,2%. Neutropenia occurs in 14,8% of neonates and thrombocytopenia in 40,6%. 18,8% of infants had sepsis and 2,2% necrotizing enterocolitis IIb. 13,9% of infants developed intraventricular hemorrhage and 8,7% retinopathy of prematurity.

25,4% needed invasive ventilation (mean 5,6 days). Median length of hospital stay was 19 days (0-162 days). Neonatal mortality was 1,36%.

## Conclusions

Respiratory morbidity and hematological abnormalities were the main complications registered in infants born to mothers with hypertensive disorders of pregnancy. It is essential to compare these results with a control group of infants born from normotensive mothers and to study long term outcomes, in order to support future decisions.

Circulation, O2 Transport and Haematology / Transfusion and volume therapy

## IMPLEMENTATION OF EVIDENCE-BASED GUIDELINES REDUCES THE FREQUENCY OF RBC TRANSFUSIONS AND LOWERS TRANSFUSION-RELATED COSTS AMONG EXTREMELY PREMATURE NEONATES (238)

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1 Division of Neonatal Medicine, Mayo Clinic, Rochester, MN, USA; 2 Department of Nursing, Mayo Clinic, Rochester, MN, USA

### Introduction /Case Report

Evidence suggests that maintenance of a high hematocrit confers no benefit among extremely low birth weight (ELBW) infants and may, in fact, result in harm. Frequent red blood cell (RBC) transfusions have been associated with severe morbidities in this population, namely necrotizing enterocolitis, bronchopulmonary dysplasia and retinopathy of prematurity.

### Patients and Methods

We established our NICU's baseline transfusion practices by reviewing the electronic medical records of all ELBW infants admitted January – December 2012. Specifically, we identified all RBC transfusions and recorded the relevant laboratory data (e.g. hemoglobin), physiologic data (e.g. level of respiratory support) and physician-documented indication for each transfusion. We then reviewed the literature and developed evidence-based RBC transfusion guidelines for use in our NICU. After implementing these guidelines in January 2014, we compared our post-intervention transfusion practices to those of 2012 in order to test our hypothesis that the guidelines would reduce the frequency of RBC transfusions.

### Results

When we applied our current RBC transfusion guidelines to those ELBW subjects transfused in 2012, only 14% of transfusions among ELBW infants would have met guidelines for transfusion [Figure 1]. However, after implementation of guidelines, 61% of transfusions were administered in adherence ( $p < 0.0001$ ). Using current cost estimates this represents a projected cost savings of \$51,000 for 2014. Unmeasurable outcomes also include morbidity associated with excessive transfusions in this vulnerable population.

### Conclusions

By adopting evidence-based RBC transfusion guidelines, we were able to successfully reduce the number of non-evidence based transfusions occurring in ELBW infants as well as reduce costs. Additionally, implementation of these guidelines likely has resulted in reduced morbidity in this medically vulnerable population.

Picture

Epidemiology / Early origins of adult disease

## CONGENITAL HEART DISEASE IN CHILDREN WITH DOWNS SYNDROME: SEVEN YEAR RETROSPECTIVE STUDY FROM SINGLE CENTRE (592)

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### Introduction /Case Report

Down syndrome continues to be one of the most common genetic defects. Congenital heart defects have been reported in 40-60% of children with Down's syndrome; atrioventricular septal defects (AVSD) being the most common type of CHD. Previous studies have reported that AVSD contributes to 30-40% of CHDs in children with congenital heart disease.

#### Aims:

To investigate the prevalence and type of congenital heart defects in children with Downs syndrome.

### Patients and Methods

A retrospective observational study was conducted and all the neonates with a diagnosis of Down syndrome between 2007 and 2015 admitted to the neonatal care unit in the Rosie hospital were included. Data was collected from electronic hospital patient records and analysed using Microsoft Excel.

### Results

59 neonates with a diagnosis of Down syndrome were identified from the BadgerNet database. Just over half of the cohort (55%) were males. 23 babies were born prematurely, of which 9 had a gestation period between 36-37 weeks whilst no babies were born under 32 weeks. Around 71% babies were born to women 35 years of age and over whilst 91% were born to women 30 years of age and over. 3% of babies were born to mothers 20 years of age and under. A confirmed antenatal diagnosis was documented in 25% neonatal discharge summaries. Just over half of the children (54%) had congenital heart defects. AVSDs were found in 31% neonates (10 of 60); half of which were diagnosed antenatally on fetal echocardiography. Eight (25%) had ventricular septal defects (VSD) and ten (31%) had secundum atrial septal defects (ASD). Two babies had a hypoplastic aortic arch while two neonates had Fallot's tetralogy.

### Conclusions

We found that in our cohort around half of children with Down syndrome had underlying congenital heart defects as reported in literature. However, atrioventricular septal defects were present in only 30% cases. The majority of neonates were born to women over 30 years of age whilst very small proportions were born to women under 20 years of age. Maternal age remains a strong risk factor for occurrence of Down syndrome.

## Epidemiology

Prediction of cephalomas: A statistic approach with logistic regression analysis (764)

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## Introduction /Case Report

Cephalomas is a well known complication at birth, related mainly to instrumental vaginal delivery. We aimed to find possible predictor factors in relation to mode of delivery i.e. Cesarean Section (CS), Emergency Cesarean Section (EMSC), Vaginal Delivery (VD), instrumental VD and maternal characteristics (Maternal Age, parity), and neonatal characteristics (Gestational Age (GA), Birth Weight (BWt), Birth Height (BHt), and Occipital-Frontal Head Circumference (OFC)).

## Patients and Methods

We retrospectively collected data from all consecutive term and late preterm deliveries in a tertiary center. For the period Jan 2010- Dec 2010 data collected from 1513 deliveries. To best describe the possible interaction between different variables and the presence of cephaloma at birth we used logistic regression approach with cephalomas as dependent variable and Gestational Age, parity, Birth Weight, Birth Height, Maternal Age and Occipital-Frontal Head Circumference as independent variables. The frequency of cephalomas was 13.94% (211/1513). Boys 58.8%, mean GA 39±1 weeks. The mode of delivery in cases with cephalomas was 72% VD (152/211) from which instrumental VD 30.9% (47/152) and CS 28% (59/211) from which EMSC 39% (n=23/59).

## Results

Mean Birth Height=51.2 ±2.3 cm, mean OFC=34.0±1.5 cm, mean Maternal Age=30±4 years. Mean Birth Weight was 3.342±409.3 gr and this was statistically increased (p=0.0008) only in cases with cephalomas born by CS and not with VD. Logistic regression analysis with cephaloma as dependent variable and the rest of the variables as independent shows that the model that best describes our data is that of the mode of delivery and its interaction with GA, parity and BHt as independent variables in the model. Increase in BHt by 1 cm increases the possibility of cephaloma by 13% (OR=1.13, 95% CI= {1.04-1.21}). Increase in GA by 1 week increases the possibility of cephaloma by 50% only in cases born by CS (OR=1.46, 95% CI= {1.12-1.91}) and not in VD (OR=0.87, 95% CI= {0.73-1.04}). Being para 2 decreases the possibility of cephaloma (OR=0.17, 95% CI= {0.11-0.26}).

## Conclusions

Birth weight and gestational age at birth increases the possibility of cephaloma only in those cases born by Cesarean section although birth height increases the possibility in relation to all mode of deliveries. Increased parity decreases the possibility of cephaloma. BHt, GA and parity in relation to mode of delivery can better predict cephaloma compared to BWt alone.

Other / Miscellanea

25 OH Vitamine D Deficiency İn Preterm Babies: Incidence and Association With Morbidities (052)

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### Introduction /Case Report

25 OH Vitamine D deficiency is common in preterm babies. However, its association with morbidities is not completely understood. Vitamin D deficiency is found to be associated with early onset sepsis and bronchopulmonary displasia in various studies. In this study we aim to investigate Vitamin D levels and its impact on morbidities in preterm babies.

### Patients and Methods

Preterm babies born before 37 weeks of gestation and admitted to our neonatal intensive care unit between January 2013 and December 2014 are included in this prospective study. 25 OH Vitamine D levels are measured in the first day of life for all babies. All babies received oral vitamine D after measurement with a dosage of 800 units per day. Control vitamine D levels are obtained in every four weeks and at discharge. Vitamine D levels of 30 ng/ml are classified as severe, moderate, mild deficiency and normal, respectively.

### Results

A total of 139 preterm babies are included in the study. Mean birth weight was 1863±863 gr. and mean gestational age was 31.9±3.4 weeks. 25 OH vitamine D levels in all babies was <30 ng/ml and in 62.2 % of cases levels were found to be <10 ng/ml. Mothers of babies with vitamine D levels less than 10 ng/ml had also been found to have significantly lower vitamine D levels. There was no difference in RDS, BPD, IVH and ROP between severe and moderate deficiency cases. 53.7 % of cases in the first control and 85.7% of cases in the second control had 25 OH vitamine D levels above 20 ng/ml.

### Conclusions

It has been reported that vitamine D deficiency is common and associated with major morbidities in preterm babies. All cases in our study had low vitamine D levels and a significant number of cases had severe deficiency. Target levels were achieved in %50 of cases in the first and %85 of cases in the second control via early administration of oral vitamine D. There was no significant difference in major morbidities between groups.

## Brain & Development / Neonatal Brain Injury and Neuroprotection

Testing for thrombophilia in mature and near term premature infants, in whom intracranial haemorrhage developed (866)

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### Introduction /Case Report

In the development of germinal matrix haemorrhage - intraventricular haemorrhage genetic prothrombotic factors act as independent risk factors in very-low-birth-weight infants.

### Patients and Methods

In our study tests for thrombophilia were carried out in term and near term (born on the 33-36. gestation week) newborns treated for intracranial haemorrhage between 01.01.2005. and 31.12.2012. in our institution. Herediter prothrombotic states: factor V Leiden mutation, prothrombin gene polymorphism (G20210A), methylenetetrahydrofolate reductase (MTHFR) polymorphism (C677T), protein C/S and antithrombin III deficiency, increased lipoprotein (a) level, increased factor VIII. activity and antiphospholipid syndrome were assessed.

Tests were done in case of the mothers as well. Inclusion criteria were met in 37 patients, but thorough examination was processed in 24 who are followed in our institution.

### Results

Prothrombotic state was detected in 11 patients (45,83%). FV Leiden mutation/homozygous/ in 1, FV Leiden mutation/heterozygous/ in 4, MTHFR C677T polymorphism in 1, I. type PC deficiency/compound heterozygous/ in 1, II. type PS deficiency in 1 and increased Lp(a)

level in 3 patients were verified. Combined occurrence of the studied risk factors were detected in three patients.

22 mothers were tested for prothrombotic state, which was detected in 14 (63,63%) cases. FV Leiden mutation /heterozygous/ in 6, I. type PC deficiency /heterozygous/ in 1, increased Lp (a) serum level in 5 and increased FVIII activity in 2 cases. Combination of risk factors were found in four of the parents. Herediter prothrombotic states were recognized in a remarkable proportion of our study sample.

### Conclusions

We have no exact data about the incidence of several prothrombotic factors in our country. The incidence of heterozygous Leiden mutation of FV. is almost 10% in Hungary. The incidence of FV Leiden allele is extremely high: 4% on the average. Heterozygous state of FV Leiden was 16.66 % among the examined children, and 27,27% among parents. Homozygous FV Leiden mutation was verified in one child.

Small sample size decreases the statistical power of our observational study.

## Brain & Development / Structural and Functional Brain Imaging

### INCREASING RELIABILITY OF CRANIAL BLOOD FLOW VELOCITY MEASUREMENTS IN PRETERM INFANTS (493)

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#### Introduction /Case Report

Preterm infants are born during critical stages of brain development, in which the adaptive capacity of the fetus to extra-uterine environment is limited. Inadequate brain perfusion has been directly linked to preterm brain damage.

Current methods to reliably measure cerebral perfusion are either invasive, not safe or not quantitative. High-end ultrasound machines with high-frequency ultrasound probes allow visualization of microvessels and regional variation. To assess whether flow velocity measurements of preterm cerebral perfusion using Doppler techniques are accurate, we conducted two in vitro experiments using microvessel flow phantoms as a model for a preterm brain.

#### Patients and Methods

Two in-house developed flow phantoms containing microvessels (inner diameter 160 and 700 microns) with attached syringe pumps, filled with blood-mimicking fluid, were used to generate non-pulsatile perfusion with peak flow velocities of 1-10 cm/s. Using presets developed for daily clinical practice, velocity measurements were performed using an Esaote scanner to determine which probe and settings provide most reliable velocity estimates.

In the second part of the study the linear ultrasound probe connected to two different Esaote ultrasound machines (MyLab Twice and MyLab 60/70) was calibrated and new presets were developed for future blood flow measurements in the internal cerebral veins in preterm infants below 32 weeks (peak flow velocity 5-7 cm/s).

#### Results

Microvessel mimicking catheters with velocities as low as 1cm/sec were adequately visualized with a linear ultrasound probe. With a convex probe velocities <2 cm/sec could not be depicted. Within settings, velocity

and diameter measurements were highly reproducible (intra class correlation 0.997 (95% CI 0.996-0.998) and 0.914 (0.864-0.946)). Overall, mean velocity was overestimated up to 3-fold, especially in high velocity ranges. Significant differences were seen in velocity measurements when using steer angle correction and in vessel diameter estimation ( $p < 0.05$ ).

In the second part of the study, calibration of the ultrasound probe resulted in highly reproducible and reliable maximum velocity results of non-pulsatile flow. Additionally, ideal Doppler settings were determined to reliably visualize two closely adjacent vessels and measure flow velocities.

## Conclusions

Visualization of microvessel size catheters mimicking small brain vessels as small as 160 micrometers is feasible. Reproducible velocity results can be obtained, although important overestimation of the values is observed if standard presets are used. Before velocity estimates of microcirculation can be used in clinical practice, calibration of the ultrasound machine for any specific Doppler purpose using a flow phantom is highly recommended.

## Brain & Development / Neurodevelopmental Outcome

### Follow-up of High Risk Group Neonates in Ukraine: Features of Guidance to Early Intervention Services (527)

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#### Introduction /Case Report

There are about 100 thousand orphans in Ukraine. The part of them are children with severe disabilities due to perinatal pathology. The neurological complications and delay of development occur in 15-52% of preterm infants worldwide.

Objective of the study was to determine the health status and characteristics of premature infant's flow to the early intervention (EI) service.

#### Patients and Methods

We included 172 young child, born prematurely. They were divided into groups depending on the gestational age at birth: Group 1 (n = 26) - late preterm children (34 - 37 weeks); Group 2 (n = 40) - moderately preterm children (32 -33 weeks); Group 3 (n = 85) - very premature infants (31 - 28 weeks); Group 4 (n = 21) - extremely premature babies (less than 28 weeks). Design of study included analysis of the age of first revenues to early intervention (EI) services. The software package STATISTICA 7.0 was used.

#### Results

The median minimum and maximum age (chronological and corrected) of first admission to EI was following: 1st gr - 5,9 (2; 21,2) and 4,5 (05,6; 19,8); 2nd gr - 7,1 (3,8; 26,9) and 5,2 (2,1; 25); 3rd gr - 8,1 (1; 49,7) and 5,8 (1; 47,6); 4th gr - 14,1 (3,2; 41,1) and 10,9 (0,2; 37,9) [Kruskal-Wallis ANOVA by Ranks; H (3,N=172) =7,91 =0,0479, MW test: p1,2=0,3294; p1,3=0,0230; p1,4=0,4774; p2,3=0,0383; p2,4=0,6299; p3,4=0,0236 ].

#### Conclusions

But the greatest incidence of children who come to the rehabilitation program observed among those born 31-28 weeks gestational age. Most of premature infants received rehabilitation services at the first year of life. Infants who were born before 28 weeks gestation were admitted to early intervention service at about 1 year old.

## Other / Involvement of parents in care

ACCEPTABILITY AND FEASIBILITY OF COLLECTING OUTCOME DATA ON THE PSYCHOLOGICAL AND SOCIAL ADAPTATION OF FATHERS TO THE BIRTH OF A VERY LOW BIRTH WEIGHT INFANT - A PILOT STUDY. (562)

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## Introduction /Case Report

Most research on families of very low birth weight infants (VLBW; <1500 g) examines maternal experiences. Less is known about paternal adaptation and experience: care may not be sufficiently sensitive to fathers' needs, and the psychological and social support needs of fathers of VLBW infants require attention. This pilot study aimed to investigate, in comparison to parents of term infants also admitted to the neonatal intensive care unit (NICU): i) the feasibility and acceptability of collecting psychological outcome data from parent couples of VLBW infants, and ii) the psychological and social adaptation of fathers to the birth of a VLBW infant.

## Patients and Methods

We recruited a target group (n=38) of parents of VLBW (<1500g) infants, and a comparison group (n=36) of parents of infants who had been born at term and also admitted to NICU. Feasibility of completing the protocol was assessed by examining participation compliance rates. Acceptability of completing the protocol was assessed through six quantitative acceptability questions. Participants completed validated psychological and social adaptation questionnaires measuring: parental attachment to the infant, partner role, individual well-being, depressive symptoms, and father work-family conflict. Group differences were analysed with t-tests. Qualitative data and field notes relating to completing the protocol were also collected.

## Results

Feasibility: Parents of VLBW infants were as likely as parents of term infants to take part. For parents who consented, completion and return of questionnaires was good (VLBW=38/57 [67%]; Term=36/59 [61%]), but recruitment of VLBW parents was challenging. Acceptability: Scores [SD] were high and did not differ between groups (VLBW=3.89 [.67] vs. Term= 3.8[.64],  $p=0.53$ ), although some parents commented on the length and applicability of the questionnaires. Psychological adaptation: Fathers in the two groups did not differ significantly on quantitative measures, but interestingly both groups indicated difficulties: 27% of VLBW and 25% of Term fathers scored over the cut-off for possible depression (compared to a recent published population estimate of 16.5%). Qualitative data showed fathers (especially of VLBW infants) wanted emotional support, and to feel included in decision-making.

## Conclusions

Collection of psychological and social adaptation data from parents of VLBW infants is feasible, acceptable, warranted, and welcomed. However, we identified some important barriers to research participation, particularly for fathers. Successful data collection from this population requires flexible, dedicated staff to aid recruitment, and short, simple questionnaires, designed or adapted specifically for use with parents of VLBW infants.

Brain & Development / Neonatal Brain Injury and Neuroprotection

THE ERYTHROPOIETIN(r-EPO) AS A NEUROPROTECTIVE AGENT ? A RETROSPECTIVE STUDY IN NICU (778)

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### Introduction /Case Report

The clinical applications of r-EPO are currently restricted to the prophylaxis and treatment of preterm anemia. Brain injury is a common in critically ill preterm and term infants. Experimental and clinical data supporting the use of erythropoietin as a neuroprotective agent for neonates who have brain injury are discussed. The rationale for Epo use in neonatal brain disease, evaluating neurological development and outcome in the brain's response to neuronal injury.

### Patients and Methods

In our retrospective study, case-control, from last five years, we enrolled 160 newborns with GA  $\leq$  32 wks, birthweight  $\leq$  2500 g, of these 79 treated and 81 control. The preterm newborns were divided into three groups for GA and birth-weight. The treatment consists of the early administration of r-Epo at a dose of 300UI/kg s.c. at 3 times weekly for 6 wks. Patients were evaluated for clinical presentation, neuroimaging, outcome after early treatment. The results were expressed as incidence of disability, morbidity and mortality in each group.

### Results

The incidence of neurological sequelae of IVH in treated was 15% vs 85% of controls. No outcome of ROP in the treated vs 16% of controls. The mortality rate in the treated group was 19% vs 81% of the control.

### Conclusions

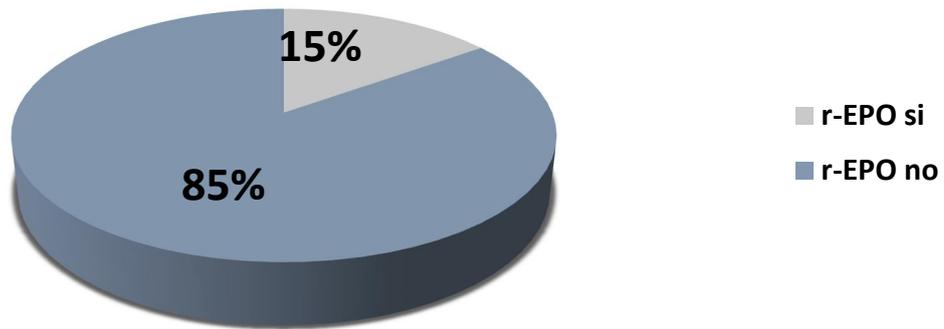
Although the perinatal period is the most critical, because the oxygenation, especially in the brain, is compromised by the concomitant presence of respiratory, cardiovascular and nutrition diseases. Our clinical study of EPO treatment in neurological diseases have accumulated positive results. Available information suggests that EPO is a promising therapeutic drug for the treatment of neurological diseases in NICU.

Table

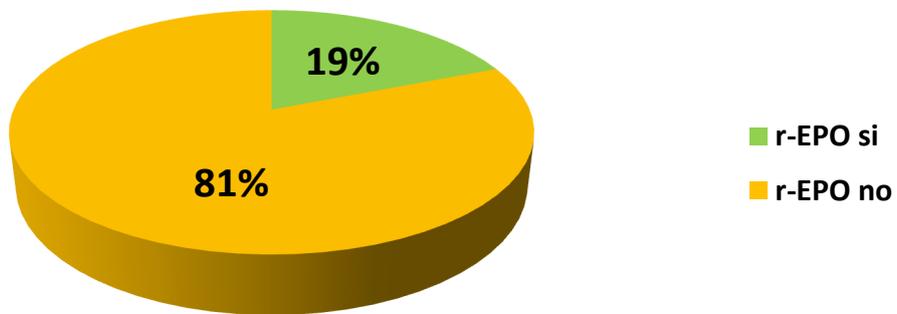
rHu-Epo treatment n°79		G.E.				
		32-30 W	29-28 W	<28 W	Tot.	Tot.%
N°patients		53	15	11	79	
Neurologic sequelae after treatment	NOT	50	12	9	71	89%
	HIE (1°-2°-3°-4°)	3	3	2	8	11%
	Leucomalacy	0	0	0	0	0
Fundus Oculi	ROP	0	0	0	0	0
	negative	53	15	11	79	
Outcome	Discharged	51	11	7	69	87%
	Obitus	2	4	4	10	13%

rHu-Epo treatment n°81		G.E.				
		32-30 W	29-28 W	<28 W	Tot.	Tot.%
N° patients		45	9	27	81	
Neurologic sequelae after treatment	NOT	31	1	4	36	44%
	HIE (1°-2°-3°-4°)	14	8	23	45	56%
	Leucomalacy	0	0	0	0	0
Fundus Oculi	ROP	2	3	8	13	16%
	negative	43	6	19	68	84%
Outcome	Discharged	35	3	1	39	49%
	Obitus	10	6	26	42	51%

**Percentage neurologic sequelae case-control groups**



**Percentage of death in case-control groups**



Circulation, O<sub>2</sub> Transport and Haematology / Systemic circulation and cardiac output

THROMBOCYTOPENIA IS NOT ASSOCIATED WITH PATENT DUCTUS ARTERIOSUS IN THE FIRST 48 HOURS OF LIFE (167)

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### Introduction /Case Report

It is assumed that platelet accumulation is essential to completely seal the constricted ductus arteriosus in newborns and recent studies have suggested that thrombocytopenia is associated with patent ductus arteriosus (PDA). We investigated this association in a Danish population of preterm infants.

### Patients and Methods

The study was designed as a matched case-control study in a population of 13786 newborns admitted to Department of Neonatology, Copenhagen University Hospital-Rigshospitalet, in Denmark from January 1996 through December 2008. We identified 221 infants, born <30 gestational weeks, who were diagnosed with haemodynamically significant PDA and matched these to up to four controls on gestational age, year of admission and gender, yielding a total of 583 controls. Data on platelet count was identified in the hospital's clinical biochemical department database. 134 cases and 313 controls had measurements of platelet counts within the first 48 hours of life. The association between PDA and thrombocytopenia (platelet count <150 x 10<sup>9</sup>/l) was estimated by conditional logistic regression.

### Results

35 cases (26,9%) had thrombocytopenia compared to 64 controls (20%) yielding an adjusted OR of PDA in neonates with thrombocytopenia versus those without of 1,25 (95% CI 0,73-2,14).

### Conclusions

Our study could not confirm an association between thrombocytopenia and PDA

Table

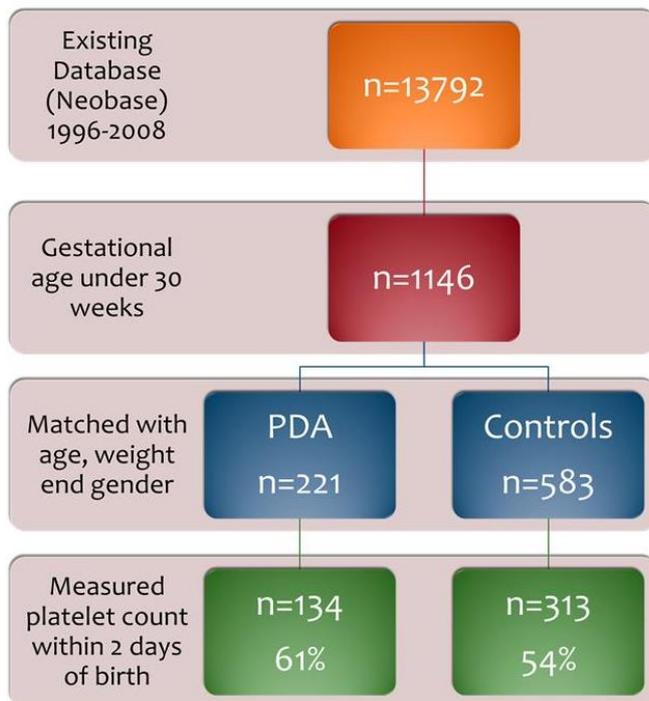
**Table 1 Characteristics of cases and controls**

	<b>Cases N=134</b>	<b>Controls N=313</b>
Females (%)	67 (50)	151 (48)
Gestational age (weeks)*	26 (25-28)	27 (25-28)
Birth weight* (g)	871 (710-955)	900 (750-1100)
Antibiotic treatment (%)	123 (92)	281 (90)
Median platelet count*	193 (148-227)	205 (164-258)
Trombocytopenia (<150x10 <sup>9</sup> /l)	35 (26)	64 (20)
Trombocytopenia <50 x10 <sup>9</sup> /l	4 (3)	5 (2)

\*median (inter quartile range)

Picture

**Figure 1**



GRADED RESTORATION OF NORMOCAPNIA BLOCKS PATHOPHYSIOLOGICAL SUPPRESSION OF SHARP WAVES IN A RAT MODEL OF BIRTH ASPHYXIA (791)

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Introduction /Case Report

Spontaneous network events are a characteristic feature of the developing brain, and they are thought to play a crucial role in the maturation of neuronal circuits. In the rodent hippocampus in vivo, sharp waves (SPW) are the first and only population event during early postnatal development. Birth asphyxia is associated with pathophysiological changes in the EEG, including either seizures or suppression of EEG activity during and immediately following asphyxia, which are often predictive of a poor neurodevelopmental outcome. The mechanisms underlying brain trauma and developmental disorders following birth asphyxia remain unknown, and effective therapies do not exist.

Patients and Methods

We used a model of infant rats that mimics the alterations in systemic CO<sub>2</sub> and O<sub>2</sub> levels during and after birth asphyxia. Infant rats (P5-7) were exposed for 45 minutes to asphyxic conditions (gas mixture containing 20% CO<sub>2</sub>, 4% O<sub>2</sub>) and left to recover either in room air for 2 hours (rapid restoration of normocapnia, RRN), or by a graded restoration of normocapnia (GRN, 10% CO<sub>2</sub> for 30minutes, followed by 5% CO<sub>2</sub> for 30 minutes, and subsequently room air for 1 hour). The impact of asphyxia and recovery on SPW activity was assessed 24 hours post-asphyxia. We recorded SPW activity along the CA1-dentate gyrus axis using multisite silicon probes under urethane anesthesia.

Results

Rats exposed to RRN after asphyxia at P5 or P6 showed strong and prolonged suppression of SPW activity when examined one day after the asphyxia. Strikingly, the fall in the rate of occurrence and amplitude of SPWs showed no significant changes when asphyxia was followed by GRN.

Conclusions

There is a widely recognized lack of therapeutic interventions to efficiently treat neurological injury caused by birth asphyxia. In the clinic, resuscitation based on RRN may have detrimental consequences. Our work suggests that GRN may prove to be an effective strategy for therapeutic intervention.

Other / Quality improvement and Safety and Error Preventio

FiO2 ADJUSTMENTS FOR SpO2 LEVEL MONITORING IN PRETERM INFANTS. (325)

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## Introduction /Case Report

The preterm infants are predisposed to episodes of intermittent hypoxia during the first 4 weeks of postnatal period. They are also more vulnerable to changes resulting from exposure to high oxygen levels. Hyperoxemic/hypoxemic episodes in preterm infants are identified by arterial oxygen saturation monitoring by pulse oximetry (SpO<sub>2</sub>), the standard, non-invasive, continuous technique that provides near-instantaneous data. These episodes are corrected by a transient decrease/increase in the fraction of inspired oxygen (FiO<sub>2</sub>), and adjusted to keep oxygen exposure at an optimum level. This work burden is significant especially in countries with restricted resources.

## Patients and Methods

**Objective & Methods:** The primary objective of the study is to collect data to observe the adherence to SpO<sub>2</sub> alarm limits during routine care. **Methods:** The camera was focused on the knob as digital export of the FiO<sub>2</sub> settings was not possible. A total of 56 neonates were recruited. Physiological data was collected from a standard Philips Patient Monitor (IntelliVue MP40) with its standard set of non-invasive parameters as per its intended use. For this, a laptop was connected to the patient monitor for communication and exporting the data. In addition to this, two cameras were connected to the USB ports of the laptop, with one focused on the FiO<sub>2</sub> knob and the other focused on the neonate to monitor body movements, crying, procedures conducted etc

## Results

Data from 4 neonates had to be rejected because of issues with the data recording. 52 neonates were distributed in 3 categories: (i) Preterm (29), (ii) Late preterm (12) and (iii) Term (11). A total of 283 hours of data was collected, comprising of approximately 1500 hypoxemic events and 3900 hyperoxemic events. The adherence to normoxemic, hyperoxemic and hypoxemic limits under each category was as follows:

Normoxemia %: (i) Preterm – 23.23%, (ii) Late preterm – 19.04% and (iii) Term – 48.27%. Hyperoxemia %: (i) Preterm – 69.36%, (ii) Late preterm – 76.95% and (iii) Term – 34.19%. Hypoxemia %: (i) Preterm – 7.41%, (ii) Late preterm – 4.01% and (iii) Term – 17.54%

In routine manual care environment, the percentage compliance to normoxemia was only around 28% probably because of the heavy nurse workload.

## Conclusions

Dedicated manual care has been found to improve maintenance of SpO<sub>2</sub> within the intended range in preterm infants. However, the nurse-patient ratio required is high and not feasible in a resource

restricted setting. The ideal solution would be to use an automated system that can control the  $FiO_2$  delivered to preterm infants, thereby maintaining  $O_2$  targets in premature infants .

Other / Quality improvement and Safety and Error Preventio

## INFLUENCE OF REPEATED PAINFUL PROCEDURES ON PAIN RESPONSE IN NEWBORNS (840)

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### Introduction /Case Report

To evaluate the effect of exposure to repetitive pain in the neonatal period on short-term pain response and to compare the results of different pain assessment methods.

### Patients and Methods

Healthy, term LGA infants (n:20) who had received at least five painful stimuli in addition to routine procedures were compared to healthy, term AGA infants (n:40). Oral Glucose Tolerance Test (OGTT) results of all the mothers and HbA1c levels of the mothers who had LGA babies, were recorded. Pulse oximeter, NIRS (Near Infrared Spectroscopy) device (Equinox Model7600) and Skin Conductance Algesimeter (Medstorm) were connected to babies before, during and after the heel lance while obtaining blood for neonatal screening test. Crying time, NIPS (neonatal infant pain scale), heart rate, peripheral oxygen saturation (SaO<sub>2</sub>), skin conductance response (peaks per sec) and regional cerebral oxygen saturation (rScO<sub>2</sub>) measurements were compared within and between the groups.

### Results

The demographic characteristics of the mothers and their babies in the study and control groups, were not statistically different except for birth weight, length and head circumference. OGTT results and HbA1c levels were within normal limits. There were no significant differences in behavioral states and physiological variables before the painful stimulus between the groups ( $p>0.05$ ). After the painful stimulus, crying time ( $p=0.018$ ) and NIPS scores ( $p=0.032$ ) were significantly higher and SaO<sub>2</sub> levels were significantly lower ( $p=0,019$ ) in the study group. Although a slight increase was detected for regional cerebral oxygen saturation after the painful stimulus, it did not reach statistical significance( $p>0.05$ ). The skin conductance activity also did not differ significantly between the groups, but the duration of time above the threshold value was longer for the study group.

### Conclusions

Newborn babies who had repeated painful exposures showed significant differences in crying time, NIPS scores and SaO<sub>2</sub> values. Although after the painful stimuli NIRS and skin conductance activity measurements showed significant difference within each group, the difference did not reach significance between the groups which may be due to our low sample size, the duration and severity of pain.

Other / Miscellanea

RETCAM-120 TO SCREENING OF THE RETINAL CHANGES IN RETINOPATHY OF PREMATURITY (084)

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Introduction /Case Report

To evaluate the use of digital retinal photographs in the assessment of retinal changes in retinopathy of prematurity (ROP).

Patients and Methods

The premature cohort consisted of 410 children born 32 weeks gestation and/or with weight below 1500 g. All infants were examined longitudinally, over a series of examinations, by indirect ophthalmoscopy (gold standard) and digital photography using the RetCam-120 Digital Retinal Camera equipped with an ROP lens. We assess the stage of ROP and we documented retinal changes, especially in the macula.

Results

Of the 410 premature infants 287 (70%) had no ROP, and 123 (30%) had ROP. Of the preterm infants with ROP macular retinal hemorrhages were found in 48 (39%) children and vitreo-retinal proliferative changes in the macula were observed in 5 (4%) patients. Of the newborns with ROP and with retinal hemorrhages, macular pigmentary changes were found in 4 (8%), and in 1 patient with vitreo-retinal proliferations. Retinal hemorrhages appeared 6 weeks after birth, macular pigmentary changes were found 6 months after birth, and vitreo-retinal proliferations were detected 3 months after birth.

Conclusions

Longitudinal digital photographs using RetCam-120 system has excellent specificity and sensitivity in detecting macular changes in ROP. Although macular hemorrhages almost always resorb without complications, our study allow the assumption that macular pigmentary changes and vitreo-retinal proliferations may lead to deprivation amblyopia. This study has shown that digital retinal photographs has promise for advances in the diagnosis of the ROP.

Other / Miscellanea

## REGULATION OF FGF23/ $\alpha$ -KLOTHO SYSTEM IN THE FETO-MATERNAL UNIT OF PREGNANCIES WITH ABNORMAL FETAL GROWTH (195)

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### Introduction /Case Report

Pregnancies complicated by abnormal fetal growth are associated with impaired mineral homeostasis, abnormal adipose tissue development and exaggerated oxidative stress. Fibroblast growth factor (FGF23) is a bone-derived hormone that enhances renal phosphorus excretion and suppresses the metabolic activation of vitamin D.  $\alpha$ -klotho acts as a cofactor of FGF23 and is critically involved in the endocrine regulation of calcium/phosphate metabolism, adipogenesis and antioxidant mechanisms. We aimed to investigate maternal/fetal FGF23/ $\alpha$ -klotho concentrations in pregnancies with abnormal fetal growth and associate them with several perinatal parameters.

### Patients and Methods

Plasma FGF23 and  $\alpha$ -klotho concentrations were determined by ELISA in 80 maternal and 80 cord blood samples from asymmetric intrauterine-growth-restricted (IUGR, n=30), large-for-gestational age (LGA, n=30) and appropriate-for-gestational-age (AGA, n=20) singleton full-term pregnancies. An intact FGF23 ELISA, which is designed to measure the biologically active full-length FGF23, was used. Fetuses were classified as IUGR, LGA or AGA, based on customized birth-weight standards, adjusted for significant determinants of fetal growth.

### Results

Maternal/fetal FGF23 and  $\alpha$ -klotho concentrations did not differ among IUGR, LGA and AGA groups and were similar in all studied groups. In a combined group, maternal FGF23 concentrations positively correlated with respective fetal ones ( $r=0.243$ ,  $p=0.040$ ). In the IUGR group, fetal  $\alpha$ -klotho concentrations increased with increasing birth-weight ( $b=2.333$ , 95%CI 0.811-3.854,  $p=0.004$ ) and were lower in multiparas [ $b=-1239.56$ , 95%CI -2081.64-(-397.48),  $p=0.005$ ]. In the LGA group, fetal FGF23 concentrations negatively correlated with the customized centiles of the studied infants ( $r=-0.393$ ,  $p=0.039$ ). Maternal FGF23 concentrations were higher in multiparas ( $b=0.382$ , 95%CI 0.091-0.673,  $p=0.012$ ). Finally, in the AGA group, maternal FGF23 concentrations negatively correlated with fetal  $\alpha$ -klotho ones ( $r=-0.517$ ,  $p=0.023$ ).

### Conclusions

Maternal/fetal FGF23/ $\alpha$ -klotho concentrations are probably not affected by abnormal fetal growth. However,  $\alpha$ -klotho is up-regulated with increasing birth-weight in IUGR fetuses. Fetal FGF23 concentrations negatively correlate with the customized centiles in the LGA group, possibly protecting against

hypocalcemia in severe cases of fetal macrosomia. FGF23/ $\alpha$ -klotho pathway may be implicated in fetal mineral homeostasis/overall metabolism.

## Brain & Development / Neurodevelopmental Outcome

### OUTCOME OF INFANTS WITH NECROTISING ENTEROCOLITIS (NEC): THE IMPACT OF LAPAROTOMY VERSUS PERITONEAL DRAINAGE ON NEURODEVELOPMENT (853)

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#### Introduction /Case Report

NEC remains a major cause of morbidity and mortality in very low birth weight infants. Randomised trials have shown no clear advantage of laparotomy (Lap) versus peritoneal drain (PD) for initial surgical management, however data on long term neurodevelopment is limited. The aim of this study was to examine growth and neurodevelopmental outcomes of infants who had surgical NEC and compare outcomes of infants who had a peritoneal drain to those who had laparotomy with bowel resection.

#### Patients and Methods

All infants with birth weight <1500g admitted to the tertiary referral unit at The Hospital for Sick Children with surgical NEC between 2001-2012 were reviewed. Infants with spontaneous intestinal perforation were excluded. Neonatal course, complications and growth and neurodevelopmental outcomes were followed to 18-24 months. Significant difference between group outcomes was assessed by Student t, Chi squared and Fisher exact tests.

#### Results

During the 12 year study period, 132 infants < 1500g were admitted with surgical NEC. Mean birth weight was 977.9±268.2g and gestational age (GA) 27.1±2.3 weeks. 78 infants had a primary laparotomy, 40 had a PD inserted and 10 had a PD followed by later laparotomy. Birth weights, GA and survival to discharge of the groups are significantly different, see Table. Follow up data was obtained on 56 infants, (85%). Rates of composite measures of neurodevelopmental impairment and severe neurodevelopmental disability are shown in Table.

#### Conclusions

Long term neurodevelopmental outcomes are not significantly different for both surgical groups, however the composite rate of severe neurodevelopmental disability and mortality is significantly higher for the drain group. Laparotomy should be undertaken for these infants if possible.

Table

Table

Variable	NEC Laparotomy	NEC Drain or Drain + Laparotomy	<i>P</i> value
N	78	50	
BW g, mean, SD	1055.6 (255.7)	866.5 (255.8)	0.0001
GA wk, mean, SD	27.8 (2.2)	26.2 (2.2)	0.0001
Survival to discharge, n (%)	48 (61%)	18 (36%)	0.005
Follow up data, n (%)	41 (85%)	15 (83%)	n.s.
Neurodevelopmental impairment, n (%)	11 (27%)	1 (7%)	n.s.
Severe neurodevelopmental disability, n (%)	9 (22%)	5 (33%)	n.s.
Death or severe neurodevelopmental disability, n(%)	39 (55%)	37 (79%)	0.006

## Other / Miscellanea

### TRANSCUTANEOUS BILIRUBIN (TCB) NOMOGRAM FOR NEWBORNS OF EAST ASIAN (EA) ETHNICITY (140)

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## Introduction /Case Report

There are limited data regarding the natural history of Transcutaneous bilirubin (TcB) levels during the first days of life, and it is incorrect to plot TcB levels on Total Serum Bilirubin-based nomograms. East Asian (EA) ethnic origin has been shown to be a major and independent risk factor for hyperbilirubinemia. The purpose of this study is to evaluate TcB levels for the first 96 hours after birth in healthy term and near-term neonates of EA ethnicity and to develop a TcB nomogram based on hour-specific TcB evaluation in these neonates. There are no existing studies done to develop nomograms for newborns of EA ethnicity that carry a distinctive independent risk factor.

## Patients and Methods

Single center, IRB approved, prospective study data collection over 12 months, from a diverse immigrant population in New York with predominant newborns admissions of EA ethnicity. Inclusion: Healthy term and late preterm neonate (GA $\geq$ 35 Wks) admitted to nursery, Exclusion: Babies with perinatal asphyxia, Rh Incompatibility, G6PD deficiency and those requiring phototherapy. Using a daily list of all deliveries, TcB measurements using the Draeger JM-103TM jaundice meter obtained every 4 hours between 10 AM and 10 PM (10 AM, 2 PM, 6 PM,10 PM) on weekdays, for all eligible infants whose ages were within 2 hours of one of the designated 4-hour time intervals (8,12,16,20,24..96 Hrs). Maternal and infant clinical data including mode of delivery, gestational age, feeding type, and BW collected.

## Results

There were total 9,021 TcB observations obtained on 1,599 neonates who met the inclusion criteria, out of 4300 neonates after excluding neonates under exclusion criteria. Study population characteristics shown in Table 1. A nomogram was constructed for this exclusive EA population, identifying the 10th, 25th, 50th, 75th, 90th and 95th percentile curves of postnatal TcB (Fig 2). The 95th percentile values at 12, 24, 48, and 72 hours were 4.8, 7.4, 11.1, and 11.9 mg/dL, respectively. There were no statistically significant association between the difference in TcB levels from 8h to 36h and mode of delivery (Kruskal-Wallis test,  $p=0.88$ , significance level=0.05), or gender (Mann-Whitney test,  $p=0.44$ , significance level=0.05).

## Conclusions

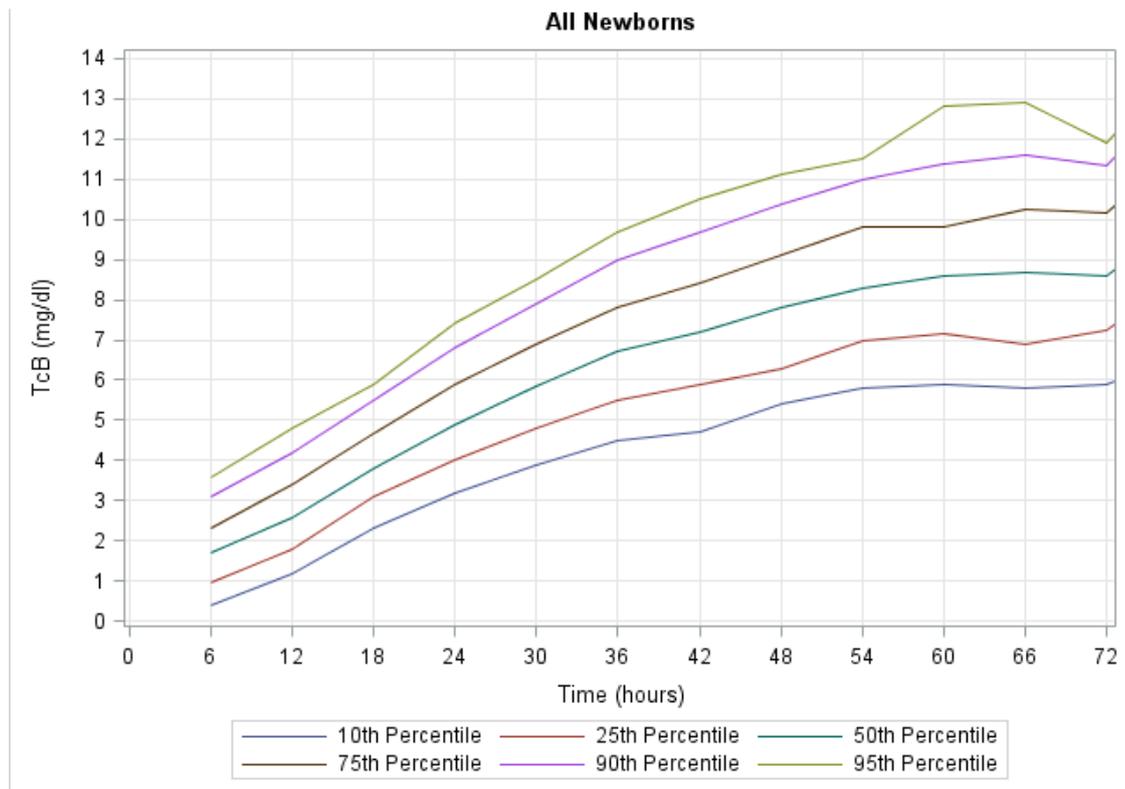
In this cohort of neonates of EA ethnicity from a diverse immigrant population in the United States the median (50th percentile) and the 75th percentile TcB values are higher than those reported in Hispanic and Caucasian population (De Luca D., et al Arch Pediatr Adolesc Med. 2009 Nov; 163(11):1054-9) , at each of the 11 time periods starting at 12 hours. The TcB levels also tend to peak earlier and plateau beyond 60 hours of postnatal life.

Table

Table 1. * (Mean ± sd)	Study population characteristics
Total number of neonates	1,599
Total no. of TcB observations	9,021
GA at birth (Weeks)	38.9±1.1
Maternal Age (yrs)	30.9±4.8
Vaginal/Assisted vaginal/ C-section (%)	64/4/32
Gender M/F (%)	54/46
Birth Weight (gms)	3306±409
Weight loss at DC	172 gms (5.2%)
TcB observations	5.6±2.7*
Feeding (%)	
• Both	62
• Formula	37
• Exclusive	1

Picture

Fig 2



## Other / NICU design and Family centres care

Using Sound Blocking Headphones on the Neonatal Intensive Care Unit to Enable Parents to Stay with their Baby during Ward Rounds and Handovers (246)

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## Introduction /Case Report

For many years to ensure confidentiality and enable full discussion during ward rounds and handovers parents were asked to attend and then leave the nursery once their baby had been discussed. This is usual practice in many NICUs, and rarely challenged. This project aimed to decrease separation for parents related to ward rounds and handovers. The duration of ward rounds depends on the structure of the NICU, many units have large nurseries especially for intensive care. During a 24 hour period this means that parents can be separated from their baby for up to 4-5 hours. Long separation during these activities can interfere with breastfeeding and bonding and increase the parents' anxiety.

## Patients and Methods

Sound blocking headphones were introduced into the NICU so parents could stay with their baby during ward rounds and handovers while information about other babies remains confidential. The Venitex Ear Defenders selected for the project were soundproof and have an inbuilt wireless radio; parents were encouraged to listen to music to ensure conversations in the ward were blocked out. Parents were aware that headphones must be worn during handovers and ward rounds but were invited to take them off when their baby was being discussed. To enable quantitative measure of the improvement pre- and post-implementation audits were carried out. We collected data about the length of the ward round, number of parents attending and time of separation. Parent and staff questionnaires were collected.

## Results

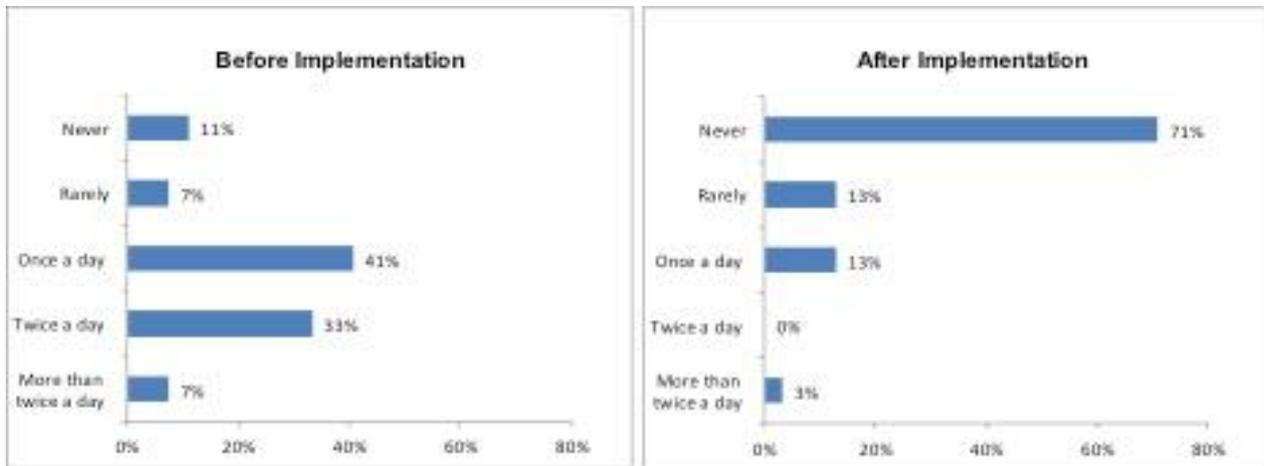
Prior to the use of headphones 22/27 (81%) of our parents experienced that they had to leave the nursery during ward rounds and handovers; 11/27 (40%) of them more than once a day. This was reduced significantly as after implementation 22/31 (71%) of the parents have never been sent out of the nursery related to these activities (Chi Square test,  $p < 0.001$ ) (Figure 1). Similarly staff reported before implementation that 81/96 (85%) of them asked parents to leave at least once a day, compared to 13/82 (16%) after implementation ( $p < 0.0001$ ). Prior implementation 21/26 (80%) of the parents were happy how we safeguarded patient confidentiality, but 2/26 (12%) were neutral and 2/26 (8%) disagreed. After introducing the headphones we have seen a significant change as 23/30 (77%) of the parents strongly agreed with the new practice, and 0 % fell into the neutral or disagree category ( $p = 0.049$ ).

## Conclusions

The result of this quality improvement study supports the innovative idea of using sound blocking headphones on the NICUs for ward round and handovers to maintain patient confidentiality without

compromising parental presence and could be shared more widely as “best practice” in units focusing on family-centered care.

Picture



## Brain & Development / Neurodevelopmental Outcome

### RISK FACTORS FOR SEVERE RETINOPATHY OF PREMATURITY IN PRETERM INFANTS $\leq 32$ WEEKS GESTATIONAL AGE (549)

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#### Introduction /Case Report

Retinopathy of prematurity (ROP) is a potentially blinding eye disorder that primarily affects premature infants born between 32 weeks of gestation. The condition was previously entirely attributed to high levels of oxygen exposure but other risk factors were described in the literature

Aim: The authors aimed to identify the incidence and risk factors for severe ROP (needing laser therapy) in preterm infants  $\leq 32$  weeks gestational age.

#### Patients and Methods

Material and methods: The prospective study was developed over a 2 years period (01.01.2010 - 31.12.2011) and as based on the information collected in the National Registry for Respiratory Distress Syndrome by 4 regional neonatal centers. All preterm infants  $\leq 32$  weeks gestational age were included and data analysis was performed using IBM SPSS Statistics 19 (for a statistical significant  $p < 0.05$ , 95% CI).

#### Results

Results: The study group comprised 621 preterm infants with a mean GA of  $29.9 \pm 2.0$  weeks, and a mean BW of  $1382.3 \pm 360.8$ g. Severe ROP occurred in 24 cases (4.02%). Preterm infants having severe ROP had significantly lower GA and BW ( $p < 0.000$ ), and Apgar scores at 1 and 5 minutes ( $p < 0.012$ ,  $0.036$ ). Diagnosis of severe ROP was significantly associated ( $p < 0.05$ ) with the presence of chorioamnionitis, the need (OR 6.1[CI 2.6-14.8]) and the length for mechanical ventilation, and duration of CPAP support and oxygen therapy. Also, severe ROP was significantly associated ( $p < 0.05$ ) with persistent ductus arteriosus (OR 4.1[CI 1.7-10.1]), cerebral hemorrhage (OR 2.4[CI 1.1-5.5]), periventricular leukomalacia (OR 5.0[CI 1.9-12.8]), chronic lung disease (OR 7.2[CI 3.1-16.6]), necrotizing enterocolitis (OR 3.4[CI 0.9-12.2.]), barotrauma (OR 4.8[CI 1.3-17.9]), and neonatal sepsis (OR 2.9[CI 1.3-7.0]).

#### Conclusions

Conclusions: The incidence of severe ROP was similar with data cited in the literature for developed countries. All the identified risk factors are suggesting that preterm infants with lower GA and BW with more complicated perinatal course have an increased risk for developing severe ROP that needs laser therapy.

Circulation, O2 Transport and Haematology

## FEASIBILITY OF USING THE ELDON CARD IN THE PERIPARTUM DIAGNOSIS OF RH INCOMPATIBILITY BETWEEN MOTHERS AND THEIR NEWBORNS (405)

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### Introduction /Case Report

Hemolytic Disease of the Foetus/Newborn (HDFN) occurs when a Rhesus (Rh) negative woman, previously sensitised to the Rh D antigen in a pregnancy with an Rh positive baby, carries another Rh positive baby in a later pregnancy. It is preventable if the blood groups of the mother and baby are known early so that appropriate management is started. Universal blood group testing is an issue in developing countries like Ghana, hence the persistence of the disease. The Eldon Card is a point of care method of ABO-Rh group testing which has been used by armed forces at field sites. It could potentially be used to fill this gap for universal blood group testing and contribute to the reduction of HDFN.

### Patients and Methods

This will be a cross-sectional blinded study of mothers and their neonates at delivery in the labour ward of Korle-Bu Teaching Hospital. By means of a standardized form, socio-demographic, past and current obstetric details, condition of babies at birth will be documented. For each mother/baby pair, 2 ml each of maternal and cord blood will be tested by standard laboratory methods for ABO-Rh blood group at the blood bank. This will be the gold standard. Additionally, capillary blood from the mother and baby will be tested with the Eldon Card kit by trained doctors and nurses to determine their ABO-Rh blood groups. Results of the Eldon card method will be compared to the gold standard. Ethical approval and informed consent will be obtained.

### Results

The Eldon card will be a rapid and easy to handle method of determining the ABO-Rh blood groups of mothers and their newborns at the point of care. The results of the Eldon card method will be comparable to those of the gold standard method.

### Conclusions

The Eldon card will be a suitable alternative method for blood group determination for mothers and their newborns at the point of care. It therefore has the potential to help reduce the morbidity and mortality associated with Haemolytic Disease of the Foetus/Newborn by improving access to blood group testing, and thus creating the opportunity for timely management.

Other / Organization of perinatal care

ANALYSIS OF THE ASSOCIATIONS BETWEEN ANGIOTENSIN-CONVERTING ENZYME GENE POLYMORPHISM AND DEVELOPMENT OF ARTERIAL HYPOTENSION IN THE PRETERM INFANTS WITH EARLY NEONATAL SEPSIS (881)

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#### Introduction /Case Report

The objective of this study was to examine the associations between angiotensin-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism and development of arterial hypotension in the preterm infants with early neonatal sepsis.

#### Patients and Methods

Prospective observational study included 118 preterm infants with early neonatal sepsis (n=57 with arterial hypotension and n=61 without arterial hypotension) admitted to the neonatal intensive care units of children's hospitals of Poltava region: Control group consisted of healthy term infants from the same region (n=31). Both groups of patients were genotyped for the insertion/deletion polymorphism of the ACE gene. Arterial hypotension were compared in patients with II, ID, and DD genotypes of the ACE gene. Associations between different ACE genotypes and arterial hypotension were analyzed.

#### Results

Distribution of infants in relation to the three variations of ACE gene I/D polymorphism was identical in the study: in the infants with arterial hypotension - 21,05 %, 50,88 % and 28,07 %; in the infants without arterial hypotension (29,5% 49,2% and 21,2% p=0,498; in the infants of control groups – 39,5 %, 44,7 % and 15,8 %, respectively). Arterial hypotension in the infants with early neonatal sepsis was while no associations with II, ID and DD genotypes were found.

#### Conclusions

Arterial hypotension is not associated with a I/D polymorphism ACE gene in preterm infants with early neonatal sepsis.

Nutrition and gastroenterology / Breast feeding

## THE COMPARISON OF ADJUSTED VERSUS TARGETED HUMAN MILK FORTIFICATION ON GROWTH PARAMETERS OF VERY LOW BIRTH WEIGHT INFANTS (652)

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### Introduction /Case Report

Breast milk supplements are supporting the use of breast milk of very low birth weight (VLBW) infants and also aim to fulfil the needs of premature babies in the best way. Breast milk might seem insufficient for the efficient provision of essential protein, calcium, phosphorus and other nutrients for extra uterine growth of VLBW premature infants and therefore growth retardation is encountered frequently. This study aimed to compare the effects of fortification methods on growth in addition to breast milk supplements.

### Patients and Methods

In each group, 20 infants were included to this study under 1500 g and under 32 wks at birth in our hospital between June 2014 and December 2014. Standard protein supplement were provided to the first group. Additional protein levels were provided to the second group via adjusting the protein levels according to defined serum BUN while additional protein levels (adjustable ) were provided to the third group via tailoring breast milk content according to the ESPGHAN recommended protein level (targeted/tailored) of breast milk and infants were fed by this method twice a week. Infants were followed for four weeks and head circumference, weight and height percentiles were compared.

### Results

No significant difference was observed between standard supplemented group and the 2 groups during the first week. The difference of heights was found, between the first group and other groups in weeks 2, 3 and 4 ( $p: 0.032$ ,  $p = 0.025$ ,  $p = 0.0001$ ); Weight gain was similar during the first two weeks but then difference in weight gain between the groups were observed in the third and fourth weeks (respectively;  $p: 0.002$ ,  $p = 0.0001$ ). For head circumference, there was no significant difference between the groups during the four weeks. Body weight and height percentiles were significantly lower in the group with standard enrichment method at the end of a one-month follow-up compared to the two other groups. There was no statistically significant difference between Adjustable and Targeted enrichment methods considering the effects on the growth.

### Conclusions

According to this study, it can be stated that when three different enrichment methods were compared, the babies get better weight and better grow fed with set (adjusted) and targeted (tailored-targeted) methods than standard enrichment method at an early stage.

## Brain & Development / Neurodevelopmental Outcome

The influence of prenatal exposure to endocrine disrupting chemicals on behavioral development in children (147)

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### Introduction /Case Report

In recent years, prevalence rates of behavioral disorders in children have increased. One factor of importance might be exposure to endocrine disrupting chemicals (EDCs), which are widely used in everyday life. Several epidemiological studies, human clinical observations and animal models indicate that exposure to EDCs may have adverse health effects. The prenatal period might be a particularly sensitive period for EDC exposure as rapid structural and functional changes take place, in particular with regard to brain development. The aim of the current paper is to study the relationship between prenatal exposure to EDCs and behavioral development in children.

### Patients and Methods

Women were recruited at the first antenatal visit to the midwife. At the age of 18 months parents filled out the Child Behavior Checklist 1.5-5 to assess the behavioral development of the child. The scales 'Externalizing' and 'Attention Deficit Hyperactivity Problems' were used for the analysis. Umbilical cord blood (UCB) and breast milk (BM) were collected for the analysis of EDCs, which included DDE, PCB-153, PFOA, PFOS and dioxins. PCB-153 was included as a dichotomous variable, comparing samples below LOQ with samples above LOQ.

Linear regression models were composed for each compound. The variables family history of ADHD, educational level, smoking/alcohol use/illicit drug use during pregnancy were checked for confounding effects. Stratification for boys and girls was applied.

### Results

The total number of included mother-child pairs varied between 44 and 65, depending on the compound. When analyzing the whole study population, participants exposed to the highest levels of dioxins, showed significantly higher scores on the ADHD scale of the CBCL (1.32;  $p=0.03$ ). After stratification, the effect remained significant for boys (1.73;  $p=0.02$ ), but not for girls. In addition, boys exposed to the highest levels of PFOA, scored significantly lower on 'Externalizing Problems' (-5.21;  $p=0.04$ ). After adjustment, the effects did not remain significant. Girls presenting PCB-153 levels above LOQ showed a significantly lower score on the scale 'ADHD' than those exposed to levels below LOQ (-1.51;  $p=0.02$ ). This effects remained significant after adjustment. No significant associations were found between prenatal exposure to DDE and PFOS and ADHD or Externalizing Problems.

## Conclusions

Prenatal exposure to higher levels of PFOA was related to less externalizing behavior, while higher exposure levels to dioxins were related to more ADHD-like behavior. These effects were only found in boys. Girls prenatally exposed to quantifiable levels of PCB-153 scored lower on the ADHD scale. Considering the burden developmental disorders place on the medical and educational system, it should be a priority to identify modifiable risk factors.

Table

Table 1: Regression coefficients for EDC exposure and ADHD for the whole study population

Compound	N	Q1	Q2		Q3	
			$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value
<b>DDE Total</b>						
<i>Crude model</i>	71	Ref.	0.16 (-1.01, 1.26)	0.79	0.87 (-0.20, 1.80)	0.08
<i>Adjusted model</i>	69	Ref.	-0.06 (-1.26, 1.04)	0.91	0.55 (-0.45, 1.42)	0.26
<b>Dioxins Total</b>						
<i>Crude model</i>	50	Ref.	0.29 (-0.79, 1.43)	0.64	1.32 (0.13, 2.49)	0.03*
<i>Adjusted model</i>	48	Ref.	0.91 (-0.33, 1.98)	0.15	1.41 (0.03, 2.93)	0.06
<b>PFOA Total</b>						
<i>Crude model</i>	62	Ref.	0.20 (-0.94, 1.35)	0.73	-0.34 (-1.50, 0.80)	0.53
<i>Adjusted model</i>	58	Ref.	0.21 (-1.08, 1.53)	0.79	-0.67 (-1.88, 0.46)	0.29
<b>PFOS Total</b>						
<i>Crude model</i>	63	Ref.	0.45 (-0.68, 1.65)	0.42	-0.31 (-1.44, 0.72)	0.59
<i>Adjusted model</i>	59	Ref.	0.30 (-1.01, 1.57)	0.65	-0.35 (-1.52, 0.71)	0.59

Table 2: Regression coefficients for EDC exposure and ADHD, stratified for gender

Compound	BOYS						GIRLS					
	N	Q1	Q2	Q3			N	Q1	Q2	Q3		
			$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value			$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value
<b>DDE Total</b>	<51.5		51.5-109.8			>109.8	<45.0		45.0-82.0			>82.0
<i>Crude model</i>	38	Ref.	-0.63 (-2.36, 1.16)	0.47	0.49 (-0.85, 1.79)	0.46	27	Ref.	0.26 (-1.25, 1.79)	0.74	1.25 (-0.31, 2.75)	0.11
<i>Adjusted model</i>	36	Ref.	-1.03 (-3.02, 0.68)	0.29	0.35 (-1.52, 1.68)	0.69	26	Ref.	0.34 (-1.66, 2.33)	0.71	1.29 (-0.59, 2.93)	0.15
<b>Dioxins Total</b>	<2.5		2.5-4.9			>4.9	<2.7		2.7-4.5			>4.5
<i>Crude model</i>	27	Ref.	0.60 (-1.11, 2.09)	0.45	1.73 (0.31, 2.94)	0.02*	19	Ref.	-1.00 <sup>43</sup> (-2.00, 1.97)	0.99	0.50 (-1.75, 2.50)	0.62
<i>Adjusted model</i>	26	Ref.	1.36 (-0.06, 2.56)	0.08	1.52 (0.09, 2.86)	0.05	18	Ref.	0.22 (-2.00, 2.45)	0.85	0.50 (-1.88, 2.52)	0.63
<b>PFOA Total</b>	<579.9		579.9-990.0			>990.0	<393.3		393.3-689.9			>689.9
<i>Crude model</i>	38	Ref.	-0.50 (-3.38, 1.67)	0.67	-1.29 (-4.20, 0.56)	0.24	20	Ref.	0.21 (-1.00, 1.50)	0.75	0.38 (-2.00, 4.11)	0.83
<i>Adjusted model</i>	36	Ref.	-1.01 (-4.19, 2.82)	0.54	-1.97 (-4.99, 1.60)	0.26	19	Ref.	0.67 (-0.33, 2.00)	0.38	1.33 (-1.87, 5.33)	0.53
<b>PFOS Total</b>	<1199.8		1199.8-1899.8			>1899.8	<603.3		603.3-1466.4			>1466.4
<i>Crude model</i>	38	Ref.	-0.36 (-4.00, 1.93)	0.86	-0.80 (-4.21, 1.53)	0.67	21	Ref.	0.21 (-1.37, 1.57)	0.77	0.71 (-1.25, 2.77)	0.49
<i>Adjusted model</i>	36	Ref.	-0.44 (-4.79, 2.50)	0.83	-0.70 (-4.38, 2.45)	0.75	20	Ref.	0.30 (-1.33, 2.00)	0.76	0.55 (-2.14, 3.55)	0.69

Table 3: Regression coefficients for EDC exposure and externalizing behavior, stratified for gender

Compound	BOYS						GIRLS					
	N	Q1	Q2		Q3		N	Q1	Q2		Q3	
			$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value			$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value
<b>DDE Total</b>		<b>&lt;51.5</b>	<b>51.5-109.8</b>		<b>&gt;109.8</b>		<b>&lt;45.0</b>	<b>45.0-82.0</b>		<b>&gt;82.0</b>		
<i>Crude model</i>	38	Ref.	0.11 (-6.12, 7.30)	0.96	1.21 (-2.52, 5.10)	0.55	27	Ref.	1.31 (-3.93, 7.42)	0.64	1.31 (-7.07, 2.60)	0.34
<i>Adjusted model</i>		Ref.	-0.23 (-7.58, 6.08)	0.94	1.45 (-4.12, 5.99)	0.59	26	Ref.	2.68 (-3.21, 10.64)	0.39	-1.14 (-5.09, 3.91)	0.63
<b>Dioxins Total</b>		<b>&lt;2.5</b>	<b>2.5-4.9</b>		<b>&gt;4.9</b>		<b>&lt;2.7</b>	<b>2.7-4.5</b>		<b>&gt;4.5</b>		
<i>Crude model</i>	27	Ref.	2.83 (-2.95, 7.90)	0.32	5.13 (0.00, 9.68)	0.06	19	Ref.	-0.79 (-5.84, 4.80)	0.77	-2.17 (-9.83, 6.34)	0.65
<i>Adjusted model</i>		Ref.	4.05 (-2.41, 9.33)	0.20	4.86 (-0.86, 9.19)	0.08	18	Ref.	-2.63 (-10.54, 3.89)	0.45	-2.69 (-11.26, 6.18)	0.55
<b>PFOA Total</b>		<b>&lt;579.9</b>	<b>579.9-990.0</b>		<b>&gt;990.0</b>		<b>&lt;393.3</b>	<b>393.3-689.9</b>		<b>&gt;689.9</b>		
<i>Crude model</i>	38	Ref.	-3.00 (-7.95, 3.01)	0.29	-5.21 (-9.32, 0.65)	0.04*	20	Ref.	0.43 (-5.52, 7.37)	0.88	1.43 (-3.53, 6.31)	0.61
<i>Adjusted model</i>		Ref.	-2.33 (-7.91, 7.21)	0.51	-5.54 (-10.68, 4.00)	0.12	19	Ref.	1.17 (-5.00, 9.78)	0.76	7.17 (-2.29, 17.39)	0.22
<b>PFOS Total</b>		<b>&lt;1199.8</b>	<b>1199.8-1899.8</b>		<b>&gt;1899.8</b>		<b>&lt;603.3</b>	<b>603.3-1466.4</b>		<b>&gt;1466.4</b>		
<i>Crude model</i>	38	Ref.	2.49 (-5.81, 9.26)	0.56	-0.07 (-8.30, 6.52)	0.99	21	Ref.	-3.57 (-9.65, 3.33)	0.30	-1.74 (-6.83, 3.47)	0.49
<i>Adjusted model</i>		Ref.	2.74 (-5.61, 10.64)	0.52	-0.01 (-8.06, 7.20)	1.00	20	Ref.	-2.00 (-9.37, 5.67)	0.56	-0.17 (-6.02, 6.30)	0.95

Table 4: Regression coefficients for exposure to PCB-153, ADHD and externalizing behavior, stratified for gender

Outcome	BOYS				GIRLS			
	N	<LOQ	>LOQ		N	<LOQ	>LOQ	
			$\beta$ (95% CI)	p-value			$\beta$ (95% CI)	p-value
<b>ADHD</b>								
<i>Crude model</i>	38	Ref.	-0.39 (-1.52, 0.73)	0.48	27	Ref.	-1.51 (-2.68, 0.38)	0.02*
<i>Adj. model</i>	37	Ref.	-0.46 (-1.58, 0.72)	0.45	27	Ref.	-1.60 (-2.94, 0.24)	0.04*
<b>Externalizing</b>								
<i>Crude model</i>	38	Ref.	-0.34 (-4.14, 3.44)	0.87	27	Ref.	0.79 (-3.67, 5.00)	0.71
<i>Adj. model</i>	36	Ref.	-0.66 (-4.49, 3.41)	0.77	26	Ref.	-0.29 (-5.02, 3.64)	0.89

## Brain & Development / Neurodevelopmental Outcome

### ASSESSMENT OF NEURODEVELOPMENT IN LATE PRETERM NEWBORN AT 24 MONTHS OF AGE USING THE AGES & STAGES QUESTIONNAIRES. (557)

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#### Introduction /Case Report

Prematurity is the main reason for neonatal morbidity and mortality. It has become one of the greatest problems in public health. This increase may be attributed to late preterm (LP) babies (34+0 - 35 +6 ). Neurological development of these newborns is one of the most important concerns for neonatologists and research teams. Early detection of neurodevelopmental disorders is essential to make an intervention to correct or mitigate them. The Ages & Stages Questionnaires (ASQ-3) is a surveillance method for detecting children at risk of developmental delay.

The aim of this study is to evaluate the psychomotor development of late preterm infants at 24 months.

#### Patients and Methods

A retrospective cohort study was conducted on late preterm babies who were born at a level III hospital along one year period (2011). Cerebral palsy, polimalformative syndromes, genetics and metabolic disorders were excluded. The preterm babies were assessed by ASQ-3 at 24 months of age. Five psychomotor fields were evaluated: communication, gross and fine motor function, problem solving and sociability). Demographic and perinatal variables were collected. Continuous variables were described using mean and standard deviation. The categorical ones were described as frequencies and proportions, and compared applying the Chi-square test and Mann-Whitney test. A cut-off was determined for the total score of ASQ-3 able to detect the risk of developmental deficit by a ROC analysis.

#### Results

100 late preterm were contacted. 69 of them completed the questionnaire. In our population, the bigger sensitivity (75%) and specificity (85,2%) are provided by a total score 235. Positive predictive value 52,9% and negative predictive value 93,9% have been obtained using this cut-off score. From all analyzed patients, 17 babies (24,6%) showed a risk of psychomotor deficit (total score < 235). No significant statistically relationship was detected with demographic and perinatal variables. Breastfeeding could be a protector factor (14,3% late preterm who received breast milk achieved a total score < 235 versus 23,5% in not breast fed group).

#### Conclusions

According to these results our late preterm newborns show an increased risk of psychomotor deficit. ASQ-3 test could be a good and easy method to assess these babies. Specific monitoring programs should be designed to attend this population

## Brain & Development / Neurodevelopmental Outcome

### OUTCOME FOR LIVEBIRTHS WITH EXTREMELY LOW BIRTH WEIGHT IN ESTONIA: IS THERE ANY IMPROVEMENTS? (841)

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#### Introduction /Case Report

Survival until hospital discharge of extremely low birth weight infants (ELBWI, <1000g) born before 29 gestational weeks in Estonia has increased from 48% in 2002–03 to 64% (2007–08) and 80% in 2011–12. Decreased mortality concern for higher impairment rates in survived children. Two years of corrected age (2yCA) is considered an acceptable time for assessment of high-risk infants for long-term morbidities. PARCA structured questionnaire has been used for parental report of child developmental skills, health and diseases. The aim was to evaluate the outcome of the Estonian national one-year 2011–12 liveborn ELBWI cohort at 2yCA and compare with the earlier cohorts.

#### Patients and Methods

National population-based cohort of Estonian VLGA infants born between 01.05.2011–30.04.2012 was studied prospectively within the EPICE (Effective Perinatal Intensive Care in Europe) project. Parents of surviving at 2yCA infants were asked to fill in PARCA questionnaire describing infants' treatment needs, vision, hearing, and ability to walk, sit and understand instructions, as well as number of words the infant can say. Data of the subgroup of liveborn infants with birth weight <1000g and gestational age < 29 weeks were taken for the current subanalysis. Severe neurodevelopmental impairment (NDI) was considered as blindness, deafness, inability to say 5 words or understand instructions, or cerebral palsy with Gross Motor Function Classification System (GMFCS), levels 3–5.

#### Results

The follow-up rate was 100%. The median (range) birth weight was 920 (452-992)g and gestational age 26 (23-28.2) weeks. All infants survived after hospital discharge. There were no children at 2yCA with blindness, deafness or on seizure medications. 7% (n=2) of infants were unable to walk without assistance and unable to sit without support. Survival of live-born ELBW infants without severe NDI at 2yCA was 73%. This outcome has improved significantly ( $p<0.05$ ) when compared with results of the previously studied similar national cohorts from 2007–08 and 2002–03 (survival without severe NDI respectively 58% and 38%).

#### Conclusions

Along with the increased survival until discharge from hospital, the overall outcome measured as survival without severe NDI for liveborn ELBWI at 2yCA has improved in Estonia significantly, if measured by parental reports. Further analysis of performed Bayley (BSID-III) tests will show more appropriately the developmental outcome, as this group of high-risk patients can have often moderate developmental or behavioral problems.

## Other / Miscellanea

### Body Composition Assessment in Preterm Infants: Comparison of Air Displacement Plethysmography and Dual-Energy X-Ray Absorptiometry (874)

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#### Introduction /Case Report

Fat and lean mass accretion in preterm infants determines the risk for chronic diseases. Assessing nutrition is the best way to curtail inappropriate growth of these body compartments. Infant body composition is an emerging field promising a more clinically relevant assessment of adequacy of nutrition compared to the current practice of weight gain evaluation. Hence, there is a need to establish the validity of body composition techniques. Air displacement plethysmography (ADP) and dual X-ray absorptiometry (DXA) have been independently validated against established reference methods. However, there is little to no literature comparing ADP with DXA, particularly in the preterm population

#### Patients and Methods

55 concurrent DXA (Hologic Discovery QDR 4500, Hologic Inc.) and ADP (PEA POD, COSMED) measurements were compared from 50 preterm infants (born <30 weeks of gestation). Measurements were performed at three time points: <40 weeks of corrected gestational age, term and 3 months corrected age (n=14, 21, and 20 respectively). The actual range of age at measurement was 32 weeks of gestation to 3.8 months corrected age. Infants were measured with DXA while wearing a disposable diaper, swaddled in a cotton blanket, and laying supine on the scanning bed. ADP measurements were performed with the infant nude, wearing only a wig cap. In addition, total mass measurements from DXA and ADP were compared against a third method, an electronic scale (Smart Scale® Model 65)

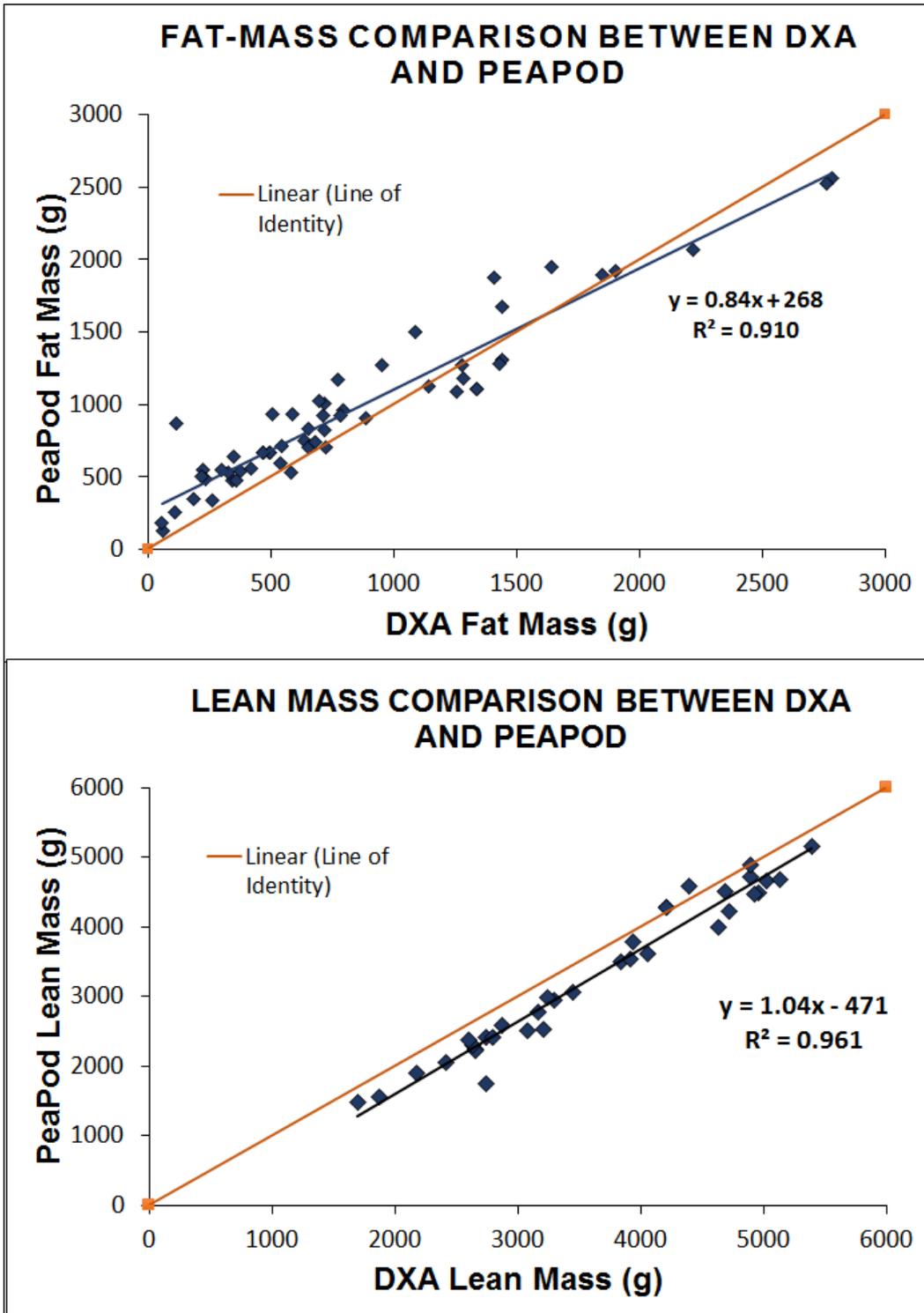
#### Results

DXA and ADP were significantly correlated for total body mass ( $R^2= 0.997$ ), absolute fat mass ( $R^2= 0.910$ ), absolute fat-free mass ( $R^2= 0.961$ ) and %fat mass ( $R^2= 0.713$ ). However, the Bland-Altman analysis revealed significant bias ( $p \leq 0.001$ ) in all of these estimates. Both the DXA and ADP total mass against the independent electronic scale showed a high correlation ( $R^2= 0.995$  and  $R^2= 0.998$  respectively). However, only the DXA total mass showed a significant bias from the electronic scale ( $p < 0.001$ ) in the Bland-Altman analysis. This bias was not found for ADP total mass ( $p=0.887$ )

#### Conclusions

Body composition estimates by DXA and ADP were highly correlated, but significantly biased. DXA mass deviates systematically from both the independent scale and the ADP scale, and %fat mass is underestimated compared to ADP. Literature suggests that this discrepancy is not attributable to the mass of the diaper or blanket. Further studies are needed to identify the basis of the large inter-method biases

Picture



RESUSCITATION WITH HYDROGEN GAS INHIBITS GENE EXPRESSION OF IL-18 IN PREFRONTAL CORTEX AFTER SEVERE HYPOXIA IN A MODEL OF NEWBORN PIGS (646)

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Introduction /Case Report

Birth asphyxia is a leading cause of neurodevelopmental sequelae in newborns infants. Hypoxia plays a crucial role in activating the cytokine pathway with over-expression in the brain. Resuscitation with room air is a well-studied delivery room management. It down-regulates the cascade of pro-inflammatory interleukins in comparison with 100% oxygen. Recently, hydrogen gas in an experimental rodent model was found to preserve brain tissue from post-hypoxic injury. We hypothesized that resuscitation with the mixture of room air and 2.0 % hydrogen gas will provide anti-inflammatory effect comparable with room air.

Patients and Methods

Thirty-five newborn pigs were included in the study. Animals were exposed to severe hypoxia until base excess was  $-20$  mmol/l or mean arterial blood pressure 20 mmHg. The pigs were randomized into 3 groups: resuscitation with room air (RA)(n=15) or mixture of room air and 2.0 % hydrogen (H2-RA)(n=16) or control group (n=4). Mean arterial blood pressure, ECG, and oxygen saturation were monitored. The observation period for groups was 9.5 hours after the end of hypoxia time point. Tissue samples from prefrontal cortex were snap frozen in liquid nitrogen and stored at  $-80^{\circ}\text{C}$  until analysis. Real time PCR was used to measure mRNA expression for interleukins  $1\beta$  and 18, tumor necrosis factor alpha (TNF $\alpha$ ), and brain-derived neurotrophic factor (BDNF). Statistical analysis was performed using SPSS.

Results

There was a down-regulation of cerebral gene expression\* for the pro-inflammatory cytokine IL-18 after resuscitation with the mixture of room air and 2.0 % hydrogen gas. H2-RA group versus RA group ( $0.69\pm 0.43$  vs.  $1.55\pm 0.75$ ,  $p < .01$ ) and H2-RA group versus control group ( $0.69\pm 0.43$  vs.  $1.16\pm 0.60$ ,  $p < .05$ ). BDNF mRNA was significantly over-expressed in RA and H2-RA groups versus control group ( $10.56\pm 8.29$  vs.  $1.1\pm 0.54$ ,  $p < .01$ ; and  $9.65\pm 12.61$  vs.  $1.1\pm 0.54$ ,  $p < .05$ ). Moreover, fold change for IL- $1\beta$  for both groups of hypoxia (RA and H2-RA) in comparison with the control group ( $4.42\pm 3.67$  vs.  $1.94\pm 2.24$ ,  $p < .05$ ; and  $4.02\pm 2.7$  vs.  $1.94\pm 2.24$ ,  $p < .05$ ). Gene expression of TNF $\alpha$  did not show significant differences between studied groups.

Conclusions

IL-18 mRNA was significantly down-regulated after resuscitation with room air supplemented with 2% hydrogen gas in a contrast to room air alone indicating an anti-inflammatory effect of hydrogen gas. BDNF and IL- $1\beta$  mRNA were significantly up-regulated in both groups exposed to hypoxia. Studies of histopathology and biomarkers are ongoing.

Other

## URINARY KIDNEY INJURY MOLECULE-1 REFLECTS THE SEVERITY OF CLINICAL CONDITIONS IN NEWBORN INFANTS TREATED IN NICU (603)

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### Introduction /Case Report

Kidney injury molecule-1 (KIM-1) is postulated new sensitive marker of acute kidney injury (AKI), especially proximal tubule injury. KIM-1 became recognized in pre-clinical studies, however its' clinical usefulness requires confirmation. Evaluation of a soluble form of KIM-1 in urine samples may reduce the necessity of blood testing for kidney injury monitoring in neonates at high risk for AKI. Some of the previously analyzed structural markers, including NGAL, are affected by inflammatory processes that limit its clinical application in septic patients. Searching for a marker less influenced by inflammation, we tested KIM-1 levels in urine of septic newborns with and without AKI.

### Patients and Methods

Fifty-six newborns admitted to Neonatal Intensive Care Unit (NICU), including 27 septic and 29 non-septic patients were enrolled. Urinary KIM-1 concentrations were assessed during the three subsequent days. In the control group 95% CI of the mean urinary KIM-1 was 0.04-2.02 ng/ml (reference range). AKI was diagnosed according to pRIFLE criteria, on the basis of serial measurements of serum creatinine and urinary output monitoring. Urinary KIM-1 concentrations were assessed by ELISA (BioAssay) in frozen samples. Severity of clinical conditions was evaluated on the basis of Neonatal Therapeutic Intervention Scoring System (NTISS). C-reactive protein (CRP) and procalcitonin (PCT) serum levels were used for the monitoring of inflammatory reaction.

### Results

Median values of KIM-1 were significantly greater in septic than non septic newborns [1.42 (0.48-2.12) vs 0.66 (0.22-1.34) ng/ml] on the first day, [0.98 (0.50-2.32) vs 0.42 (0.14-1.20) ng/ml] on the second day, and [0.80 (0.24-1.68) vs 0.80 (0.14-1.46) ng/ml] on the third day, however the differences were statistically significant only in the first assessment. KIM-1 levels were not related to birth weight, gestational age, 5' Apgar score, but were associated with NTISS value, serum CRP and PCT levels. Among septic newborns, there were 8 newborns who developed AKI (risk or injury). In this group of patients, KIM-1 values were slightly greater than in non-AKI patients: 1.02 (0.46-1.62) ng/ml on the first day, 1.24 (0.38-2.20) ng/ml on the second day, and 1.02 (0.42-1.48) ng/ml on the third day of observation. The difference between AKI and non-AKI was not statistically significant.

### Conclusions

1. Increased urinary KIM-1 concentration in septic newborns is affected by severity of clinical conditions and inflammation. 2. High variability of urinary KIM-1 levels diminishes its usefulness in the diagnosis of

mild and moderate acute kidney injury episodes in septic newborns. 3. Our preliminary findings preclude elimination of serial measurements of serum creatinine in the monitoring of newborns at high risk of AKI.

Other / Involvement of parents in care

## HEALTH PROFESSIONALS' VIEWS AND PRACTICES ON PARENT PARTICIPATION (523)

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### Introduction /Case Report

Objective: Determining views and practices of health professionals, who worked as nurse in paediatric clinic, on parent participation.

### Patients and Methods

Descriptive-correlational research was performed with 155 health professionals, working as nurse in paediatric clinics at four hospitals in Konya, 2014. Data were collected using "Information Form" and "Health Professionals' Views and Practices on Parent Participation Questionnaire" which was developed according to literature. Number, percentage, mean, standard deviation, chi square test were used.

### Results

They (87.1%) allowed parent participation; parents' gender and communication skills, child's disease and age were found effective. Parent participation were different invasive procedures (45.1%-67.2% expressed allowing family presence; except 82.6%-86.5% of them didn't allow life-threatening process), other applications (mostly participation with nurse) during diagnosis-treatment. Participation with nurse and allowing family presence were mentioned for medicine administration, using electronical devices and evaluation vital signs. Making by themselves, participation with nurse, allowing family presence were stated to child's needs-hygiene. Reducing child's fear, increasing child's coping, turning professional communication to social could be result of parent participation. Female, 19-32 year-old, baccalaureate degree health professionals allowed it (respectively  $p=0.001$ ;  $p=0.039$ ;  $p=0.045$ )

### Conclusions

Most of health professionals support parent participation in different way and levels. Allowing parent participation was affected by health professionals (gender, age, education level), child (age and disease) and parent (gender and communication ability).

Nutrition and gastroenterology / Nutrition of the Very Preterm

CALCIUM AND PHOSPHORUS ADMINISTRATION FOR INFANTS WITH A BIRTH WEIGHT LESS THAN 400 GRAMS (087)

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### Introduction /Case Report

The required calcium and phosphorus dose to prevent osteopenia of prematurity in extremely low birth weight infants is 150-200 mg/kg/day and 100-150 mg/kg/day, respectively. However, it is unknown whether these amounts are also sufficient for infants weighing less than 400 grams. The accumulation of calcium and phosphorus during pregnancy for SGA infants is less than AGA infants. Therefore, it follows that the required dose of calcium and phosphorus for such infants after birth would be higher than the recommended dosage. This study reports the amount of calcium and phosphorus administered in the course of osteopenia of prematurity in the cases of seven infants weighing less than 400 grams.

### Patients and Methods

All the infants received total parenteral nutrition (TPN). Enteral feeding was started at a dose of 0.5 ml every three or six hours when the condition of the infants was stabilized. Amount of enteral feeding was gradually increased and when the total amount of milk reached 120 ml/kg/day, fluid therapy was stopped and 200 IU of vitamin D was started. Human milk fortifier was also administered. Since all the infants had developed severe chronic lung disease, total water intake was also restricted by 140 ml/kg/day. All the infants received additional calcium and phosphorus supplements. Serum levels of calcium, phosphorus, creatinine and alkaline phosphatase were measured as required or every week and bone X-ray were taken every month. Data was collected through 120 days of age.

### Results

The birth weight of the infants ranged between 265 grams and 389 grams. One patient died at 11 months of age. Calcium administration was initiated from birth but phosphorus administration began from 2 to 4 days of age. During TPN, sodium phosphate buffer was used for 3 infants and potassium phosphate was used for 4 infants. The maximum amount of calcium and phosphorus during TPN was 48-91 mg/kg/day and 45-93 mg/kg/day, respectively. Full feeding was reached at 12 days to 36 days of age. After full feeding, the maximum amount of calcium and phosphorus was 140-235 mg/kg/day and 75-144 mg/kg/day, respectively. Serum levels of calcium and phosphorus fluctuated before 40 days of age. Serum alkaline phosphatase ranged between 1627 and 3845 IU/dl at most. Pathological fracture of the femur was observed in one infant weighing 265 grams. All the infants showed cupping and flaring by X-ray.

### Conclusions

The amount of calcium and phosphorus required for infants weighing less than 400 grams reached the recommended dosage after full feeding. However, all infants showed the findings of osteopenia of

prematurity by X-ray. Therefore, the recommended dosage of calcium and phosphorus might be insufficient for those infants and the stabilization of serum levels of calcium and phosphorus during this early period of infancy is possibly important.

## Other / Miscellanea

### SERUM LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR - TEMPORAL CHANGES IN RELATION TO RETINOPATHY OF PREMATURITY (235)

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## Introduction /Case Report

The role of vascular endothelial growth factor (VEGF) in the pathogenesis of retinopathy of prematurity (ROP) has been clearly established. However, despite that little is known about temporal changes of circulating VEGF levels in the preterm neonate, off-label treatment with anti-VEGF is becoming more commonplace.

The aim of this study was to investigate longitudinal serum levels of circulating VEGF in preterm infants in relation to ROP.

## Patients and Methods

The study was conducted as a prospective longitudinal cohort study between January 2005 and May 2007, and consisted of 52 infants born at <31 weeks gestational age (GA). All infants were screened for ROP according to a routine protocol. Thirty-three infants were classified as non-ROP, 10 as non-proliferative ROP (stages 1 and 2), and 9 as proliferative ROP (stage 3 and treated for ROP). Plasma samples were collected at birth. Then serum samples were collected at 3 days postnatal age, followed by weekly collection of samples until at least a postmenstrual age (PMA) of 35 weeks. Circulating levels of VEGF were analyzed by Luminex multiplex technology. All statistical analyses were performed by non-parametric tests.

## Results

VEGF levels did not differ in cord blood between infants with different degrees of ROP. In contrast, the longitudinal VEGF serum levels differed between groups, with significantly increased VEGF levels at first detection of ROP (34 – 36 weeks PMA) in infants with proliferative ROP as compared to infants without ROP; median (range) VEGF levels at PMA 34 weeks were 1768 (538; 6463) in infants with proliferative ROP vs 1076 (17; 3770) pg/ml in infants without ROP,  $p < 0.05$ . Corresponding levels at PMA 35 weeks were 2139 (1116; 7729) vs 1058 (1; 3767) pg/ml,  $p < 0.001$ , and at PMA 36 weeks 1835 (700; 3574) vs 817 (117; 2208) pg/ml,  $p < 0.05$ . After adjustment for GA at birth, differences remained significant at PMA 34 and 35 weeks. At the time for laser therapy (median (range) PMA 39 (34 – 40) weeks) VEGF levels did not significantly differ between ROP groups.

## Conclusions

The current findings, displaying elevated circulatory levels of VEGF at the time of ROP detection, but not at the time of ROP treatment support the need for studies highlighting the temporal pattern of VEGF in relation to ROP treatment.

Other / Quality improvement and Safety and Error Preventio

## SCREENING FOR QTc PROLONGATION IN NEONATES BY REAL-TIME BEDSIDE MONITORING (142)

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### Introduction /Case Report

Neonates admitted to the NICU undergo continuous cardiorespiratory monitoring with data that is displayed on the bedside monitor and often downloaded to the electronic medical record (EMR). We previously showed that neonatal QTc values as measured by bedside monitoring undergo developmental progression before reaching a stable baseline after 96 hours of life. Use of this bedside tool is a potential way to screen for QTc prolongation in hospitalized neonates. This pragmatic, retrospective study attempted to describe trends in bedside monitor QTc values compared to those measured from standard 12-lead ECGs temporally related in time.

### Patients and Methods

Twelve -lead ECGs obtained after 96 hours of life on infants admitted to our level II/III NICU from December 2012 – June 2014 were obtained for manual QTc interval measurement performed by a trained electrophysiologist (EP). This measurement as well as the value found on the 12-lead ECG image uploaded to the EMR was compared to the bedside monitor value that coincided temporally with 12-lead attainment. Based on data from our previous study a monitor QTc value of 475 ms was considered prolonged. Cutoffs of 440 ms and 475 ms were both used for 12-lead comparisons.

### Results

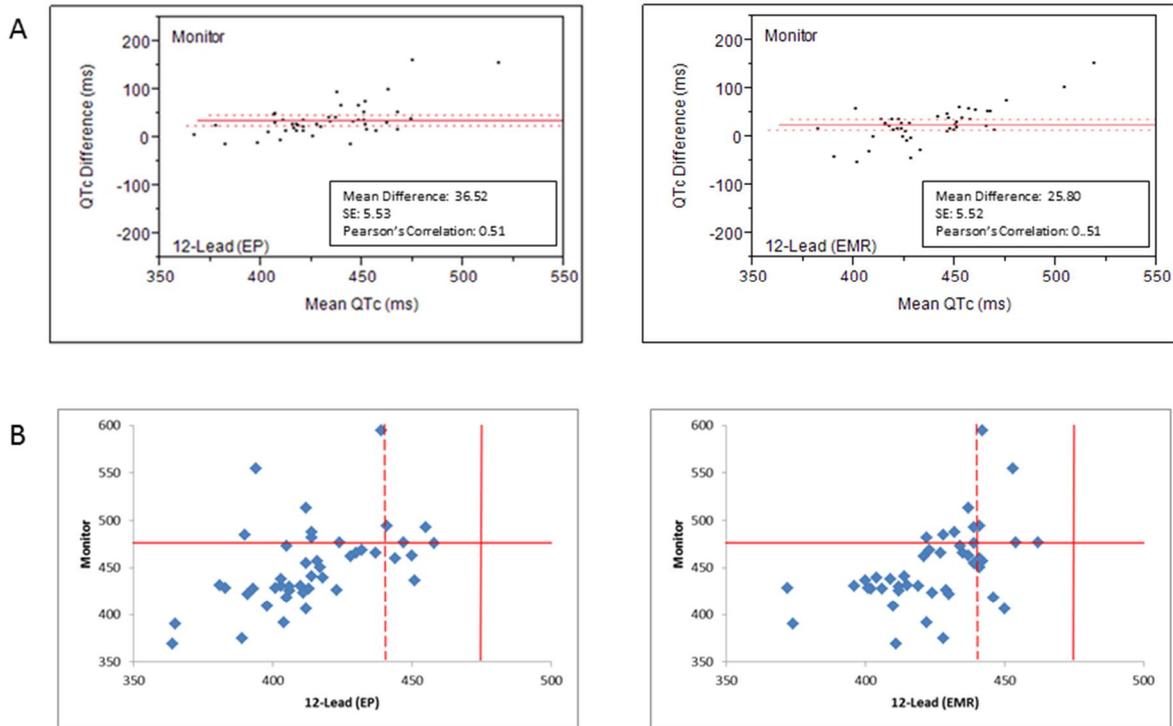
A total of 44 12-lead ECGs were performed on 38 (27 preterm) patients. Median age at the time of ECG was 12 days of life.

Bland-Altman modeling [Figure 1A] demonstrated poor agreement of bedside values compared with standard 12-lead ECG QTc measurements. Monitor measurements averaged ~25-35 ms longer than 12-lead ECG measurements. A scatter plot of dichotomous values [Figure 1B] shows poor-to-fair agreement (Kappa for all analyses <0.35) between monitor and 12-lead QTc measurements for categorizing patients as having QTc prolongation.

### Conclusions

Bedside monitor QTc values were consistently longer than those measured on 12-lead recordings. Categorization of QTc prolongation based on monitor readings did not agree with various 12-lead cutoffs. Prospective validation of real-time bedside QTc monitoring is needed to guide neonatal providers on how best to use this potentially useful tool.

Picture



**Figure 1:** [A] QTc measurement differences plotted vs mean QTc values. Mean (solid) and  $\pm 2$  standard deviations (dashed) of the difference are plotted as horizontal lines. [B] Dichotomous testing of QTc prolongation detection. A QTc value of 475 ms (solid) was considered prolonged for monitor values with 440 ms (dashed) and 475 (solid) being used as a cutoff for 12-lead values.

EMERGING REGULATORY COMPETENCIES IN PRETERM BABIES: IMPLICATIONS FOR EARLY PSYCHOLOGICAL INTERVENTION (517)

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Introduction /Case Report

Self-regulation is a key to competent functioning across the lifespan. At the same time, this is the very domain, where the development of preterm children can be compromised due to: specific biological risk factors and immaturity, the quality of early experience, and challenges to parent-child relationship. The aim of this study was to assess and compare emerging self-regulatory competencies (ESRC) in extremely preterm, very & moderately preterm, and full term babies aged 40-44 gestational weeks. The following dimensions of ESRC in early infancy were considered: autonomic regulation, motor regulation, organization & regulation of behavioral states, and regulation of attention/orienting.

Patients and Methods

The study was conducted as a part of a longitudinal project on the relational and biological predictors of self-regulation in preterm children. The subjects were 90 babies and their parents recruited from three hospitals in Warsaw, Poland. Three equal sized groups (3 x n=30) were enrolled: "extremely preterm" (p1), "very & moderately preterm" (p2), and "full term" (c). At the age of 40-44 weeks GA, infants were assessed with the Neonatal Behavioral Assessment scale (NBAS). The assessments took place at home and were supplemented with semi-structured interviews with both parents. NBAS raw scores were transformed using data reduction system (Lester et al., 1982). Child's developmental status, biological risk factors, socio-economic variables, and parental depression were controlled for.

Results

Mean results for each of the NBAS clusters in the three groups are presented in table 1. The effect of "GROUP" on dependent variables turned out to be significant ( $F(10, 162) = 5.065$ ;  $p < 0.001$ ; observed power: 0.999,  $\alpha = 0.05$ ; figure 1), yet in univariate ANOVA this was not confirmed in the case of RANGE of STATES. In the post hoc comparisons it was shown that: 1) babies from group p1 were significantly less competent in ORIENTATION than babies of either group p2 ( $p < 0.043$ ) or c ( $p < 0.045$ ), 2) full term babies were more competent in MOTOR REGULATION than preterm babies from group p1 ( $p < 0.001$ ) and p2 ( $p = 0.03$ ) (similar result was obtained for REGULATION of STATES). Significant differences were also found in ORIENTATION ( $p < 0.001$ ) and MOTOR REGULATION ( $p = 0.02$ ) in preemies of varying biological risk, to the disadvantage of babies with higher risk index.

Conclusions

These results point to interesting differences in early regulatory competencies of preterm versus full term babies. Specifically, preterm babies' lower results in ORIENTATION (an early measure of orienting/attention regulation) and REGULATION of STATES (a measure of regulation of arousal) may shed some light on the

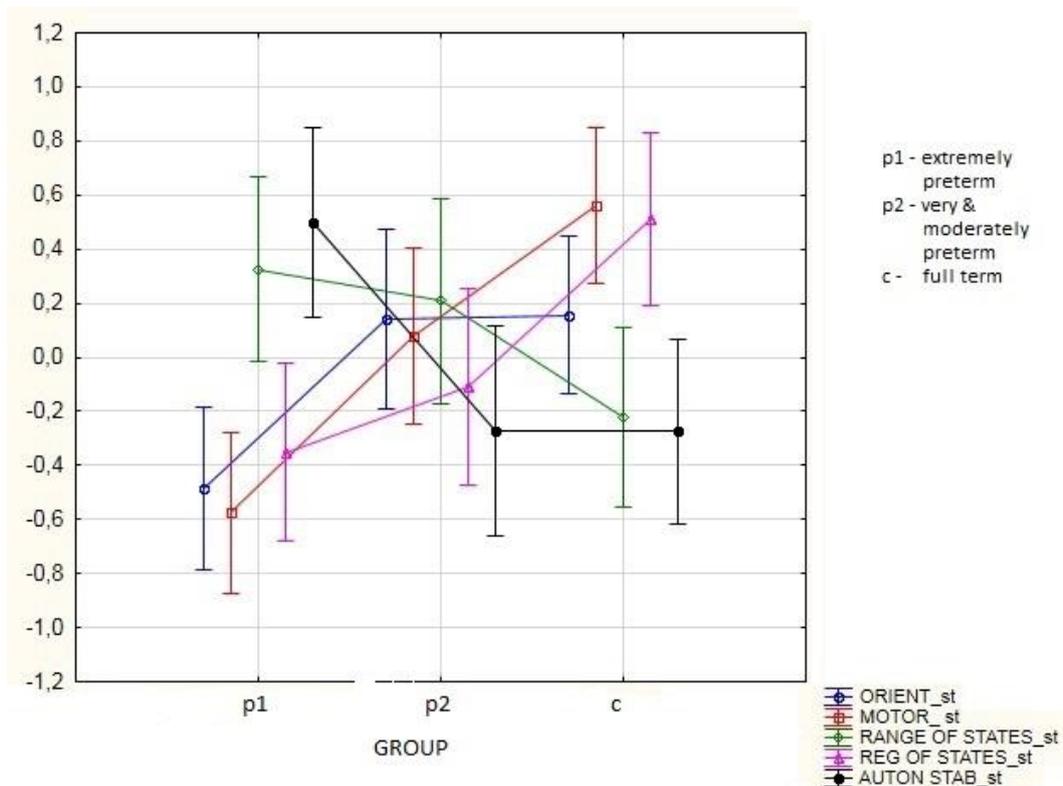
difficulties that might arise in parent-child interactions. Implications for early psychological intervention will be discussed.

Table

Table 1: NBAS clusters: mean results for the three analyzed groups.

NBAS Cluster	Group	n (valid)	Mean	Minimum	Maximum	Standard deviation
Orientation	p1	30	40.367	8.0	62.0	11.300
	p2	28	47.429	32.0	99.0	12.399
	c	30	47.133	28.0	58.0	8.415
Motor regulation	p1	30	24.667	13.0	35.0	6.200
	p2	29	26.621	10.0	36.0	5.931
	c	30	30.700	18.0	35.0	3.816
Range of states	p1	30	14.633	6.0	23.0	3.508
	p2	29	14.000	5.0	19.0	3.505
	c	30	12.633	6.0	19.0	4.123
State regulation	p1	30	15.467	4.0	30.0	5.631
	p2	29	16.069	5.0	32.0	6.204
	c	30	20.133	10.0	32.0	6.033
Autonomic stability	p1	30	16.333	7.0	24.0	4.342
	p2	29	14.379	10.0	22.0	2.691
	c	30	14.100	9.0	19.0	2.203

Picture



## Brain & Development / Neonatal Brain Injury and Neuroprotection

Elevated Granulocyte-macrophage colony stimulating factor is associated with low Apgar scores in Preterm infants (836)

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### Introduction /Case Report

Persistent inflammation and activation of innate immune cells has been associated with neonatal brain injury. Activated neutrophils and monocytes may be a target for treatment of inflammatory disease in preterm infants and cytokines may be biomarkers for neonatal outcomes.

### Patients and Methods

In a tertiary referral university neonatal intensive care unit, serial blood samples were analysed from preterm infants (<32 weeks gestation) on day 0, 1, 3 and 7 of life in this pilot study. Serum levels of Vascular Endothelial Growth Factor (VEGF), Granulocyte-Colony Stimulating Factor (G-CSF) and Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) were measured with Cord pH, Cord base excess, pH and Apgar score. Spearman's correlation was used to compare these parameters.

### Results

Preterm infants (n=51) enrolled had a gestation of 27.9+/-1.6 weeks and a birthweight of 1.1+/-0.3kg. Serum GM-CSF levels on day 1 statistically correlated with VEGF ( $p=0.001$ ) and negatively correlated with Apgar score at 5min ( $p=0.023$ ). There were no significant correlations across the remaining parameters measured.

### Conclusions

Elevated GM-CSF correlated with low Apgar scores at 5 minutes and may indicate a potent stimulation of innate immunity in preterm infants who require resuscitation.

Other / Quality improvement and Safety and Error Preventio

## MORTALITY AND MORBIDITY OF PREMATURE INFANTS: A QUALITY CONTROL STUDY IN A NICU (300)

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### Introduction /Case Report

Recent advances in perinatal care improved the survival rate of premature infants and substantially decreased the occurrence of disability. The goal of this study was to analyze mortality and morbidity rates in a cohort of premature infants admitted to a neonatal intensive care unit (NICU), in order to evaluate the quality of care and establish a plan to avoid preventable deaths.

### Patients and Methods

Descriptive study of all the newborns <32 weeks (W) admitted to a NICU, January 2008 -December 2014. Necrotizing enterocolitis (NEC) was diagnosed if one clinical finding (bilious gastric aspirate or emesis, abdominal distension or stool blood) and one radiographic finding (pneumatosis intestinalis, hepatobiliary gas or pneumoperitoneum) were identified. Bronchopulmonary dysplasia (BPD) was defined as oxygen requirement at 36W. Severe retinopathy of prematurity (ROP) was characterized as severely abnormal blood vessel growth or detached retina (stages≥III). Severe peri-intraventricular hemorrhage was considered for grade≥3, according to Volpe, or whenever periventricular hemorrhagic parenchymal infarction or post-hemorrhagic ventricular dilatation occurred. T-test was used for comparisons.

### Results

There were 624 newborns <32W admitted to our unit in the last 7 years. Among these, 218 were born <28W (35%), 238 were extremely low birth weight infants (ELBW) (38%) and 23 were transferred from another unit (4%). Major congenital malformations were identified in 49 (8%). Complete antenatal corticosteroids administration occurred in 73%. Severe ROP was diagnosed in 4%, NEC in 7%, severe PIVH in 9% and BPD in 21% of the infants. Seventy newborns had early-onset sepsis (11%). In 14% (10/70) the causative agent was identified. The overall mortality was 14%. The mortality of ELBW infants was 26%. The mortality of 24W infants was 48%. Mortality was higher in outborn infants (22%), in infants with major congenital malformations (24%) and in those without complete antenatal corticosteroids administration (18%). The mortality was associated with the SNAPPE-II score ( $p<0.001$ ).

### Conclusions

The mortality of the newborns <32W admitted to our unit was 14%, being higher in ELBW infants and in those with congenital malformations, transferred from another unit or without antenatal corticosteroids treatment. Our results were similar to the ones reported by other centers. Continuous quality control, as well as identification of preventable deaths, are important steps in order to improve outcomes in prematurity in each particular setting.

Table

SNAPPE-II Score	Mortality
0-9	2%
10-19	9%
20-29	7%
30-39	20%
40-49	23%
50-59	31%
60-69	42%
70-79	50%
>80	76%

## Nutrition and gastroenterology / Breast feeding

### ADMINISTRATION OF OROPHARYNGEAL COLOSTRUM IS SAFE IN PREMATURE INFANTS AND MAY PROMOTE EARLY BREAST MILK FEEDINGS (136)

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#### Introduction /Case Report

Recent evidence suggests that oropharyngeal colostrum (OC) may provide immunological benefits to premature infants, and be a complementary source of nutrition for infants not yet able to receive enteral feedings. The feasibility of oropharyngeal colostrum has been demonstrated in premature infants, however, the safety and efficacy of oropharyngeal colostrum has not been extensively studied in the very low birth weight (VLBW) and extremely low birth weight (ELBW) population. The objective of this study was to determine the safety of oropharyngeal colostrum by evaluating its impact on nutritional, growth, and clinical outcomes in VLBW premature infants

#### Patients and Methods

A retrospective cohort study was conducted on infants (< 1500 grams) admitted to the Morristown Medical Center, NJ,USA Neonatal ICU (NICU) in 2012 (n=89) and 2014 (n=92). In 2013 an OC protocol was adopted for infants not receiving enteral feeds, but whose mothers provided their own breast milk. Our protocol was stratified by birth weight, such that infants weighing < 1000 grams received 0.1 mL OC every 2 – 4 hours, and infants 1000 - 1500 grams received 0.2 mL OC every 2 – 4 hours, for the first 48 hours of age. Demographics, nutritional milestones, mortality and morbidity were assessed. Comparisons, adjusted for weight (< 1500 grams, < 1000 grams and < 750 grams), were made between infants who did and did not receive OC using student t-test and Mann Whitney U test, where appropriate.

#### Results

There were 197 infants included in this study, of which 75 (42%) received OC and 102 (58%) did not receive OC. Nutritional outcome measures, including the day of life (DOL) feeding began, the DOL infants regained birth weight, and the DOL infants reached 120 ml/kg/day of feeds, were similar between OC and non-OC groups, irrespective of weight. (Tables 1-3) The odds of VLBW infants receiving breast milk as their first feed is 1.96 times higher after administration of OC compared to no administration of OC (OR: 1.96, 95% CI 1.06 to 3.62,  $p < 0.03$ ). Mortality and morbidity rates, including necrotizing enterocolitis (medical and surgical), spontaneous perforations, sepsis, and ventilatory associated pneumonia, were also statistically similar between OC and non-OC groups.

#### Conclusions

This study demonstrates that administration of oropharyngeal colostrum in infants < 1500 grams is feasible and safe within the first 48 hours of life. Moreover, we demonstrate that OC for infants < 1000 grams and < 750 grams is also equally as feasible and safe, and can be implemented in a community hospital NICU

setting. Most importantly, this study suggests that infants who receive oropharyngeal colostrum care may be more likely to receive breast milk as their first enteral feed.

Table

<b>Table 1: Outcomes in Infants <math>\leq</math> 1500 grams</b>			
	No Colostrum	Oral Colostrum	P - value
	(n = 102)	(n = 75)	
<b><i>Demographic</i></b>			
Gestational age (weeks)	29 (26, 31)	28 (26, 29)	0,18
Birth weight (grams)	1100 (820, 1371)	1010 (780, 1240)	0,15
<b>Gender</b>			
(Male/Female)	45/57	41/34	0,17
<b>Race</b>			
White	68 (67%)	53 (71%)	0,08
Non-white	34 (33%)	22 (29%)	
<b><i>Nutritional</i></b>			
Day feedings began	2 (1, 3)	2 (1, 3)	0,43
Day regained birth weight	11 (8, 13)	9 (7, 12)	0,42
Day reach 120 ml/kg/day	12 (9, 17)	16 (12, 23)	0,26
<b>1st feeding</b>			
EBM	50	49	0,07
Formula	52	26	
<b><i>Morbidity and Mortality</i></b>			
Medical NEC	4	4	0,66
<b>Surgical Abdominal</b>			
SIP	2	4	0,44
Surgical NEC	2	0	0,15
Sepsis	5	5	0,62
VAP	1	3	0,23
Death	6	4	0,27

Data are presented as, median (Intraquartile ranges)

Non-white (African American/Hispanic/Asian/Other)

EBM, expressed breast milk;

NEC, necrotizing enterocolitis; SIP, spontaneous bowel perforation

VAP, ventilator associated pneumonia

**Table 2: Outcomes in Infants  $\leq$  1000 grams**

	No Colostrum (n = 43)	Oral Colostrum (n = 37)	P - value
<b>Demographic</b>			
Gestational age (weeks)	25 (26, 27)	26 (25, 28)	0,83
Birth weight (grams)	790 (675, 910)	697 (780, 885)	0,73
Gender (Male/Female)	38/25	18/19	0,15
Race			
White	23 (53%)	25 (68%)	0,83
Non-white	20 (47%)	12 (32%)	
<b>Nutritional</b>			
Day feedings began	2 (1, 4)	2 (2, 3)	0,42
Day regained birth weight	11 (8, 12)	9 (7, 11)	0,31
Day reach 120 ml/kg/day	17 (13, 27)	22 (18, 26)	0,87
1st feeding			
EBM	25	30	0,03
Formula	18	7	
<b>Morbidity and Mortality</b>			
Medical NEC	4	2	0,51
Surgical Abdominal			0,14
SIP	1	4	0,14
Surgical NEC	1	0	0,32
Sepsis	5	5	0,81
VAP	1	3	0,26
Death	4	5	0,56

Data are presented as, median (Intraquartile ranges)

Non-white (African American/Hispanic/Asian/Other)

EBM, expressed breast milk;

NEC, necrotizing enterocolitis; SIP, spontaneous bowel perforation

VAP, ventilator associated pneumonia

**Table 3: Outcomes in Infants  $\leq$  750 grams**

	No Colostrum (n = 20)	Oral Colostrum (n = 15)	P - value
<b>Demographic</b>			
Gestational age (weeks)	24 (25, 26)	24 (25, 26)	0,17
Birth weight (grams)	670 (536, 750)	680 (620, 710)	0,58
Gender (Male/Female)	13/7	8/7	0,31
Race			
White	10 (50%)	12 (80%)	0,81
Non-white	10 (50%)	3 (20%)	
<b>Nutritional</b>			
Day feedings began	3 (2, 5)	3 (2, 3)	0,23
Day regained birth weight	11 (7, 13)	8 (7, 12)	0,82
Day reach 120 ml/kg/day	25 (18, 34)	25 (18, 25)	0,58
1st feeding			
EBM	14	14	0,07
Formula	6	1	
<b>Morbidity and Mortality</b>			
Medical NEC	3	1	0,43
Surgical Abdominal			0,22
SIP	1	3	0,22
Surgical NEC	1	0	0,33
Sepsis	4	3	0,91
VAP	0	2	0,16
Death	3	3	0,71

Data are presented as, median (Intraquartile ranges)

Non-white (African American/Hispanic/Asian/Other)

EBM, expressed breast milk;

NEC, necrotizing enterocolitis; SIP, spontaneous bowel perforation

VAP, ventilator associated pneumonia

Other / Involvement of parents in care

THE PEDIATRIC PRENATAL VISIT: WELCOME TO THE NEONATAL UNIT (725)

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Introduction /Case Report

As a result of the close collaboration between all perinatal assistencial teams and in order to provide the best quality of care to pregnant women whose sons is expected needed hospitalary income at the Neonatal Unit, Obstetrician and Neonatal Services started up a new Pediatric Prenatal Care (PPC) on October 2013.

Objectives:

- 1.- Focusing the fetus as a patient.
- 2.- Share decision making.
- 3.- Give information about prognosis, follow-up and quality of life
- 4.- Promoting breastfeeding
- 5.- Showing postnatal environment
- 6.- Taking care of the psicological needs

Patients and Methods

All women with high risk pregnancies (congenital defects, preterm delivery risk, multiple gestation, intrauterine growth retardation, fetal therapy, preeclampsia, cancer,...) are sent to the PPC.

Professional attendance is given at the PPC external consultation as an outpatient, at the room where patient is admitted or, exceptionally at the delivery room,

A visit to the Neonatology Unit is offered to the parents and close family, showing the different areas where the newborn will remain. Knowing the postnatal environment decreases parental and familiar anxiety and improves the comunication between professionals and parents.

Two guides, edited by our Neonatal Unit: The "Parental Guide" and "How to breastfeed my prematur newborn" are also given to the parents.

Results

158 gestants ( and their familiars) have been included in the PPC program from october 2013 to december 2014.

The interview lasts usually one hour and, more than one meeting was needed if fetal or maternal relevant changes ocured. The interview format is adapted to each particular gestational circumstances with special emphasis on achieving the best communication and empathy,been open minded to hear and solve doubts and questions.

Periodic and regular contact is established in order to include emotional conditions and to increase interdisciplinary coordination.

Pregnant women expressed their personal gratitude for the received care and the usefulness of the PPC program

#### Conclusions

PPC program is an healthcare that has allowed a quality care increasing.

The impact on the pregnant women and their close family is excellent

Increases the relationship and confidence between parents and professionals

raises the breastfeeding rate.

## Other / Quality improvement and Safety and Error Preventio

The impact of staffing and intensity levels on medication errors in a Neonatal Intensive Care Units (597)

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### Introduction /Case Report

Patient safety incident reports are on the increase. The number of incidents reported to the National Patient safety agency, England rose by 2.3% in 2012 compared to the preceding year. Neonatal Intensive care units (NICU) are high risk environments with increased risk of errors. The reported incidence of such adverse events varies between 0.97 per 1000 NICU patient days to 14.7 per 1000 NICU patient days. Medication errors are one of the commonest adverse incidents in NICU and are multi-factorial in causation. In our study, we have evaluated the relationship between staffing and activity levels on medication errors as there is currently no study demonstrating this relationship.

### Patients and Methods

This study was conducted in a regional (tertiary) NICU in England. Adverse clinical incidents are reported using a non-punitive, voluntary, reporting system (Datix) which has been in place since 2002. The staffing and activity levels were benchmarked with the British Association of Perinatal Medicine (BAPM) recommendations. All the medication errors reported on Datix over a two year period (2010 & 2011) were analysed. The staffing and activity levels for the months with the highest and lowest in 2011 were further explored for any relationships and associations.

### Results

There was more than two fold increase in medication errors reported in 2011; 140 compared to 65 in 2010 (Table 1). This was despite no change in clinical practice during both years. In 2011, the month of July had the highest reported errors (24 errors in 12 of the 31 days) while November had the lowest reported errors (4 errors in 3 of the 30 days).

The average bed occupancy for July 2011 was 107% (range: 83% - 117%) which was similar to November 2011 average of 104% (range: 83% - 117%). Both months also had equal number of days (14) when occupancy levels were 100% or greater. However, July 2011 had fewer days when actual nurse staffing levels fell below recommended numbers compared to November 2011 (21days versus 25days). Likewise, deficient staffing levels occurred in more of the error days in November 2011 than in July 2011 (figure 1).

### Conclusions

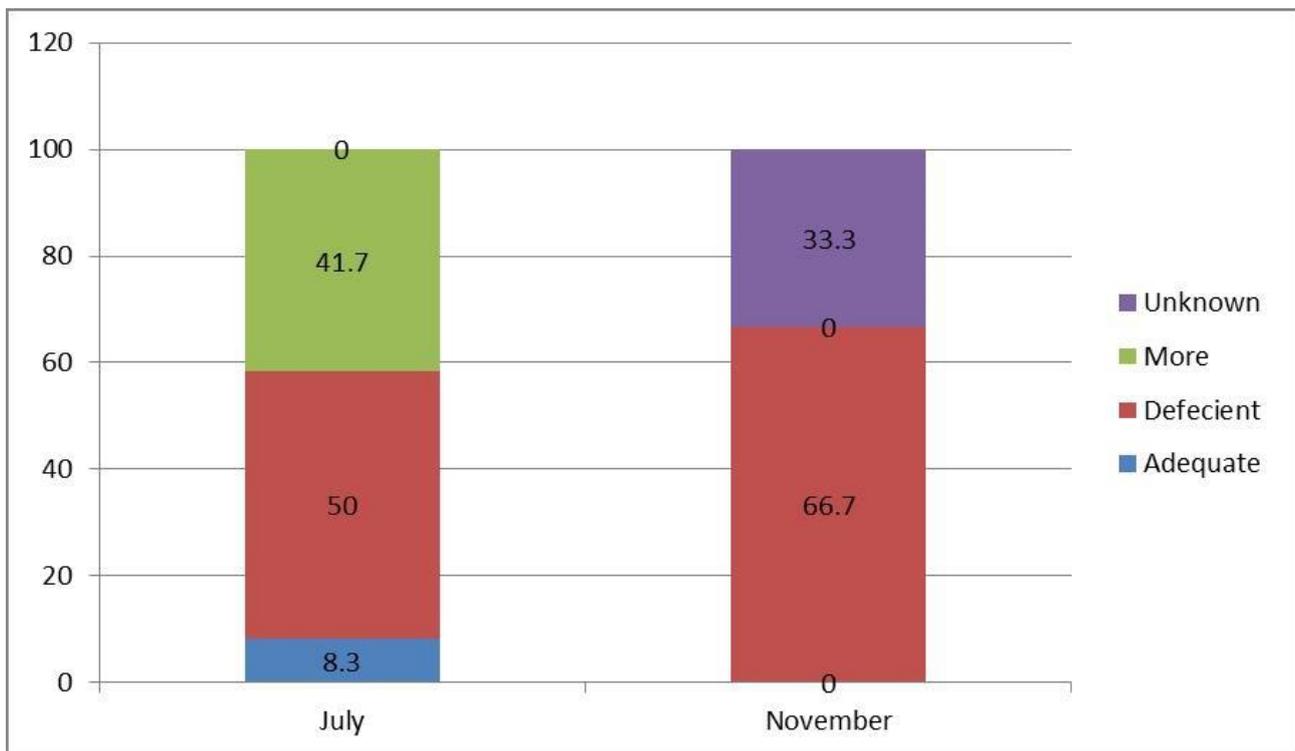
Our study findings show that there is increasing medication errors reported in NICU and occupancy levels are consistently higher than BAPM recommendation of 70%. There was no direct correlation between deficient nursing staff and bed occupancy levels with medication errors. These findings challenge conventional beliefs. Medication errors are most likely multifactorial which warrants further evaluation in a larger study to aid understanding.

Table

**Table 1: Medication incidents by month compared over the 2 years of the study**

	2010	2011
January	7	5
February	2	23
March	3	8
April	6	18
May	8	11
June	8	10
July	10	24
August	6	11
September	1	10
October	5	10
November	4	4
December	5	5
<b>Total</b>	<b>65</b>	<b>140</b>

Picture



PERCEPTION OF TASTE IN NEWBORN INFANTS, CORTICAL ACTIVATION AND COMFORT BEHAVIOUR (738)

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Introduction /Case Report

Human foetuses react to different tastes of the amniotic fluid and early breast-feeding can change future taste preferences. Preterm born infants are most often fed by naso-gastric tubes (NG) and will not always receive any maternal taste stimuli. They are also often exposed to glucose and other nosocomial tastes. We aimed to measure cortical activation in cortical gustatory areas to breast milk, glucose and water and to evaluate comfort behaviour.

Patients and Methods

We used a multichannel NIRS device to record bilaterally cortical activation in the gustatory cortex (GC) and primary somatosensory (S1), during 30s (10s baseline, 10s presentation, 10s post-stimuli). We also video recorded the infant's behaviour and two nurses performed behavioural scoring using a new comfort score ranging 0-2 in 4 10s periods. Zero points: no reaction, 1: lip movement with closed lips, relaxed forehead, 2: lips open, tongue to the palate, relaxed forehead. Gustatory stimuli were presented in controlled conditions (silent room, active sleep, randomized order) using a NG put 1 cm behind the lips. Twenty-nine infants were included (16 preterm and 13 full term). After systematic artefact removal HbO<sub>2</sub> changes from baseline were compared using ANOVA and post-hoc analysis.

Results

Both breast milk and water elicited haemodynamic changes (increase in HbO<sub>2</sub>) in S1 bilaterally and in GC bilaterally for breast milk and on the right side for water. Glucose gave a late decrease in HbO<sub>2</sub> in S1 and left GC (table 1). All tastes induced a significant increase in the comfort scale as compared to baseline. Glucose gave a significantly higher total comfort score than all the other taste stimuli (2.8 glucose, 2.0 water, 1.3 breast milk) (fig 1).

Conclusions

Gustatory stimulation with breast milk and water elicit cortical activation in newborn infants. Glucose triggers strong comfort behaviour and a decreased HbO<sub>2</sub> in gustatory and somatosensory areas. Breast milk and water can also trigger comforting behaviour.

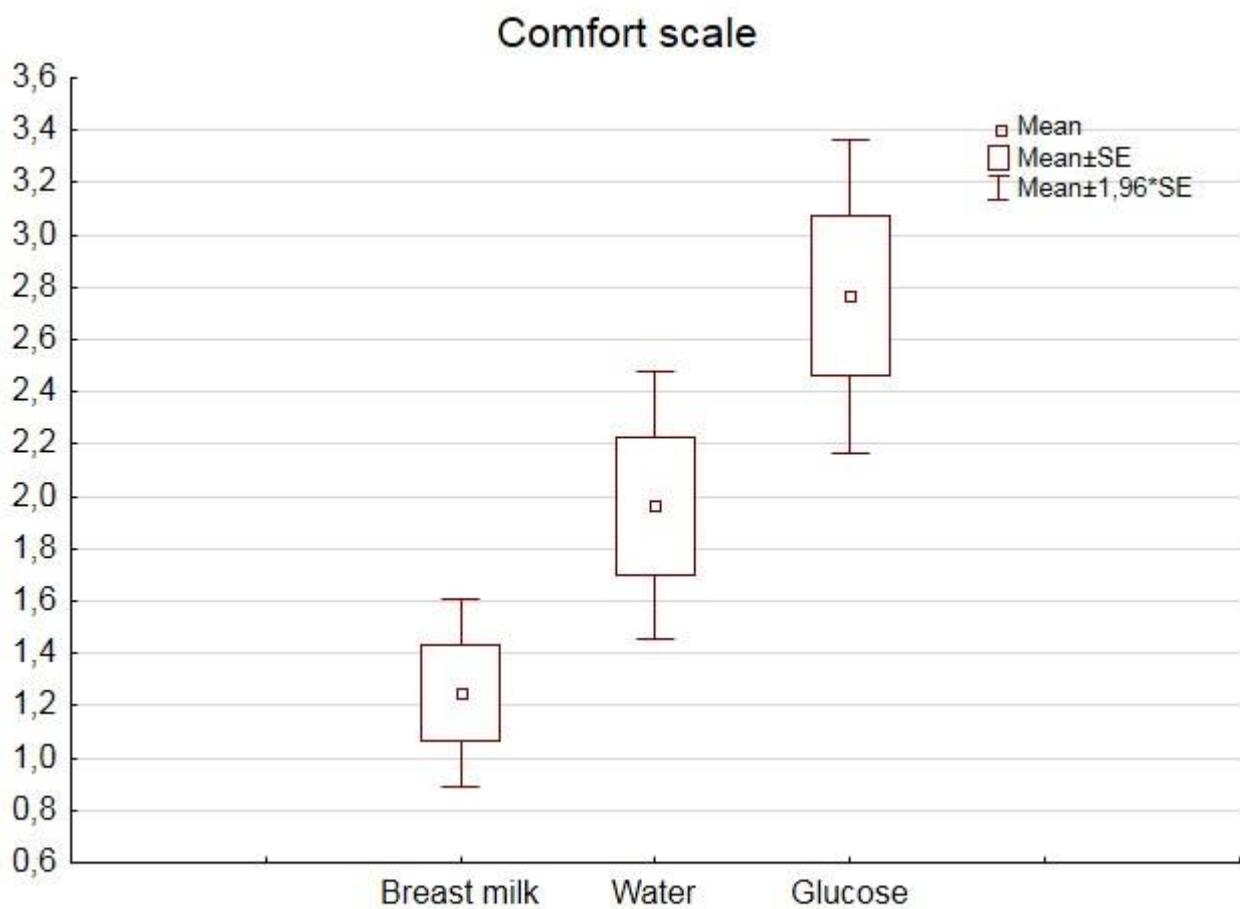
Table

**Table 1: Hemodynamic changes in gustatory and somatosensory areas**

location	Breast milk	Water	Glucose
<b>S1 Left</b>	↑ <0,001	↑ <0,001	↓ <0,001
<b>S1 Right</b>	↑ <0,001	↑ <0,001	↓ <0,001
<b>GC Left</b>	↑ <0,001	-	↓ <0,001
<b>GC Right</b>	↑ <0,001	↑ 0,001	-

Arrows indicate significant change in HbO<sub>2</sub> using ANOVA

Picture



THERAPEUTIC HYPOTHERMIA FOR HYPOXIC ISCHEMIC ENCEPHALOPATHY: ASSOCIATION BETWEEN DISTURBED COAGULATION AND THE RISK OF CLINICALLY SIGNIFICANT BLEEDING (807)

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Introduction /Case Report

Laboratory evidence of disturbed coagulation is a common finding in infants with hypoxic ischemic encephalopathy (HIE). Additionally, coagulopathy is also a potential side-effect of therapeutic hypothermia (TH). However, a recent meta analysis did not demonstrate increased incidence of clinically significant bleeding in cooled versus non-cooled infants. We aim to identify clinical and laboratory findings associated with a higher risk of bleeding in a group of infants with HIE undergoing TH.

Patients and Methods

Infants with HIE treated with TH between 2009-2014 were included in this retrospective study. We excluded four patients who died during treatment (all deaths unrelated to coagulopathy). Laboratory tests were performed according to the unit's protocol (at 12, 24, 48, 72 and 96h). Laboratory evidence of disturbed coagulation was defined as platelet (PLT) count  $<150 \times 10^9/L$ , fibrinogen (Fib)  $<150 \text{mg/dL}$ , activated partial thromboplastin time (aPTT) or prothrombin time (PT) twice the normal value. Bleeding was defined as clinically significant if fatal, associated with a drop in haemoglobin of 2 g/dL in 24 hours, involving a critical organ system or requiring surgery. Bleeding group (BG) and non-bleeding group (NBG) were compared concerning demographical, clinical and laboratory data.

Results

64 infants were included with a mean ( $\pm$ SD) birthweight of  $3.12 \pm 0.60$  kg and gestational age of  $39.1 \pm 1.6$  wks. BG included 16 infants (25%), who presented intracranial (13), gastrointestinal (7) and pulmonary (4) bleeding. There were no statistically significant differences between BG and NBG regarding baseline characteristics. At least one altered value for PLT, Fib, aPTT or TP was detected in 75% of BG and 77.1% of NBG. Mean laboratory values (initial PLT, Fib, aPTT and TP; minimum PLT and Fib; maximum aPTT and TP) and frequency of infants presenting laboratory changes were not significantly different between both groups.

Conclusions

The incidence of significant bleeding in our sample was lower than described in similar studies. Laboratorial evidence of disturbed coagulation was not statistically associated with clinical bleeding and was commonly observed in both BG and NBG, as verified in recent meta analysis. Further studies are needed to clarify clinical and laboratory findings associated with a higher risk of bleeding and to guide the use of blood products in infants with HIE undergoing TH.

## Brain & Development / Neurodevelopmental Outcome

### THE AGES AND STAGES QUESTIONNAIRE AND NEURODEVELOPMENTAL IMPAIRMENT IN TWO-YEAR OLD PRETERM-BORN CHILDREN (274)

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#### Introduction /Case Report

Examining large groups of children with the Bayley Scales of Infant and Toddler Development (BSID) is money and time consuming. Therefore alternative methods to detect severe neurodevelopmental impairment (NDI) are being investigated, including the use of the Ages and Stages Questionnaire third edition, (ASQ) as first step to determine which children should go on to formal neurodevelopmental testing. Our objective was to analyze the usefulness of the ASQ using the original ASQ domain score and a combined "ASQ total score" to predict severe NDI.

#### Patients and Methods

We included 224 children at 22-26 months' corrected age, born <32 weeks gestation' in 2007-2008 who had concurrent results on ASQ and BSIDIII. Severe NDI was defined as a score <70 on the Cognitive - or Motor Score of the BSIDIII, or severe impairment on neurological examination or audiovisual screening. Severe NDI was compared with abnormal ASQ scores (< -2SD on any domain) and the combined "ASQ total score". To compensate for possible overestimation of the BSIDIII, adjusted BSIDIII thresholds <80 and < 85 were also analyzed. Youden's index was used to identify a cut-off score for the "ASQ total score" predicting severe NDI which maximized sensitivity and specificity where sensitivity exceeded 80%.

#### Results

61 children (27%) had abnormal ASQ scores, ten (4.5%) children had severe NDI with original BSIDIII thresholds (<70), twelve children had NDI with BSID thresholds < 80 and fifteen with thresholds < 85. ASQ had excellent sensitivity (100%) with acceptable specificity (76%) to detect severe NDI; negative predictive value (NPV) was 100%. When using the ASQ as first-step, a formal neuropsychological assessment could have been omitted in 163 (73%) of the children without missing any case of severe NDI. Sensitivity and NPV remained high with adjusted BSID thresholds. Optimum ASQ total-score cut-off was 188, resulting in a sensitivity of 96% and specificity of 90% with an area under the ROC curve (AUC) of 96%,  $P < 0.0001$  to detect severe NDI with BSIDIII threshold < 70.

#### Conclusions

The Ages and Stages Questionnaire is a reliable and useful first step in a two-step neurodevelopmental assessment method to predict severe NDI in preterm-born children at age two. Both the original scoring method and the "ASQ total score" yield excellent results. The optimum cut-off for the "ASQ total score" to predict severe NDI in preterm infants < 32 weeks is 188. None declared

## Brain & Development / Neurodevelopmental Outcome

ARE THERE ANY SIGNIFICANT DIFFERENCES IN THE QUALITY OF LIFE AMONG CHILDREN WITH EPILEPSY, CEREBRAL PALSY, MENINGOMYELOCELE AND CONTROL IN HUNGARY FROM THE POINT OF VIEW OF NUTRITIONAL ASPECT? (822)

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### Introduction /Case Report

To study the Quality of Life of children and adolescents with chronic neurological diseases is important part of their treatment. KidScreen-52 test is valued for measuring HrQoL of different groups of healthy and ill children and their parents. The aim of this study was to investigate quality of life (QoL) and nutritional aspects among children with neurological diseases (epilepsy (E), meningomyelocele (MMC), cerebral palsy (CP)) and controls.

### Patients and Methods

KidScreen-52 children-adolescents and parental version questionnaires were used.

The examined ten dimensions were: physical well-being, psychological well-being, moods and emotions, relation and home life, autonomy, parents, financial resources, social support and peers, school environment and social acceptance - bullying.

The parental questionnaire contained physical parameters, as weights and lengths. Body mass index (BMI) was calculated based on these parameters. Five BMI categories were used: underweight severe, underweight mild, normal, overweight, obesity.

584 family were enrolled - 255 control, 99 CP, 86 MMC and 144 epilepsy families. Age limits were between 7-19 years.

Statistical analysis was performed by SPSS-19 statistical software and KidScreen SPSS – syntax.

### Results

All patients and their parents thought that they had lowest QoL than controls. The control, E,MMC groups had similar BMI characteristics, but CP group was underweight at a level of  $p: 0,003$ . There were QoL differences neither between nutritional groups of control and diseases nor between different types of diseases. Physical well-being had lower scores in each disabled group. But the “Could you run well?” question was low rated in children with obesity.

The children’s groups of severe underweight and obesity scored the lowest in the category of segregate feelings of Moods and Emotions.

The outlook played the main role among obese children ( $p: 0,005$ ). Developing friendships were harder in all the adipose groups.

Level of social acceptance was lower in all groups of diseases ( $p \leq 0.05$ ), but severe bullying was in the groups of obesity.

## Conclusions

Our study is that it is based on the opinion of the children, so we were able to compare the opinions not only of the age-matched healthy and disabled girls and boys, but of the younger and older (adolescent) populations, as well.

Obesity has been disadvantageous in the view of normal population and diseases. It has influence on physical, psychical, emotional, social acceptance and friendly relations.

## Brain & Development / Neurodevelopmental Outcome

### DIFFERENT RISK FACTORS FOR SEVERE RETINOPATHY OF PREMATURE IN PRETERM INFANTS LESS THAN 28 WEEKS GESTATION COMPARED TO THOSE OF 28 TO 32 WEEKS OF GESTATION (553)

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#### Introduction /Case Report

Retinopathy of prematurity (ROP), described previously as entirely attributed to high levels of oxygen exposure is recognizing, in fact, many other risk factors the most important ones being extreme prematurity and retinal immaturity.

Aim: The authors aimed to identify the incidence and risk factors for severe ROP (needing laser therapy) in preterm infants <28 weeks gestational age compared to those born at 28-32 weeks of gestation.

#### Patients and Methods

Material and methods: The prospective study was developed over a 2 years period (01.01.2010 - 31.12.2011) and as based on the information collected in the National Registry for Respiratory Distress Syndrome by 4 regional neonatal centers. All preterm infants  $\leq$  32 weeks gestational age were included and data analysis was performed using IBM SPSS Statistics 19 (for a statistical significant  $p < 0.05$ , 95% CI).

#### Results

The study comprised 83 preterm infants with GA < 28 weeks and 538 infants with GA 28-32 weeks. Severe ROP was found with an incidence of 14.45% at  $\leq$  28 weeks and of 2.23% between 28-32 weeks. Perinatal data analysis revealed that in preterm infants  $\leq$  28 weeks GA only prolonged mechanical ventilation (MV) and PDA (OR 7.16[CI 0.88-58.59]) were correlated with severe ROP ( $p < 0.5$ ). Instead, in preterm infants with GA between 28-32 weeks, severe ROP was associated with significantly ( $p < 0.05$ ) lower BW, GA, oxygen saturation during resuscitation, prolonged oxygen therapy, and significantly associated ( $p < 0.05$ ) with birth outside the regional center (OR 4.06[CI 1.28-12.84]), chorioamnionitis (OR 9.41[CI 2.35-37.72]), need for MV (OR 4.01[CI 1.27-12.68]), chronic lung disease (OR 4.54[CI 1.18-17.49]), neonatal sepsis (OR 4.04[CI 1.25-13.05]), and maternal fetal infections (OR 4.98[CI 1.29-19.27]).

#### Conclusions

The incidence of severe ROP in the study groups was similar with data in the literature. In less mature infants it seems that immaturity by itself represents the most important risk factor for ROP, prolonged MV and PDA being the only risk factors identified in this study. In more mature preterm infants the identified risk factors are suggesting an increased risk for those with lower GA and BW, more complicated perinatal course, mainly by conditions involving different inflammatory pathways.

Other / Miscellanea

## HYPERTENSIVE DISORDERS OF PREGNANCY ERASE GENDER DIFFERENCES IN CORD BLOOD TESTOSTERONE IN PRETERM INFANTS (726)

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### Introduction /Case Report

The primary aim was to study gender differences in estradiol and testosterone at birth.

The secondary aim was to study if gender differences in sex hormone levels at birth account for the differences seen in IGF-I levels, and to study if children born after hypertensive disorder of pregnancy (HDP) have altered estradiol and testosterone levels.

### Patients and Methods

177 singletons (73 girls, 104 boys) born after 32-37 weeks of gestation were studied. 34 of these children (16 girls, 18 boys) were born after HDP. The levels of estradiol, testosterone and IGF-I were analysed in umbilical cord vein sera.

### Results

In infants born after healthy pregnancies, boys had similar levels of estradiol (16702 vs. 13917 pmol/L) but higher levels of testosterone (4.0 vs. 3.1 nmol/L) than girls. After HDP the gender difference in testosterone was erased. Testosterone correlated to gestational age in both girls ( $r=0.35$ ,  $p=0.003$ ) and boys ( $r=0.47$ ,  $p=0.000$ ). Only in boys did testosterone correlate to birth weight, birth length, and head circumference. There was also a strong correlation between testosterone and estradiol in both boys ( $r=0.35$ ,  $p=0.000$ ) and girls ( $r=0.58$ ,  $p=0.000$ ). Estradiol correlated to birth weight in boys only ( $r=0.26$ ,  $p=0.008$ ).

### Conclusions

Testosterone correlated to gestational age and in boys also to size at birth, and might be an important anabolic hormone during pregnancy. Hypertensive disorders of pregnancy seem to erase the gender difference in testosterone in umbilical cord sera.

## Other / Miscellanea

Influence of neonatal respiratory system immaturity on incidence of retinopathy of prematurity (864)

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## Introduction /Case Report

Retinopathy of prematurity (ROP) is a disease related to abnormal vascularization of immature retina in preterm neonates. Although this disease was known for many years, risk factors of ROP are still being investigated. Aim of the study was to analyze risk factors of severe ROP effecting from immaturity of respiratory system in neonates with birth weight  $\leq 1500$ g.

## Patients and Methods

A retrospective analysis of medical records of 337 patients of the Department of Neonatology Medical University of Gdansk, Poland was performed. These were preterm neonates with birth weight  $\leq 1500$ g. The analyzed risk factors were effecting from immaturity of respiratory system: incidence of respiratory distress syndrome, need for mechanical or non-invasive ventilation, oxygen therapy, treatment with surfactant or caffeine citrate. Children were divided into two groups: group of neonates with diagnosis of severe ROP (ROP  $\geq$  stage 3 and/or plus disease) and group of the remaining neonates (without ROP and with mild ROP).

## Results

In neonates with severe ROP respiratory distress syndrome was observed with increased incidence (80% vs 56%). Those children required longer mechanical ventilation, CPAP ventilation, oxygen therapy and higher concentrations of oxygen. Mechanical ventilation longer than 2 weeks was more frequently performed in group of neonates with severe ROP. Oxygen therapy was used with the same frequency in both groups, but it was longer and with higher oxygen concentration in the group of severe ROP. Oxygen concentration  $\geq 50\%$  was used in 52% of all analyzed neonates – 88% of children with severe ROP and 45% of remaining neonates. Surfactant (49% vs 20%) and caffeine citrate (84% vs 70%) were more frequently used in group of children with severe ROP.

## Conclusions

Risk factors effecting from immaturity of respiratory system were observed with higher incidence in the group of neonates with severe ROP. Longer ventilation, oxygen therapy and higher concentration of oxygen were connected with severe ROP. Surfactant and caffeine citrate therapy were also used more frequently in group of neonates with severe ROP.

## Brain & Development / Structural and Functional Brain Imaging

### CORRELATION BETWEEN BRAIN ULTRASOUND AND MRI AND SHORT-TERM DEVELOPMENT (INFANTS 23-27 GW): A PROSPECTIVE COHORT STUDY (150)

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#### Introduction /Case Report

Extremely premature preterms (<28 GW) are at risk of abnormal development. Neuroimaging, primarily using cranial ultrasound (CUS) is routinely recommended, whereas a brain MRI performed at term seems to have better predictive value for the development

of these infants. It provides a more detailed assessment of white matter and cerebellum,

the injury of which seems to have significant influence on the development. The aim

of the study was to assess the correlation between CUS and MRI and a short-term development assessment (up to 1 year of age) of extremely premature infants.

#### Patients and Methods

20 infants were included in the study born <28 GW and hospitalized

in the NICU between 01.06 and 31.12.2013. All infants had an early (3-14 day of life)

and late cranial ultrasound (around 38-40 weeks of postconceptional age). Near term MRI was performed in an incubator compatible with the MRI system. All the MR studies were judged by the same radiologist who assessed intraventricular haemorrhage, ventricular enlargement, white matter damage, cerebellum, myelination. Neurological assessment was done at the corrected age of 3-6-9-12 months, based on Amiel-Tisson scale, elements

of Prechtl's Assessment of General Movements and milestones assessment.

#### Results

The study population was divided into two groups: group I (23-25 GW = 6 infants), group II (26-27 GW = 14 infants). In each group the diagnosis made on the basis of CUS

was compared with the brain MRI. In 11 infants (55%; 4 from group I and 7 from group II), additional information about brain damage was gained from the MRI. The damage concerned mostly the cerebellum. Attendance at follow-up neurological assessment was 100%. In group I the development of 2 infants was described as doubtful, the other 4 infants develop normally. In group II 8 infants developed normally, in 3 infants the development was doubtful and in 3 significantly delayed. In 3 infants from group I (50%) and 1 infant from group II (7%) developmental abnormalities were much more significant than the MRI findings could indicate.

## Conclusions

1. In 55% of cases MRI brought additional information on brain damage compared to ultrasound. 2. In group I even with small changes on MRI the development was described as doubtful or delayed. 3. In group II there was a much better correlation between changes on MRI and infant's development. 4. For better prediction of further development it is important to consider selected pre- and postnatal factors and others after discharge from hospital.

Other / Medical Education and Training

## NURSING PRACTICES OF PAIN MANAGEMENT DURING EXAMINATION of RETINOPATHY of PREMATURITY: A QUALITATIVE RESEARCH (222)

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### Introduction /Case Report

This study was conducted qualitatively in order to determine the knowledge of nurses regarding the pain felt by newborns during examination of retinopathy of prematurity (ROP), which is a painful procedure, as well as their emotions and thoughts about the practice and the interventions aimed at killing the pain.

### Patients and Methods

The data of study were obtained by using the semi-structured interview form, which was prepared by researchers and involved open-ended questions and demographic characteristics. Personal and profound interviews were performed with participants and the interviews were recorded on a tape recorder. The sampling was made by using the homogeneous sampling method and the size of sample was ended when the saturation point was reached in the study. Researcher nurses listened to the interview records and then put them in writing. In accordance with the thematic analysis of answers given by participants, two main themes were formed for the study and sub-codes were developed for these themes. Coding was performed in the computer environment by using the MAXQDA qualitative data analysis program.

### Results

In the study; as a result of interviews with 6 nurses, a saturation point was reached. The interviews lasted for averagely  $10.88 \pm 1.86$  /mn. As a result of the thematic analysis; two main themes were formed as “pain in newborns” and “examination of retinopathy of prematurity”, as well as sub-codes for these themes. Participant nurses stated that they could identify pain in newborns mainly crying, flexion/extension in extremities and increasing in the heart rate among the physiological changes. Regarding the question “what do you feel during the retinopathy examination?”, the participant nurses stated that they felt sorry and bad, it was a painful procedure for newborns and the examination was highly essential for infants. They stated that the most efficient methods of decreasing the pain involved touching the infants, giving a pacifier, talking to them, and swaddling them.

### Conclusions

It was thought that the nurses did not use objective assessment instruments in defining the pain in newborns; however, the non-pharmacological methods they used in decreasing the pain were in accordance with literature. As the nurses need to acquire relevant information; it could be recommended to add relevant training programs to the in-service training programs and plan studies of the pain management protocol in order to reflect current information on the field of clinic practices.

## Other / Neonatal Transportation

### KEY PERFORMANCE INDICATORS IN NEONATAL TRANSPORT - WHAT IS REALLY IMPORTANT? (329)

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#### Introduction /Case Report

Neonatal transport of ill newborn can be characterised as a high-risk medical procedure under often unpredictable, unknown and austere conditions. The number of inter-facility transports and the distances to be travelled are increasing due to a development towards regionalisation of secondary and tertiary care centers. The complexity of available techniques to support these sick infants en route underlines the necessity to maintain special expertise. Transport service programs, however, are often fragmented and heterogenous and specialised transport teams are not always available. Hence, there is a need for the identification of key performance indicators in neonatal transport.

#### Patients and Methods

Generally there are only few and limited studies on prehospital care of children. However, the use of specialised transport teams has been shown to diminish the risk of unexpected adverse events as well as mortality when compared to non-specialised teams. The unprepared introduction of new procedures has proven dangerous to the patient, raising mortal complications significantly. Personal errors are key reasons for adverse events and near-misses, including stress and anxiety, inadequate training and experience, concern about causing harm or pain and predominance of errors of omission over errors of commission. TRIPS is a promising scoring tool validated for neonatal transport to predict mortality and risk of IVH.

#### Results

We tested the TRIPS score in nearly 100 neonatal and paediatric intensive care patients. We found the scoring easy and clinically relevant, and could demonstrate a significant decrease in the TRIPS score measured before, during and after the transport.

#### Conclusions

Key performance indicators in neonatal transport should be identified as soon as possible. TRIPS score predicts mortality and also helps in characterising the patients, the severity of disease and thereby the complexity of the transport. TRIPS score should be implemented by all neonatal transport services. Overall there is an immediate need for consensus on quality and outcome measures for neonatal transports, the registration of adverse events, and the establishment of a transport database.

Other / Quality improvement and Safety and Error Preventio

AN IMPROVEMENT PROJECT TO REDUCE CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTION (CLABSI) IN NEWBORN INFANTS (506)

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Introduction /Case Report

Central line associated blood stream infections (CLABSI) is the most common cause of late onset sepsis in the newborn population. The use and duration of central lines have been described as independent risk factors for late onset sepsis. It is associated with significant mortality, morbidity and high economic costs. Increasingly, these infections are recognized as preventable adverse events. The aim of this study was to evaluate the effectiveness of a central line care bundle as a means of reducing the rate of CLABSI.

Patients and Methods

A prospective study of CLABSI rates was carried out in a university affiliated tertiary neonatal unit between December 2010 and June 2014.

Patients:

All neonates who had central lines in situ on admission or inserted during admission were included. Central lines were defined as all surgically inserted central lines (SICC), umbilical lines (UAC,UVC) and peripherally inserted central catheters (PICC).

Methods:

The study was designed using improvement methodology. A base line rate of CLABSI per 1000 central line days (CLD) was monitored each month during the first 4 months followed by implementation of care bundle and monthly monitoring of rate of CLABSI for rest of the study period. All positive blood cultures were reviewed monthly to identify CLABSI using pre-defined criteria.

Results

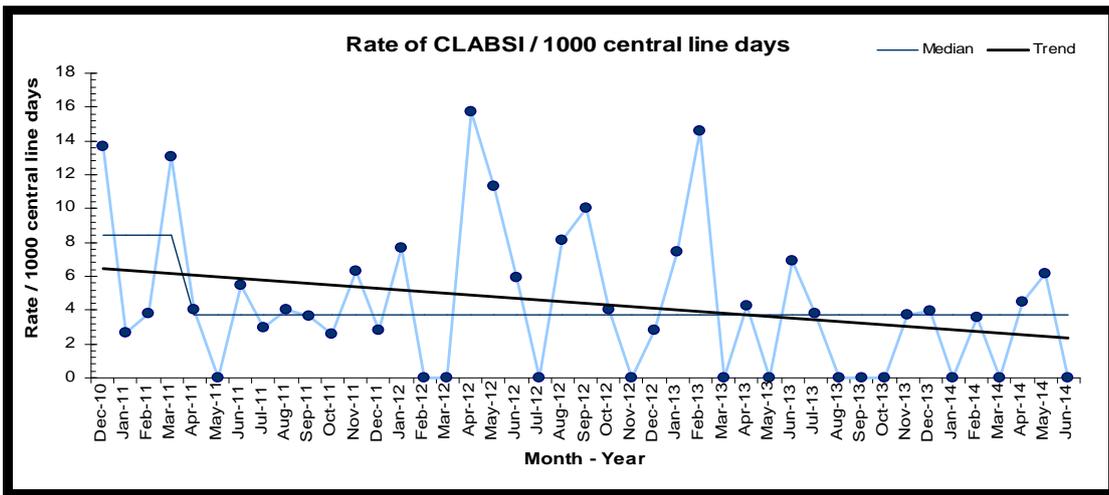
The measurement for improvement was done through monitoring process and outcome measures. The data was analysed using Statistical Process Charts. Run charts were used for process measures and control charts were used for outcome measures.

The mean gestational age of the infants in the cohort was 33.4 weeks and birth weight was 2124g. In the study period, 350 children had 571 central lines during their stay. 315 lines were PICCs, 161 were SICCs and 95 UAC, UVC or both. Together they amounted to 12,204 CLD. There were 53 CLABSI identified, resulting in the overall CLABSI rate of 4.3/1000 CLD. However, the baseline rate between December 2010 and March 2011 was 8.3/1000 CLD and post intervention (implementation of care bundle) the rate has fallen to 3.7/1000 CLD (55%).

## Conclusions

Following implementation of the central line insertion and maintenance care bundle there was trend towards reduction in the rate of CLABSI. A better compliance with processes may help to further reduce the rate of CLABSI and reduce morbidity.

## Table



## Brain & Development / Neurodevelopmental Outcome

### PLACENTAL PATHOLOGY AND EARLY NEUROLOGICAL MORBIDITY IN MODERATE PRETERM INFANTS (540)

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#### Introduction /Case Report

The placenta plays an essential role during pregnancy for growth and development of the fetus and dysfunction causes long-term neurological complications. Roescher et al. investigated the association between placental pathology and neurological morbidity in preterm infants <32 weeks' gestation. Aim of our study was to assess if there is an association between placental pathology and short term neurological outcome in moderate preterm infants (32/0-33/6 weeks' gestation).

#### Patients and Methods

Placentas of 71 moderate preterm infants (GA: 32-33 weeks, BW: 1218-2610 grams) were examined for histopathology. To determine the infants' neurological condition shortly after birth we assessed the quality of general movements (GMs) and assigned a Motor optimality score (MOS), respectively.

#### Results

The histopathologic examination showed pathologies in 83% of the placentas: Maternal vascular underperfusion (n=30), ascending intrauterine infection (n = 10), chorangiosis (n = 6), foetal thrombotic vasculopathy (n = 4), massive perivillous fibrinoid deposition (n=4), umbilical cord abnormalities (n=3), villitis of unknown aetiology (n=1), chronic deciduitis (n = 1). There were no significant associations between the placental lesions and GMs or the MOS.

#### Conclusions

In the majority of moderate preterm births in our study placental lesions could be found.

However, our study revealed that placental pathologies were not associated with the early neurological outcome of moderate preterm infants as measured by the quality of their general movements.

## Brain & Development / Neurodevelopmental Outcome

### HURDLES OF A NATIONAL SURVEILLANCE OF CEREBRAL PALSY. OVERVIEW OF THE FIRST EIGHT SURVEYED YEARS IN PORTUGAL (BIRTH-COHORTS 2001-2008) (612)

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#### Introduction /Case Report

Active epidemiological surveillance of cerebral palsy (CP) in childhood potentially provides evidence for trends in prevalence, severity and inclusion and to support adequate care. An overview of the first 8 years of the Portuguese national surveillance program, focusing on difficulties and drawbacks, is presented.

#### Patients and Methods

The Portuguese Surveillance of Cerebral Palsy at 5 years of age is a national registry (cross-sectional study) that actively registers children at the target age 5-years-old with CP, using multiple sources and active recapture strategies (allowing indefinite register of missed cases). It shares definitions, classifications and tools with SCPE. MRI is classified by its predominant pattern. Registered children with CP born in 2001-2008, survivors at 5 years of age or deceased at an earlier age with definite diagnosis of CP, were included. 1172 cases were registered, 52 (4.4%) deceased cases. Official demographic data are used as population denominators. Prevalence rates of CP at age 5 are given for birth-cohorts (BC).

#### Results

BC prevalence was 1.99‰ in 2006, 1.45-1.68‰ in 2007-10 and  $\leq 0.7\%$  onwards. Cases born in Portugal are 94%; 99% of survivors lived in Portugal. Sources are healthcare (81%), education (17%); the deaths register (1.7%); notifiers are physicians (94%) (physiatrists 65%, paediatric neurologists 18%, paediatricians 17%), therapists, nurses, teachers, social workers; multiple notifiers or sources contributed for 25.7% and 16.6% of the cases respectively. Clinical questionnaire is absent in 73 cases (6%). Missing values for CP classification 7%, birth variables 13-24%, GMFCS/BFMR 14-16%, cognition 20%, hearing impairment 23%, MRI classification 54%. No temporal trend was seen for cases reported with predominant spastic CP; cases reported with GMFCS grades IV-V are 36-43% in 2001-4 BC and 45-53% in 2005-8 BC. Cases born at term are 54-60% in 2001-6 BC, in 2007-8 BC 54-59% are born preterm.

#### Conclusions

A sustained, active epidemiological surveillance of CP requires a great effort to reach adequate coverage, validity and representativeness. Multiple sources and recapture strategies are used for accurate description of this condition on a populational and regional basis. Support from private and state institutions is primal. Special care should be taken when analyzing data from periods with inadequate coverage or notification biases.

Brain & Development / Neonatal Brain Injury and Neuroprotection

## DEVELOPMENTAL EXPRESSION PATTERNS OF KCC2 AND FUNCTIONALLY-ASSOCIATED MOLECULES IN THE HUMAN BRAIN (789)

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### Introduction /Case Report

Work on rodents has shown that steep up-regulation of KCC2, a neuron-specific Cl<sup>-</sup> extruder of the cation-chloride cotransporter (CCC) family, commences in supraspinal structures at around birth, leading to the establishment of hyperpolarizing GABAergic responses. KCC2 is also a structural protein in dendritic spinogenesis, thereby coordinating the development of GABAergic and glutamatergic transmission.

### Patients and Methods

Here, using microarrays, we describe in the human cerebrum, thalamus and cerebellum the spatiotemporal expression profiles of the entire CCC family, and of molecules which are known on the basis of rodent studies to functionally associate with KCC2. These include  $\alpha$  and  $\beta$  Na-K ATPase subunits, TrkB and synaptophysin. Translation of KCC2 mRNA into protein was validated immunohistochemically.

### Results

KCC2 mRNA was observed already at the 10th postconceptional week (PCW) in the amygdala, cerebellum and thalamus. KCC2-immunoreactive (KCC2-ir) neurons were abundant in the neocortical subplate at 18 PCW. Commencing at 19-24 PCW, most subplate and cortical plate neurons became KCC2-ir by 25 PCW. The mRNA expression profiles of Na-K ATPase  $\alpha$  and  $\beta$  isoforms as well as TrkB were consistent with what is known from studies on rodents about their interactions with KCC2.

### Conclusions

The present data show that, in the human brain, expression of KCC2 and its functionally-associated proteins begins in the early fetal period. Our work facilitates translation of results on CCC functions from animal studies to the human and, more specifically, refutes the view that the poor efficacy of anticonvulsants in the term human neonate is attributable to a lack of KCC2.

## Other / Miscellanea

Precision of Transcutaneous Bilirubin in Newborn with G6PD Deficiency: A single-center retrospective cross-sectional study (122)

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## Introduction /Case Report

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a double-edged sword for precision of transcutaneous bilirubin (TcB). In the one hand, G6PD deficiency is associated with low hemoglobin levels and TcB precision improves at low levels of hemoglobin. On the other hand, G6PD deficiency is associated with high serum bilirubin (SBR) and TcB precision reduces at high SBR. We know of no previous study that has evaluated TcB in G6PD deficient newborns. Thus, we aimed to evaluate TcB precision in G6PD deficient newborns.

## Patients and Methods

A retrospective, cross-sectional study in Almana General Hospital (AGH), Al Ahsa, Saudi Arabia. In AGH, TcB is measured by MBJ20 routinely every 8 hours for all newborns. We included newborns born at  $\geq 35$  weeks of gestation without blood group incompatibility. We compared 64 TcB-SBR pairs of G6PD deficient with that of 118 TcB-SBR pairs of normal newborns. We excluded TcB-SBR pairs if more than 2 hours elapsed between TcB and SBR measurements. An independent samples t-test was used to compare mean SBR of G6PD deficient and normal newborns. A paired sample t-test and Pearson correlation were used to compare between TcB and SBR. A Bland-Altman analysis was performed to evaluate agreement between TcB and SBR.

## Results

Timing of SBR were comparable in G6PD deficient and normal newborns ( $46 \pm 24$  vs.  $48 \pm 25$  hours of age,  $P = .64$ ). Means of SBR were comparable in G6PD deficient and normal newborns ( $168 \pm 40$ , maximum 237 vs.  $170 \pm 48$ , maximum 276  $\mu\text{mol/L}$ ,  $P = .74$ ). The SBR were more than 205  $\mu\text{mol/L}$  in 11 G6PD deficient and in 26 (22%) normal newborns (Chi-Squared  $P = .44$ ). Correlation between TcB and SBR was 0.75 in G6PD deficient vs. 0.77 in normal newborns ( $P = .37$ ). The bias between TcB and SBR was less in G6PD deficient than normal newborns (63  $\mu\text{mol/L}$  [Limits of agreement: 23 to 149] versus 80  $\mu\text{mol/L}$  [Limits of agreement: 5 to 165],  $P = .01$ ).

## Conclusions

Precision of TcB was better G6PD deficient than normal newborns; nevertheless, it was poor in both. These results need to be confirmed in a larger prospective study using different brands of transcutaneous bilirubinometer.

## Other / Involvement of parents in care

A survey of the bereavement support services utilised by families who have experienced a perinatal loss. (230)

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## Introduction /Case Report

To describe the types of bereavement services utilised by families in the ACT and surrounding NSW who have experienced a perinatal loss and to evaluate whether these services have met the needs of bereaved families.

## Patients and Methods

Women who experienced a perinatal loss between 1st Jan 2009 to 31st Dec 2012 from the ACT Perinatal Mortality Database were sent a survey consisting of the modified Perinatal Post Traumatic Stress Disorder (PTSD) questionnaire, items addressing use of bereavement services, and the Inventory of Complicated Grief. Respondents provided free text comments, which were triangulated against the final results.

## Results

44 women were included in the study (32% response rate); 77% had a perinatal PTSD score which indicated the need for support from mental health services and 75% accessed services. The lowest and highest quartile of PTSD scores were less and more likely to access SKACT services respectively. 45% of surveyed women used SKACT and accessed counseling (90%), support groups (50%), playgroups (15%), and the helpline (10%). 55% of women surveyed accessed non-SKACT services and predominantly used psychologists (75%) and GPs (33%). 68% met the criteria for complicated grief and the lowest quartile had the lowest rates of use of either service. 50% of respondents provided written comments to support their answers.

## Conclusions

A high proportion of women following a perinatal loss had high PTSD scores, complicated grief and utilised local bereavement services. Continuation of current support services is supported with modifications that may potentially improve recovery following a perinatal loss.

Brain & Development / Neonatal Brain Injury and Neuroprotection

## THE ROLE OF NEONATAL NON-INVASIVE BRAIN MONITORING (ELECTRICAL ACTIVITY AND OXYGENATION) IN PERINATAL ASPHYXIA (851)

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### Introduction /Case Report

Over the last period it recognizes the value of early predictors of postpartum neonatal brain electrical activity for long-term evolution of neurodevelopment of infants with perinatal hypoxic-ischemic injury. The aim is to highlight the correlation between the type of amplitude-integrated electroencefalographic trace (aEEG), cerebral oxygenation after birth and degree of brain damage.

### Patients and Methods

The lot includes 42 inborn or outborn newborns with moderate and severe perinatal asphyxia. Inclusion criteria in the study were VG: 37 weeks, SA 5 minutes below 7, umbilical cord pH <7.15 and BE <-15 mmol / l. Clinical evaluation of the degree of hypoxic ischemic encephalopathy was made according to Sarnat-Sarnat classification. Monitoring electrical activity was performed by Brainz (Natus) device with 5 electrodes and cerebral saturation was monitored with a device NIRS -INVOS (Somametics).

### Results

Newborns without hypoxic-ischemic encephalopathy (HIE) and those with HIE Sarnat grade I had normal or mildly abnormal aEEG trace in the first 24-48 hours and then normal trace. Cerebral oxygenation and tissue oxygen extraction fraction of the brain are normal (ScO<sub>2</sub> average 72% and FTOE average 0.4). Infants with grade II EHI all aEEG trace from normal to severely pathological. Cerebral Oxygenation is correlated with the appearance and evolution aEEG trace. HIE grade III invariably associated with pathological aspect aEEG, increasing cerebral oxygenation and decreasing FTOE.

### Conclusions

This noninvasive brain monitoring modalities can be used easily at the bedside immediately, provide useful information in management of perinatal asphyxia (medication, indication for and monitoring of hypothermia) and on the long-term prognosis.

## Other / Miscellanea

### Investigation Of Incidence, Severity And Etiology Of Neonatal Vitamine D Deficiency and Assesment Of Treatment Success (051)

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## Introduction /Case Report

There is a high incidence of vitamine D deficiency in developing countries. Various studies from our country have reported rates of severe deficiency as high as %50-92. However, there are limited number of studies evaluating the outcomes of treatment. In this study we aim to investigate the incidence, severity and etiology of neonatal vitamine D deficiency and evaluate outcomes of treatment.

## Patients and Methods

Preterm and term babies admitted to NICU between January 2012- December 2014 have been enrolled in this prospective study. 25 OH vitamine D level is measured in all babies in the first day of life. All babies received oral vitamine D after measurement with a dosage of 800 units per day for preterm babies and 400 units per day for term babies. Control vitamine D levels are obtained in every four weeks and at discharge. Vitamine D levels of < 10 ng/ml, 10-20 ng/ml, 20-30 ng/ml and >30 ng/ml are classified as severe, moderate, mild deficiency and normal, respectively.

## Results

A total of 230 babies are included in the study. All babies in the study had an vitamine D level below 30 ng/ml and %61.7 had severe, %34 had moderate and %4.3 had mild deficiency. Mothers of babies with vitamine D levels below 10 ng/ml were found to have significantly lower vitamine D levels. Only 11 (% 4.7) mothers received supplemental vitamine D during pregnancy and similarly only %4.0 of mothers had an educational status above secondary school. There was no difference in mothers' clothing style between groups, however babies born in spring-summer season had significantly higher rates of severe vitamine D deficiency. In first follow-up, vitamine D levels were >20 ng/ml in %32 of babies with severe and moderate deficiency, this rate had increased up to %59 in second control.

## Conclusions

Vitamine D deficiency is common in developing countries such as ours. All cases in our study had low vitamine D levels, and majority of cases had severe deficiency. Additionally, maternal vitamine D levels were also low and directly correlated with neonatal vitamine D deficinecy. We conclude that adequate maternal vitamine D supplementation is essential in preventing neonatal vitamine D deficinecy.

Other / Quality improvement and Safety and Error Preventio

ASSESSMENT OF THE INCIDENCE OF EARLY NEONATAL HYPOGLYCEMIA PERFORMING UNIVERSAL "POINT OF CARE" BLOOD GLUCOSE SCREENING. CAN WE VALIDATE ALL ACCEPTED RISK FACTORS? (207)

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### Introduction /Case Report

Selective screening for early neonatal hypoglycemia is generally performed when one or more risk factors are present. Because of finding high incidence of hypoglycemia among infants of mothers with missing data of glucose tolerance test during pregnancy, a universal neonatal blood glucose screening strategy was adopted in our nursery. Since this approach may be controversial, we decided to study the incidence of early postnatal hypoglycemia in our nursery population and to assess whether the classically accepted hypoglycemia risk factors could be validated in this setup. To our knowledge, this is the first study to evaluate hypoglycemia risk factors in the nursery using universal screening

### Patients and Methods

Blood glucose concentrations of all infants admitted to the nurseries of Shaare Zedek Medical Center, Jerusalem Israel, between June 1st and September 9th 2014 were recorded using "point of care" analyzer ACCU-CHEK Performa (Roche, Indianapolis, IN). Potential hypoglycemia risk factors and other demographic data were recorded, and their possible association with the first blood glucose concentration was evaluated. Two different hypoglycemia cutoffs (blood glucose concentrations inferior to 40 or to 47 mg/100ml) were analyzed independently. Cases with no information on maternal glucose tolerance test or diabetes were excluded

### Results

Of 3991 infants admitted during the study period, 315 had no maternal glucose tolerance test and 14 had no available glucose values, remaining 3662 eligible subjects. Mean birth weight was  $3322 \pm 439$  gr and gestational age was  $39.4 \pm 1.3$  (range 36-42 weeks). First glucose was checked at a mean age of 1:08h ( $\pm 1:54$ ). At this time 120 infants (3.3%) and 432 infants (11.8%) had blood glucose levels under 40 and 47 mg/100 ml respectively. From the evaluated risk factors, large or small for gestational age, or birth weight  $>3800$ gr were not associated with early neonatal hypoglycemia, while maternal diabetes, low birth weight ( $<2500$ gr), cesarean section and twin delivery had a significant association on univariate analyzes. When significant parameters on univariate analysis were re-tested using multivariate analyzes, only gestational age remained clinically and statistically significant ( $p < 0.0001$ )

### Conclusions

Of all classical risk factors, gestational age was the only one validated after multivariate analysis. We speculate that tight management of diabetes neutralized high weight, and low weight's influence was via colinearity with young gestational age. Long term follow up is necessary in order to evaluate the

consequences of transient neonatal hypoglycemia and whether there is a clinical validation for selective or universal early glucose screening

## Other / Medical Education and Training

### IMPROVING PERIPHERAL OXYGEN SATURATION ALARM LIMIT'S SETTINGS IN VERY LOW BIRTH WEIGHT INFANTS' MONITORS: A QUALITY IMPROVEMENT PROJECT (424)

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#### Introduction /Case Report

Peripheral oxygen saturation (SpO<sub>2</sub>) alarm settings on neonatal monitors influence oxygen administration in preterm infants. Incorrect oxygen supplementation has been related to death, Retinopathy of Prematurity (ROP), bronchopulmonary dysplasia and necrotizing enterocolitis in these patients. Actually 30% of Very Low Birth Weight (VLBW) infants admitted to our unit have some degree of ROP. Recent publications recommend SpO<sub>2</sub> targets between 90-95% in extremely preterm infants requiring oxygen.

Objective: to improve SpO<sub>2</sub>s alarm limits set on monitors for VLBW infants admitted to our neonatal unit.

#### Patients and Methods

Infants with gestational age <32 weeks or birth weight <1500g admitted in our unit were included. SpO<sub>2</sub> alarm limits set on monitors were recorded in three consecutive random days during morning, afternoon and night shifts and were used as our baseline pre intervention data. Four one hour training sessions were then performed to all the neonatal nursing staff. In these, the team described findings of actual SpO<sub>2</sub> limits adjusted in our monitors and new target SpO<sub>2</sub> recommendations. Tables with the new limits of SpO<sub>2</sub> for different gestational ages were developed and attached to each patient's folder in a visible location. Finally SpO<sub>2</sub> alarm limits were analyzed one and two months after training to the neonatal staff had finished.

#### Results

27 patients (140 observations) were included: 78.5% were admitted in intensive care and 21.5% in intermediate care. Median gestational age was 28 weeks (IQR=5) and median birth weight 1100g (IQR=550). 40.7% of newborns were supplemented with oxygen, 16.4% required mechanical ventilation and 47.8% noninvasive ventilation. In the baseline observation a high percentage of alarm settings were incorrect (median lower SpO<sub>2</sub> alarm limit set on the monitors 85%, range 12; median high SpO<sub>2</sub> limit 100%, range 5). Alarm adjustment was similar between infants supplemented with oxygen or not. One month after staff training had finished, upper and lower SpO<sub>2</sub> alarm limits were correct in 87.5% of patients. Pre/post-training correct alarm settings' difference was statistically significant with p<0.05. This results were maintained 2 months after staff training.

#### Conclusions

Nurses' training contributes to quality improvement of care. We are performing new studies in order to evaluate maintenance of better alarm control over time, measuring of real percentage of time patients are in the recommended oxygen saturation levels and impact of this changes in the incidence of ROP in our Unit.

Other / Miscellanea

SERUM NGAL AND COPEPTIN LEVELS AS EARLY MARKERS OF ACUTE KIDNEY INJURY IN ASPHYXIATED NEONATES. (165)

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### Introduction /Case Report

Recent reports have revealed increased concentration of neutrophil gelatinase-associated lipocalin (NGAL) in cardiovascular diseases and after episodes of hypoxia. Neutrophil gelatinase-associated lipocalin (NGAL) is postulated to be a potentially new and highly specific and sensitive marker of acute kidney injury (AKI). Copeptin, derived from a pre-pro-hormone consisting of vasopressin, is also involved in multiple cardiovascular and renal pathways and functions. The aim of the study was to determine the clinical utility of serum NGAL and copeptin as an early marker of acute kidney injury in asphyxiated neonates.

### Patients and Methods

In our prospective cohort study, 43 neonates with acute incidence of perinatal asphyxia were enrolled as the study group. In order to assess the comparison of novel biomarkers in umbilical blood and after 24 hours of newborns' life, we included 30 healthy newborns, residing in our unit during the study, as the control group. Serum molality, NGAL, copeptin and creatinine levels were analyzed in umbilical cord blood and 24 hours after birth. Patients were subsequently discriminated into AKI (n=8) and no-AKI (n=35) groups.

### Results

Among neonates with AKI stage 1, NGAL levels were elevated in comparison to those newborns without AKI, both in umbilical cord blood (174.3 [117.8-230.7] ng/ml vs 88.5 [59.1-118.0]ng/ml;  $p<0,0001$ ) and 24 hours after birth (152.5 [80.1-224.8]ng/ml vs 74.9 [55.5-94.4]ng/ml;  $p<0,001$ ). However, we did not observe any difference in the concentration of copeptin, neither in umbilical cord blood (660.1 [273.5-1026.6]pg/ml vs 520.8 [456.3-585.4]pg/ml;  $p=0.32$ ), nor 24 hours after birth (439.9 [310.3-569.5]pg/ml vs 455.1 [394,8-515.3]pg/ml;  $p=0.51$ ). Furthermore, we also did not discriminate any significant differences in the concentration of creatinine and serum molality between the analyzed groups.

### Conclusions

We suggest that serum NGAL levels may be an early marker to predict AKI in neonates after perinatal asphyxia.

Other / Quality improvement and Safety and Error Preventio

## VARIABILITY IN POLICIES REGARDING SCREENING FOR RETINOPATHY OF PREMATURETY AMONG EUROPEAN EURONEONET PARTICIPANTS (541)

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### Introduction /Case Report

To describe differences in screening rates for retinopathy of prematurity (ROP) among European countries with Neonatal Intensive Care Units (NICUs) with stable participation in the EuroNeoNet (ENN) project.

### Patients and Methods

Data from a subset of ENN very low gestational age / very low birthweight (VLGA/VLBW) infants (<32 weeks or <1501 g) were studied. Analyses were restricted to NICUs with data provided for at least five years from 2006-2012. Neonates of <23 wk of gestational age (GA) and those transferred to another NICU or who died in the NICU during the first year of life were excluded. Proportions of neonates who underwent retinal examination were assessed and analyzed according to GA (23-29 wk vs.  $\geq 30$  wk) and weight (< 1,250 vs.  $\geq 1,250$  g). Differences among countries were explored using logistic random effects regression analysis taking into account clustering of neonates in NICUs, apart from Sweden due to the specific regional-based transfer policy where the clustering unit was used.

### Results

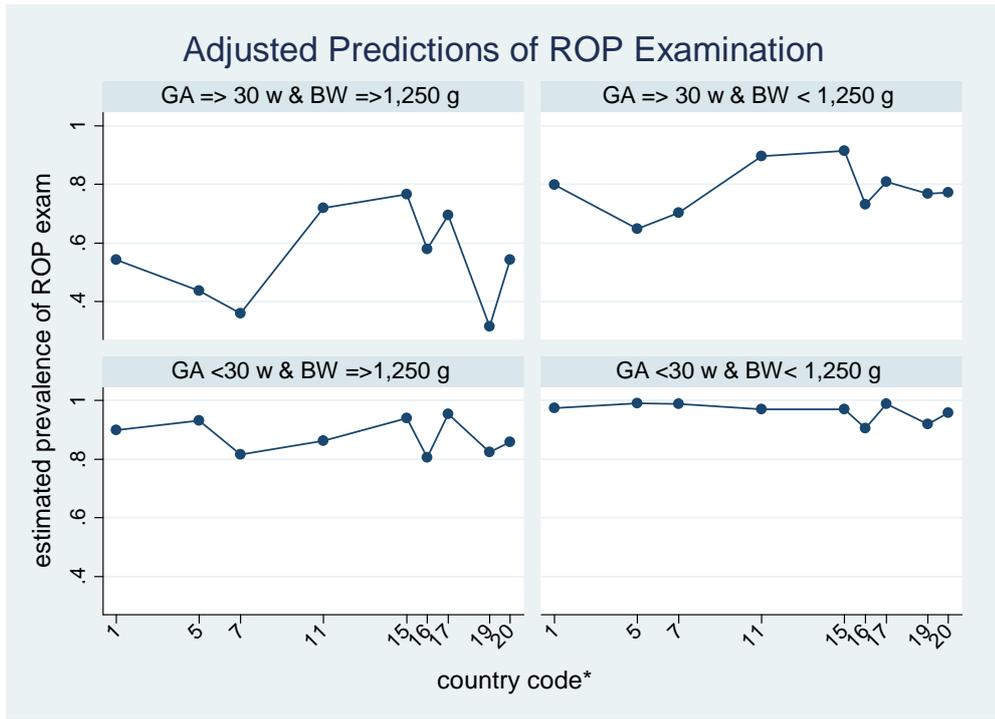
19,211 infants in 80 NICUs from nine European countries and Turkey were included in the analysis. The overall rate of retinal examination was 79.4% with significant differences by GA and weight ( $\geq 30$ wk and  $\geq 1,250$  g: 63.0%;  $\geq 30$ wk and <1,250 g: 82.5%; <30wk and  $\geq 1,250$  g: 86.2%; <30wk and <1,250g: 94.0%) ( $p < 0.001$ ). Screening rates among countries varied from 91.9% to 99.7% for the <30wk and <1,250 g stratum ( $p < 0.001$ ) and from 31.7 to 96.0% for the  $\geq 30$ wk and  $\geq 1,250$  g subgroup ( $p < 0.001$ ). The overall prevalence of severe ROP (grades  $\geq 3$ ) among tested infants was 4.2%. Among extremely preterm infants (<28 wk and <1,000 g; n=3,216), 126 neonates (3.9 %) were not tested for ROP. Rates of non-testing for this very high risk population ranged among participating countries from 0% to 5.6% ( $p < 0.001$ ). Participating countries had assigned identification codes.

### Conclusions

There is wide variability in retinal examination rates for VLBW/VLGA infants in ENN participating countries. Almost one in twenty five extremely preterm infants did not undergo screening for retinopathy.

Funded by EC DG-SANCO (Contract number: 530078).

Table



Other / Quality improvement and Safety and Error Preventio

## DEVELOPMENTAL ENAMEL DEFECTS IN VERY AND EXTREMELY LOW BIRTHWEIGHT INFANTS AT THE AGE OF ONE YEAR (613)

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### Introduction /Case Report

Very low birthweight infants (VLBW) and extremely low birthweight infants (ELBW) suffer from neonatal complications and morbidity that may affect a mineralisation of primary teeth and occurrence of developmental enamel defects (DDE). The prenatal factors associated with DDE are infections, metabolic diseases, nutritional deficiencies and maternal intake of some drugs. The perinatal and postnatal factors of DDE are birth complications, infections, metabolic disorders, congenital cardiac defects, nutritional deficiencies and intake of some medicaments. In addition to systemic factors, trauma caused by a laryngoscope can be associated with DDE.

### Patients and Methods

The aim of the study was to evaluate the prevalence and possible risk factors of DDE in primary incisors of VLBW and ELBW infants. A cross-sectional study was carried out with 132 one-year old infants. The perinatal (gestational age, birthweight) and postnatal variables (frequency of laryngoscopies, number of teeth with enamel defects) were collected through hospital records and clinical examination. The presence of DDE was evaluated with the Developmental Defects of Enamel Index. Qualitative changes in enamel translucency without loss of surfaces were categorized as opacity. Enamel hypoplasia was diagnosed when a quantitative alteration in the enamel surfaces was identified. The obtained data were statistically evaluated using the chi-squared test and the multifactorial analysis.

### Results

The research cohort consists of 132 one – year old (corrected age) very and extremely preterm Caucasian infants. There are 62 boys (47 %) and 70 girls (53 %) with mean gestational age 28.8 weeks (range 24 – 35), mean birthweight 1119.7 g (range 570 – 1490), mean number of laryngoscopies 1.075 (range 0 – 4) and mean number of erupted teeth 5.6 (range 1 – 12). The prevalence of DDE was 34.1 % and the teeth most affected were maxillary central incisors in 52.2 %. In 14 infants (10.6 %) enamel hypomineralisation were diagnosed, in 31 infants (23.5 %) enamel hypoplasia were present (Fig. 1) and in 2 infants (1.5 %) had combined defects. The gestational age (prevalence  $p=0.22$ ), gender ( $p=0.054$ ) and frequency of laryngoscopies ( $p=0.053$ ) correlated negatively to the number of primary teeth with DDE. The significant statistical relationship was between ELBW and DDE in primary incisors ( $p=0.009$ ).

### Conclusions

The prevalence of DDE in primary teeth observed in previous studies is higher in VLBW and ELBW infants than in term infants (Tab. 1). In our study the prevalence of DDE in primary incisors was 34.1 % (48 % in ELBW and 24.4 % in VLBW) (Tab.1). We found that the occurrence of DDE in primary incisors was

significantly related to ELBW infants. Concerning local etiological factors of DDE, frequency of laryngoscopies probably has an important role.

Table

Tab. 1: Prevalence of DDE in primary teeth

	Birthweight (BW)											
	NBW			LBW			VLBW			ELBW		
author	No	age	p.	No	age	p.	No	age	p.	No	age	p.
Seow et al. (1987)	47	9-42	12.7	33	9-42	27.3	77	9-42	62.3	-	-	-
Lai et al. (1997)	25	30	45	-	-	-	25	30	96.6	-	-	-
Franco et al. (2007)	61	31-35	24.6	61	18-34	57.4	-	-	-	-	-	-
Bansal et al. (2012)	50	9-35	18	64	9-35	26.5	58	9-35	74.1	-	-	-
Nelson et al. (2013)	234	18-20	8	-	-	-	234	18-20	31.0	-	-	-
Cadova et al. (2015)	-	-	-	-	-	-	82	12	24.4	50	12	48.0

NBW – normal birthweight, LBW – low birthweight, VLB – very low birthweight, ELBW – extremely low birthweight

No – number infants in cohort

age – age in months during examination

p. – prevalence [%]

Picture



## Brain & Development / Structural and Functional Brain Imaging

Adenosine levels in VLBW and correlation with MRI : insights and speculations (893)

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### Introduction /Case Report

Background: Extracellular adenosine (Ado) increases during hypoxic conditions and inflammation. It acts via different receptors and it seems to play a role also in promoting diffuse white matter injury in the developing brain. Ado level has never been correlated to cerebral MRI in very low birth weight (VLBW) infants.

Aim: The aim of the study was to determine the plasmatic levels of Ado in VLBW infants and to determine its relationship with MRI at term equivalent age.

### Patients and Methods

Material and methods: Blood samples were collected at 4 different times after delivery (T1=3 days, T2=15 days, T3=30 days, and T4= 340 days) according to samples performed for screening for metabolic diseases in VLBW. In addition, MRI at term equivalent age (mean GA 40 weeks), was analysed. We considered IVH (intraventricular haemorrhage), CBH (Cerebellar Haemorrhage), punctate white matter lesions (PWML) mimicking minor forms of PVL (periventricular leucomalacia) and PLIC (Posterior Limbs of Internal Capsule) maturation.

### Results

Fifty-six premature infants (mean GA 28 weeks, mean birth weight 1095 g, male 43%) who admitted to our neonatal intensive care unit were included in the study. The median Ado concentration was 0.75  $\mu$ M at 3 days, with progressive and significant higher values at the following times (1.01  $\mu$ M at 15 days, 1.46 at 30 days, 1.44  $\mu$ M at >40 days,  $p < 0.001$ ).

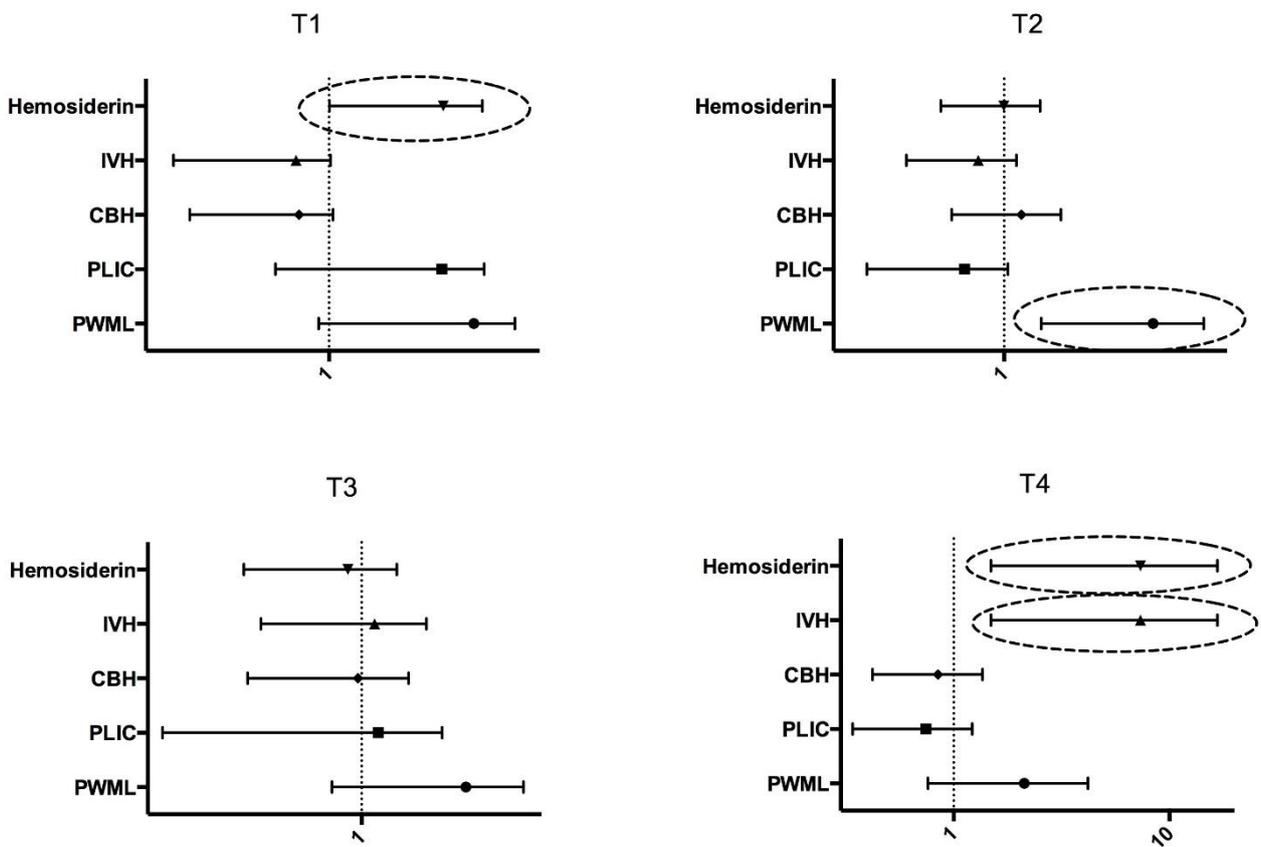
Ado levels at Time 1 positively correlated with the presence of blood or degradation products as hemosiderin evidenced by SWI (susceptibility weighted imaging) ( $p < 0.01$ ).

Adenosine levels at Time 2 were significantly higher in infants with white matter lesions (WML) at 40 weeks of GA ( $p < 0.01$ ). At Time 4 Ado levels were correlated to hemosiderin at SWI ( $p < 0.01$ ).

## Conclusions

Adenosine level at T1 and T4 is significantly correlated with the presence of blood at MR performed at term equivalent age; we remain uncertain of the reasons of these time interval differences. T2 levels of adenosine were associated with the development of PWML confirming the potential role of adenosine as a marker, at specific time point, in the developing of those minor forms of white matter lesions (PWML).

## Picture



## Other / Miscellanea

Exploring clinicians' views and experiences of offering two consent pathways in a trial of timing of clamping at very preterm birth: A qualitative study (193)

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## Introduction /Case Report

When preterm birth is imminent recruitment to trials requires approaching women at a difficult time, often with limited time to make a decision. The Cord Pilot Trial compared alternative policies for timing of cord clamping at very preterm birth. So high risk women were not excluded, we developed an oral assent pathway for use when birth was imminent. After a brief description of the trial, if the woman agreed to participate she was randomised, with written consent for participation in follow up was after the birth. A third of women were recruited using this consent pathway. This study explored clinicians' experiences of offering the two consent pathways

## Patients and Methods

A qualitative interview design with semi-structured interviews. Clinicians were recruited from all eight sites participating in the Cord Pilot Trial. 17 clinicians from a range of disciplines were interviewed. Eleven participants had experience of offering both the one stage written consent pathway, and two stage oral assent pathway. Six participants had experience of only offering one stage written consent. Results were analysed using systematic thematic analysis.

## Results

Five consultant neonatologists, 5 neonatal nurses, 4 midwives, 2 neonatology registrars and 1 paediatric registrar were interviewed. Five themes were identified: 1) Consent as a continual process; 2) Consent as a record versus consent as a legal document; 3) Team approach to consent; 4) Different consent pathways for different trials; 5) Balance between time and information.

## Conclusions

Overall, clinicians thought that the one stage written consent pathway was the optimal method of offering consent. However, clinicians were positive about the use of oral assent for straightforward, acceptable trials where there is limited time for offering participation. Clinicians thought that recording oral assent should be improved, to mitigate the risk of not having enough evidence that consent had been given and its validity.

Brain & Development / Placenta and prenatal factors

HIGH GRADE INTRAVENTRICULAR HEMORRHAGE IN VERY LOW BIRTH WEIGHT INFANTS – DOES THE MODE OF DELIVERY MATTER? (752)

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#### Introduction /Case Report

High grade intraventricular hemorrhage (grade 3-4) carries a poor prognosis for very low birth weight infant. There are very few studies on the impact of the mode of delivery on this outcome.

The objective of this study was to compare the incidence of high grade IVH according to the mode of delivery in VLBW infants.

#### Patients and Methods

We investigated 1386 VLBW infants that were born at Assaf Harofeh Medical Center in Israel. 410 were born by spontaneous vaginal delivery and 976 by cesarean section. Demographic and outcome data were collected and analyzed by appropriate statistical methods.

#### Results

The 2 groups were comparable for demographics, morbidity and mortality variables. In the vaginal delivery mode 6.8% develop high grade IVH, whereas in the caesarean section group 5.8% develops it. This finding did not reach statistical significance.

#### Conclusions

Our study had one of the largest cohorts that addressed this question. We did not find any effect of the mode of delivery on the incidence of high grade intraventricular hemorrhage.

## Brain & Development / Neurodevelopmental Outcome

### Neurodevelopmental Outcomes of Preterm Infants with Low Grade Intraventricular Hemorrhage (332)

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#### Introduction /Case Report

As the survival rate of preterm infants has improved, it has become more important to improve morbidity and quality of life in this population. It is well known that intraventricular hemorrhage (IVH) is related to mortality and neurological sequelae in preterm infants. However, neurodevelopmental outcomes in preterm infants with low grade IVH have been controversial. The aim of the study was to investigate neurodevelopmental outcomes of preterm infants with low grade IVH compared to those without IVH.

#### Patients and Methods

This was a retrospective cohort study including preterm infants less than 32 weeks of gestation between January 2009 and December 2011 at Seoul National University Children's hospital. Serial brain sonography were reviewed for IVH grading and study population were categorized into 3 groups; no IVH, low grade IVH (grade I - II), and high grade IVH (grade III - IV). Korean-Ages and Stages Questionnaires (K-ASQ) at corrected age (CA) 8 months and 18 months, and the Gross Motor Function Classification System (GMFCS) at CA 12 months and 24 months were reviewed for evaluating the neurodevelopmental outcomes of the study population. Presence of cerebral palsy (CP), deafness and blindness were also collected.

#### Results

A total of 204 premature infants were enrolled and 18 infants were excluded. Number of the no IVH, low grade, and high grade IVH group were 77, 95, and 14 respectively. There were no significant differences between the no IVH group and the low grade group in K-ASQ at CA 8 months and 18 months. The GMFCS mean score was lower in the low grade group than the no IVH group at CA 24 months but it was not statistically significant. The incidences of CP or neurodevelopmental impairment (NDI) were not significantly different between the no IVH group and the low grade group. Among study groups, the number of infants who had the score below the cutoff in K-ASQ or the combined NDI (score below the cutoff of any five parts in K-ASQ, CP, blindness or deafness), and who were above GMFCS level II were the highest in the high grade group. And the GMFCS mean score was the lowest in the high grade group.

#### Conclusions

Our study indicated that there was no difference in neurodevelopmental outcomes between preterm infants without IVH and those with low grade IVH. Only high grade IVH was associated with poor neurodevelopmental outcomes.

## Brain & Development / Neurodevelopmental Outcome

### NEURODEVELOPMENTAL OUTCOME FOLLOWING NEONATAL PERFORATOR STROKE (227)

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### Introduction /Case Report

Data on outcome of neonatal perforator stroke are scarce. We aim to assess outcome after neonatal perforator stroke in the largest cohort so far.

### Patients and Methods

Survivors from a cohort of children diagnosed with neonatal perforator stroke using cranial ultrasound or magnetic resonance imaging were eligible for inclusion. Recovery and Recurrence Questionnaire (RRQ) score, presence of cerebral palsy (CP) and crude outcome was assessed, specifically (1) ability to walk independently, (2) participation in regular education, and (3) presence of epilepsy.

### Results

37 patients (20 males) aged 3 to 14 years (mean 8 years) were included; 14 with isolated single perforator stroke, 4 with multiple isolated perforator strokes, and 19 with additional brain injury. Four of eighteen children with isolated perforator stroke(s) had CP, one could not walk independently, and one developed epilepsy. In 4 of 18 posterior limb of internal capsule (PLIC) was involved, 3 of these had CP. Eleven of nineteen children with additional brain injury had CP, three were not able to walk independently. Three of nine children with concomitant cortical middle cerebral artery stroke developed epilepsy.

### Conclusions

Perforator stroke patterns can be of use in predicting long-term outcome and guiding counselling and surveillance. Motor outcome was favourable in children with isolated perforator stroke(s), except when PLIC was involved.

Table

**Table 1. Patient characteristics**

	No. (%) or median (range)
Gestational age, weeks	35 5/7 (24 6/7 – 42)
Birth weight, grams	2320 (620 – 4440)
Male	20 (54%)
Singleton	31 (84%)
SGA	8 (22%)
Apgar score 1 minute (n= 34)	6.5 (0 – 10)
Apgar score 5 minutes (n= 35)	8 (3 – 10)
Umbilical cord pH	7.16 (6.73 – 7.39)
CRIB score (n= 34)	1 (0 – 13)
Age* at assessment RRQ, years	8.3 (3.1 – 14.6)

*Abbreviations:*

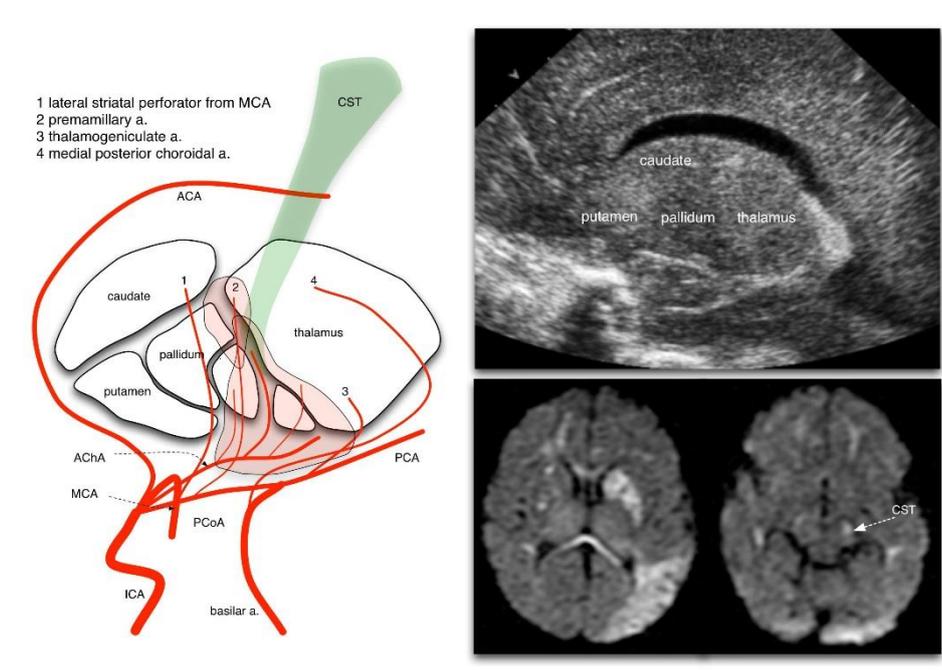
SGA= small for gestational age

CRIB= Clinical Risk Index for Babies

RRQ= Recovery and Recurrence Questionnaire

\*Age not corrected for prematurity

Picture



Brain & Development / Early developmental care

## ASSOCIATION BETWEEN THE SEVERITY OF METABOLIC ACIDOSIS AND HYPOCAPNIA DURING RECOVERY FROM ACIDOSIS IN ASPHYXIATED NEWBORNS (844)

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### Introduction /Case Report

Metabolic acidosis is a known consequence of severe perinatal asphyxia, characterized by low pH and increased base deficit (BD). pCO<sub>2</sub> also influences the acid-base imbalance and its role is controversial in neonates with hypoxic ischemic encephalopathy (HIE). Hypocapnia occurs frequently in HIE and although it lessens acidosis, it is presumably associated with poor neurodevelopmental outcome, whereas hypercapnia has been suggested to ameliorate brain damage. In the present study, we evaluated the relationship between pH, BD and pCO<sub>2</sub> levels during the first 6 hours of life and their association with neurodevelopmental outcome in neonates with moderate to severe HIE.

### Patients and Methods

This was a single centre retrospective cohort study. We assessed 104 term newborns with HIE defined by the TOBY criteria and treated with therapeutic hypothermia. A total of 296 blood gas samples were collected in the first 6 hours of life and neurodevelopmental outcomes were registered. Neurodevelopmental assessment (Bayley II test) was performed between 18-24 months. Survival without severe neurological disability was defined as both MDI and PDI > 70 (n=70). Moreover, the relationship between pH, BD and pCO<sub>2</sub> was separately analysed in the 1st, 2nd, 3rd, 4th, 5th and 6th postnatal hours using correlation analysis.

### Results

Threshold for survival without severe disability were pH 6.63 and 7.04; BD 21.6 mmol/L and 15.1 mmol/L at 3 and 6 hours of age, respectively. However, a wide range of pCO<sub>2</sub> levels were compatible with intact survival (13.6-118 Hgmm). Infants with favorable outcome had the same variability of pCO<sub>2</sub> levels as infants with bad neurodevelopmental outcome. Interestingly, a strong negative correlation was found between pCO<sub>2</sub> and BD in the 3rd and 4th hours of life ( $r = 0.52$ ;  $p = 0.0014$ ). Increased BD values were associated with lower pCO<sub>2</sub> levels probably due to increased spontaneous respiratory efforts in compensation for the severe metabolic acidosis.

### Conclusions

Some infants even with very low initial pH may survive without severe disability. There is a negative correlation between BD and pCO<sub>2</sub> during early recovery from acidosis. Future clinical studies are needed to clarify the role of pCO<sub>2</sub> variation on the recovery from acidosis following perinatal asphyxia.

## Brain & Development / Structural and Functional Brain Imaging

### FULL NEONATAL EEG MONITORING IN THE NICU: CAN WE USE CAPS APPLIED BY A PEDIATRICIAN? (336)

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#### Introduction /Case Report

There is increasing evidence of the early predictive power of full EEG recordings in preterm infants. Normal EEG maturation is associated with normal neurodevelopmental outcome of infants born preterm. There is also an increasing awareness of the high likelihood of subclinical seizures in several (common) patterns of preterm brain injury. So there is a clear need for expansion of current EEG monitoring on the NICU (neonatal intensive care unit), in order to objectify the seizure burden and investigate treatment strategies. However, full EEG monitoring in preterm infants has several obstacles: i.e. it is difficult to apply electrodes and it can be difficult to interpret the signal.

#### Patients and Methods

Infants (n= 24) born < 32 weeks gestational age (24 1/7 until 30 2/7) received a single EEG measurement with a high-density cap applied by one single pediatrician, at the corrected age of 30 weeks. Time to place the cap (TPC) started from the time the patient received cap and ended after 20 electrodes were prepared with abrasive gel/conductive paste. Time until good signal quality was recorded and was defined by TPC + time needed to adjust skin-electrode interface to achieve good signal quality with impedances < 40 kOhm.

Patient burden was classified in three groups, group 0: no reaction or arousal without crying; group 1: crying during placement; group 2: apnea/bradycardia during placement.

Data were analysed by an automatic interburst interval detection algorithm (Matic et al, 2012).

#### Results

Average time to place the EEG cap was 13 minutes (range 7 -35 minutes). A time to achieve good signal quality was 25 minutes (range 12-65 minutes). Patient burden resulted in n=14/24 for group 0; n = 5/24 for group 1; n= 5/24 for group 2. Visually, all EEG patterns had a discontinuous background with cyclicity. Automated analysis of the data was successful and revealed a mean interburst interval value of 4,5 seconds in the patient group.

## Conclusions

Although the importance of preterm EEG maturation as a potential biomarker of future neurodevelopmental outcome increases, implementation of full EEG in the neonatal department has been limited by technical and practical challenges. EEG caps can overcome some of these issues. In combination with automated analysis, clinical decision making can be facilitated. This offers potential for improvement of clinical care and for future research.

FEATURES OF EARLY CONVENTIONAL ELECTROENCEPHALOGRAPHY THAT PREDICT POOR OUTCOME IN NEONATAL HYPOXIC-ISCHAEMIC ENCEPHALOPATHY (547)

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Introduction /Case Report

The conventional electroencephalogram (cEEG) and magnetic resonance imaging (MRI) are commonly used to investigate neonates with hypoxic-ischaemic encephalopathy. The relationship between cEEG and MRI findings is unclear. Previous studies comparing cEEG and MRI have mostly used continuous cEEG monitoring rather than the 'snapshot' recordings that are more commonly performed in clinical practice. We sought to examine which features of early (first week) cEEG may best predict poor MRI and neurodevelopmental outcomes in neonates with HIE. Our hypothesis was that at least one feature of the initial cEEG done in the first postnatal week would be associated with poor outcomes.

Patients and Methods

We studied infants  $\geq 36$  weeks' gestation who were cooled in Norwich for suspected HIE and who received cEEG within 7 days of birth between Oct 2007 and Oct 2011. We devised a novel cEEG score to assess amplitude, continuity, electrographic seizures, and symmetry for features potentially associated with poor MRI or later neurodevelopmental outcomes. Discontinuity was measured via manual counting of inter-burst interval. Poor outcome was severe pattern of injury on MRI brain scan done within 3 months of birth and/or death in infancy or later major adverse neurodevelopment. MRI scans were independently categorised by two experts blinded to clinical or cEEG data as either Grade 1 (normal or only mild pattern of injury) or Grade 2 (severe pattern of injury). Groups were compared via the  $\chi^2$  test.

Results

23 infants were included. Initial cEEG was on median postnatal day 3 (IQR: 2-3 days). cEEG amplitude and total continuity were graded for all; waking continuity was gradable in 12 infants with clear wakeful periods; electrographic seizures and symmetry were gradable in all but one infant who had an inactive trace. MRI was done in 19 (83%) and neurodevelopmental outcomes were available for 22 (96%) infants. Total cEEG continuity was associated with both poor MRI ( $P=0.03$ ) and later neurodevelopmental outcomes ( $P=0.03$ ): of 5 infants with severely discontinuous traces (inter-burst interval  $>60$  s), 4 died and the 1 survivor had a severely abnormal outcome. The presence of electrographic seizures (4/23; 17%) was also associated with poor MRI ( $P = 0.03$ ) and later neurodevelopmental outcomes ( $P=0.01$ ): 2 died in early infancy and 2 had severely abnormal neurodevelopmental outcomes.

## Conclusions

Severe discontinuity of background activity and the presence of electrographic seizures were early cEEG features found to be predictive of poor MRI and neurodevelopmental outcomes. Amplitude, waking continuity, and symmetry were not of prognostic value in this cohort. A 'snapshot' first-week cEEG provides useful prognostic information in term/near-term neonates who received therapeutic hypothermia.

Brain & Development / Neonatal Brain Injury and Neuroprotection

SYSTEMIC HYPOPERFUSION IN TERM ASPHYXIATED NEWBORNS SUBMITTED TO HYPOTHERMIA:  
CORRELATION WITH CEREBRAL OXYGENATION AND SHORT TERM OUTCOME (585)

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### Introduction /Case Report

Newborns with hypoxic-ischemic encephalopathy (HIE) treated with hypothermia can have haemodynamic instability with poor systemic perfusion. Loss of cerebral autoregulation may turn them vulnerable to decreased cerebral perfusion and oxygenation, which can be associated with an adverse outcome. We aimed to assess the cerebral oxygenation and predicted outcome in newborns with HIE submitted to hypothermia and systemic hypoperfusion.

### Patients and Methods

Term newborns with HIE treated with hypothermia that survived to perform MRI at the second week of life were prospectively studied. Serum lactate measurements were performed regularly during hypothermia. Severe hypoperfusion was defined by lactate levels above 5 mmol/L during the first 24 hours. Cerebral oxygen saturation (rScO<sub>2</sub>) was measured by near-infrared spectroscopy (NIRS) during hypothermia. Short term outcome was predicted by both aEEG pattern at 48 hours and MRI on the second week of life.

### Results

Within 48 studied newborns, 10 (20%) had severe hypoperfusion at 24 hours of hypothermia. Predicted outcome was abnormal in 27 (60%). rScO<sub>2</sub> levels at 2, 4, 6, 8, 10, 12, 14, 16, 18, 20 and 24 hours were similar in patients with or without severe hypoperfusion (mean 80±8% vs 79±14%).

9 (90%) newborns with severe hypoperfusion had abnormal outcome (p<0.05). Positive predictive value for abnormal outcome was 95 % and negative predictive value was 55%.

### Conclusions

In newborns with HIE treated with hypothermia, severe hypoperfusion during the first 24 hours is predictive of abnormal short term outcome, but it is not associated with decreased values of cerebral oxygenation. As these newborns seem to have more severe brain lesions, we hypothesize that their rScO<sub>2</sub> levels reflect both decreased brain perfusion and decreased brain oxygen consumption.

SUDDEN UNEXPECTED POST-NATAL COLLAPSE AND THERAPEUTIC HYPOTHERMIA: A PORTUGUESE NICU EXPERIENCE (600)

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Introduction /Case Report

Sudden unexpected post-natal collapse (SUPC) in healthy newborns (NB) is a rare occurrence but frequently associated with fatal or long-term neurodisability outcomes. In view of limited therapeutic options, and the observed efficacy of therapeutic hypothermia (TH) in the hypoxic-ischaemic encephalopathy (HIE) without serious adverse effects, this therapeutic option has been offered to the NB that suffered SUPC by some neonatal intensive care units (NICU), although not fulfilling the standard criteria. The authors reviewed retrospectively the SUPC cases submitted to TH in their unit regarding their outcome and searching prognostic indicators.

Patients and Methods

Newborns with SUPC needing resuscitation and invasive ventilation, that underwent TH in our unit, were selected over a 55 months period (June 2010 to January 2015). NB performed whole-body cooling at core target temperature 33,5°C for 72h. Data was collected from the clinical files, concerning information on pregnancy and birth, circumstances of the event, analytical surveillance and investigation to exclude a possible underlying disease with septic, metabolic and cardiac workload, aEEG monitoring records, cerebral magnetic resonance imaging (MRI), clinical evolution in the NICU, autopsy in the deceased or evaluation at discharge and follow up.

Results

Seven cases of SUPC were found (6/7 out-born). NB had a median gestational age of 38 weeks (range 36-40), a mean birth weight 3016g (range 2335g-2395g), 3/7 were vaginal delivered (1 forceps). All NB had an Apgar score  $\geq 9$  at 5min and suffered an unexpected collapse at a median 107min of life (range 30min-22h). Five were found in an asphyxiating position, four of them in an early skin-to-skin contact with their mother/father and one in mother's bed. Six mothers were primiparous. Clinically they presented severe encephalopathy. They started TH at mean 228min after SUPC (range 34min-8h). In 2/7 aEEG pattern improved before 36h TH. Cerebral MRI (mean 8 days of life) was normal in 2/7 and lesions of HIE in 5/7. A NB had hypertrophic miocardiopathy (gestational diabetes), in 6/7 no underlying abnormalities were found. The outcome of 5/7 was death and 2/7 survived without neurologic sequella.

Conclusions

There are proven benefits of early skin-to-skin contact but the possibility of occurrence of SUPC in previous healthy NB implies a better surveillance in the first hours of life.

In our sample, most NB who suffered SUPC had poor outcome. Comparing data from this sample of NB submitted to HT, aEEG normalization with sleep-wake cycling before 36h of cooling and normal MRI seems to be related with better outcome.

Table

**Newborn clinical features**

	Initial mean pH	Initial mean BD	Initial mean Thompson Score	Initial aEEG	aEEG sleep-awake cycling ≤ 36h	Cerebral MRI
NB deceased	6,87	22,8	16,2	LV-1 BS-2 FT-2	0	Abnormal
NB survived	7,04	20,1	14,5	DC-1 BS-1	2	Normal

NB-newborn, BD- base deficit, DC- discontinuous, LV- low voltage, BS- burst suppression, FT- flat trace.

BRAIN DAMAGE ASSESSMENT FOLLOWING PERINATAL HYPOXIC-ISCHAEMIA USING AN AUTOMATED PROTOCOL FOR COMBINED REGIONAL ANALYSIS OF THE CEREBRAL BLOOD FLOW AND MR SPECTROSCOPY (616)

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### Introduction /Case Report

Perinatal hypoxia-ischemia (HI) can cause catastrophic alteration of brain metabolism and physiology<sup>1</sup>, resulting in neonatal encephalopathy. Metabolic changes detected using magnetic resonance spectroscopy (MRS) have been used as a reliable predictor of clinical outcome (thalamic Lactate/N-acetylaspartate (tLac/NAA) peak area ratio <sup>2</sup>). Similarly, abnormalities in cerebral blood flow (CBF), reflecting cerebral physiology, have been linked to HI <sup>3,4</sup>. Therefore this study aims to investigate the added value of combining thalamic MRS with automatic regional CBF analysis as a potential biomarker of outcome in HIE.

### Patients and Methods

Ethical approval and informed consent were obtained before the study. We included 14 term neonates with neonatal encephalopathy, who underwent therapeutic hypothermia. MR imaging was performed including: T1, T2 and diffusion-weighted imaging, proton MRS (calculating tLac/NAA) and pseudo-continuous arterial spin labeling (pCASL5 label duration=1.7s, PLD=1.5-2s). Subjects were divided into two groups: tLac/NAA 0.29: high risk of poor outcome (n=5). Raw ASL images were corrected for motion before averaging and CBF quantification<sup>6,7</sup>. CBF was calculated in automatically defined regions (using both an atlas <sup>8</sup> and multi-atlas methods <sup>9</sup>). Differences in mean and variance of CBF values between low- and high-risk groups were analysed.

### Results

All babies included were term (GA 38-41 weeks). They were scanned between 3-7 days of life. Examples of CBF maps and analysis of regional CBF are shown in Figure 1 and 2 respectively. Boxplots show the range, median and interquartile range. In the low risk group, all CBF values are within a tight range for all brain regions (8-47ml/100g/min), whereas in the high- risk group, the range is much broader: (7-128ml/100g/min). In this group, CBF in the lentiform nuclei and parasagittal cortex is especially high. There were statistical differences for CBF in the lentiform nuclei between the high- and low-risk groups (t-test, F-test<0.05) but not in the parasagittal cortex (t-test=0.07, F-test<0.05).

### Conclusions

ASL provides noninvasive physiological information complementing structural scans. An increase in CBF accompanies generally a raise in tLac/NAA, most notably within the deep grey matter nuclei and

parasagittal cortex. This may relate to autoregulation loss in severely affected neonates. The proposed automated method of segmentation/parcellation is more amenable to clinical implementation. We will correlate follow-up data with CBF findings.

Picture

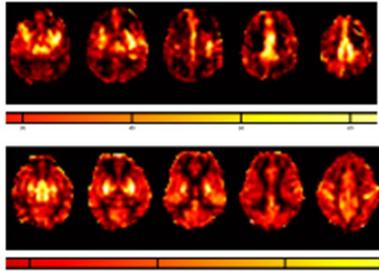


Figure 1. CBF maps of 2 neonates from the high risk group (thalamic Lac/NAA > 0.29)

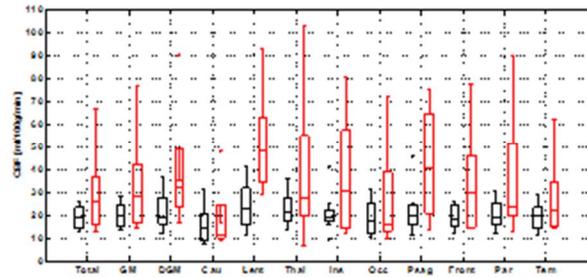


Figure 2. Results of detailed regional CBF analysis; neonates with thalamic Lac/NAA peak ratio below (black) and above (red) predictive value of 0.29

## Brain & Development / Placenta and prenatal factors

Homocysteine, vitamin B12 and folic acid levels in newborns with conotruncal heart defects and their mothers (886)

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### Introduction /Case Report

Folate and vitamin B12 deficiencies as well as hyperhomocysteinemia (HHcy) in pregnant women are related to increased occurrence of congenital anomalies, including critical congenital heart defects (CHD). Homocysteine (Hcy) interferes with epigenetic modifications of DNA structure of histone proteins. Cardiomyocyte migration disorders in association with antioxidant mechanisms dysfunction may lead to conotruncal heart defects (CTDs).

The aim of study was to compare homocysteine, vitamin B12 and folic acid levels in neonates with CTDs and septal heart defects and with control group.

### Patients and Methods

The study group consisted of 37 term newborns with a prenatal diagnosis of CHD, while the control group comprised 20 term and healthy newborns and their mothers.

Blood samples for biochemical measurements (total Hcy, vitamin B12 and folic acid levels) were taken from mother's venous blood and umbilical cord blood immediately after delivery.

### Results

The study involved 20 neonates with CTDs (CoA n=7; TGA n=11; DORV n=2) and 17 newborns with septal defects (AVSD n=4, ASD n=10, VSD n=3).

We observed a significant difference in serum Hcy levels between neonates with CTDs and those with septal defects (11,08 $\mu$ mol/l [SD 5,2] vs 8,91 $\mu$ mol/l [SD 3,9];  $p=0,02$ ) and controls (6,51 $\mu$ mol/l [SD 4,2];  $p<0,001$ ). Moreover, we noted a relevant relationship between mother's Hcy and umbilical folic acid ( $r = -0,36$ ,  $p<0,05$ ), and vitamin B12 levels ( $r = -0,25$ ;  $p<0,05$ ).

### Conclusions

Hyperhomocysteinemia observed in newborns with conotruncal heart defects may suggest the influence of disrupted Hcy metabolism on CTDs development.

Nutrition and gastroenterology / Nutrition of the Very Preterm

DO HIGHER PARENTERAL AMINO ACID AND ENERGY INTAKES AFFECT REQUIREMENTS FOR SODIUM, FLUID AND CIRCULATORY SUPPORT? (414)

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### Introduction /Case Report

We have previously shown that increasing protein and energy intake using a standardised, concentrated, additional macronutrients, parenteral (SCAMP) nutrition regimen improves early head growth in very preterm infants (VPI). This is associated with increased potassium and phosphate requirements. Such a regimen also has the potential to alter sodium, fluid and circulatory support requirements.

### Patients and Methods

**Aims:** To compare requirements for sodium, fluid and circulatory support in VPI receiving either the SCAMP regimen or a control parenteral nutrition (PN) regimen

**Methods:** Control PN was started within 6 hours and infants (<1200g; <29 weeks) were randomised to start SCAMP or remain on control PN. Actual daily nutritional, fluid and electrolyte intake and plasma electrolyte data were collected for day1-14 along with all forms of circulatory support (including fluid bolus, blood products, inotrope use and treatment of metabolic acidosis).

### Results

Infants were randomised (d2-5) to SCAMP (n=74) and control (n=76) groups. Maximum differences in protein/energy intakes were achieved day 5-8. There were no differences in the daily intake or plasma levels of sodium or chloride. There was no difference in daily fluid intake or the use of inotropes, fluid or blood product boluses. Both groups demonstrated mild hyperchloraemia (110mmol/l both groups) peaking on day 4-6. Mean (sd) bicarbonate use (mmol/kg/14d) was 5.3 (9.1) versus 3.8 (5.3) [p=0.19] in SCAMP (65% infants) and control (63% infants) groups respectively.

### Conclusions

Increasing protein and energy intake using the SCAMP nutrition regimen does not affect requirements for sodium, fluid and circulatory support when compared to a control regimen.

Nutrition and gastroenterology / Obesity and risk factors for cardiovascular diseases

## BACTERIAL AND FUNGAL GUT MICROBES IN OBESE CHILDREN: A CASE-CONTROL STUDY (521)

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### Introduction /Case Report

Composition and activity of the gut microbiota co-develop with the host from birth and are subject to a complex interplay depending on the host genome, nutrition, and life-style. With regard to pediatric metabolic disorders, gut microbiota has been poorly studied, although in recent years has emerged as a significant factor involved in obesity [1]. The fungal microbiota (mycobiota) is much less studied and, at least at our knowledge, there is no study in pediatric age evaluating any potential association of mycobiota composition with changes in adiposity [2]. The aim of this case-control study was to evaluate differences in gut microbiota and mycobiota of obese versus normal-weight children.

### Patients and Methods

Twenty-eight obese children, mean (SD) aged 10.03 (0.68), consecutively admitted to Pediatric Department, and 34 age- and sex- matched normal-weight children were included in the study. Body Mass Index (BMI) z-scores were calculated. Obesity or normal-weighting was defined according to WHO criteria[3]. Fasting blood samples were analyzed for insulin and glucose. Insulin resistance was estimated by homeostatic model assessment (HOMA) and defined as HOMA >3.16[4]. Children dietary habits were assessed through a food frequency questionnaire. Abdominal Ultrasonography (US) was performed to evaluate liver echogenicity. Composition and diversity of gut microbiota, coming from stool samples collected, were analyzed by qPCR and denaturing gradient gel electrophoresis (DGGE).

### Results

BMI z-score was 2.9 (0.66) in obese children (O group) and 0.29 (0.79) in normal-weight children (N group) ( $P < 0.001$ ). The 80% of N and the 54% of O were born by vaginal delivery. The 50% of N and the 53% of O were exclusively breastfed for 6 months. Ten obese patients were identified with insulin resistance, 4 of them had increased liver echogenicity. Compared to normal-weight children, obese children had higher dietary intakes of energy and macronutrient. Analysis of DGGE profiles showed high bacterial biodiversity and a lower richness in yeast species. *Akkermansia muciniphyla*, *Faecalibacterium prausnitzii*, *Bacteroides/Prevotella* group and *Candida* were significantly less abundant in obese children ( $P = 0.031$ ,  $P = 0.044$ ,  $P = 0.003$  and  $P = 0.047$  respectively). No significant differences were observed comparing obese children with or without insulin resistance and liver echogenicity.

### Conclusions

Our results are in agreement with recent scientific evidence showing a significant less abundance of *Akkermansia muciniphyla*, *Faecalibacterium prausnitzii* and *Bacteroides/Prevotella* in obese subjects. Shifts of some core microbial species, pre-existing or diet-induced, could actively be part of obesity etiology.

Microbiota analysis could represent a new tool for designing customized diets and improve therapeutic lifestyle strategies.

Nutrition and gastroenterology / Breast feeding

## EARLY PERSISTENT BLOOD EOSINOPHILIA IN NECROTIZING ENTEROCOLITIS: A PREDICTOR OF LATE COMPLICATIONS (458)

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### Introduction /Case Report

Eosinophils infiltrate into intestinal tissue during necrotizing enterocolitis (NEC) and adult bowel diseases. We theorized that epithelial damage releases interleukin-33 and a cascade of cytokines and chemokines that cause eosinophilic activation and recruitment to the bowel after NEC onset. We studied the influence of early persistent blood eosinophilia and medical or surgical complications during NEC.

### Patients and Methods

NEC cases and controls at MU Children's Hospital (2008 - 2013) underwent review. A five point Likert scale measured the severity of NEC during the course of NEC. We utilized a SPSS database for statistical analyses (ANOVA and receiver operator curves [AUC] and confidence intervals [CI] of diagnostic utility).

### Results

Among 50 cases with NEC, Group 1 infants (n = 15) had eosinophilia at <2 days after onset; Group 2 had NEC but no persistent eosinophilia (n = 25). Control infants without NEC and no eosinophilia were matched for birth weight and gestational age (Group 3, n = 46). Group 4 included four preterm infants with infection and ≤ 5 days of eosinophilia. Hematologic review of the four groups defined persistent eosinophilia as ≥ 5% eosinophils for ≥ 5 days after NEC onset [AUC: 0.97, 95% CI (0.92, 1.00), p<.001 for group 1 vs. group 2]. Absolute eosinophil counts were twice as high in Group 1 vs. Group 2 (p = .002). Group 1 had a mean duration of eosinophilia of 8 days vs. one day in Group 2 (p<.001). The NEC severity score was 3-fold higher in Group 1 vs. Group 2 (p<.001). Group 1 infants were 8 times more likely to have hepatic fibrosis or intestinal strictures compared to group 2 (p = .02).

### Conclusions

Early persistent blood eosinophilia is not currently a predictor of complications after onset of NEC. This biomarker identifies immature infants (group 1: BW = 911 ± 422 g & GA = 27 ± 3 wk) at high risk for adverse outcomes during the convalescence from NEC.

Nutrition and gastroenterology

## TRANSPILORIC FEEDING SHORTENS TIME TO FULL ENTERAL FEEDS IN LEFT CONGENITAL DIAPHRAGMATIC HERNIA (576)

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### Introduction /Case Report

Congenital diaphragmatic hernia (CDH) is an anomaly of the development of the diaphragm that allows the abdominal organs to enter the thorax. Respiratory and cardiovascular morbidity are the main determinants of short-term mortality, but nutrition is one an important mid-term problem during admission. Enteral nutrition is usually started through tube feeding, but no studies have addressed whether the gastric (GT) or transpiloric (TPT) route could be more advantageous for these children. Our aim was to assess the time needed to reach full enteral nutrition depending on the side of the hernia, the placement of the feeding tube and the associated complications.

### Patients and Methods

This was a retrospective study performed by reviewing clinical charts of patients with CDH admitted to our unit between 2007 and 2014. Patients with lethal chromosomal abnormalities and those that died before receiving any enteral nutrition were excluded. Variables reflecting severity of illness, nutritional support and complications were recorded. The groups were compared according with the laterality of the defect - right (RCDH, n=15) or left (LCDH, n=83) CDH- and the route of feeding (GT/TPT). Because most RCDH (93.3%) received GT feeding, feeding outcomes for GT were compared between RCDH and LCDH, while GT and TPT were compared within the LCDH group. The database was analyzed with SPSS® v22.0 statistical package.

### Results

98 patients were included, with a mean gestational age (GA) of  $37.9 \pm 2.5$  weeks; 55 (56%) were male and 7 (7%) died during admission. Most (85%) defects were on the left side. Babies with RCDH had a GA 1.9 weeks lower than LCDH ( $p 0.007$ ) and had a tendency to be less clinically ill. Forty-six (55%) LCDH patients had a TPT and there were no differences with the GT-LCDH regarding GA or anthropometry at birth, although TPT-LCDH had a tendency to require more support ( $p 0.079$ ). Within the GT group, children with RCDH took fewer days to full enteral feeding ( $16 \pm 5$  vs  $27 \pm 15$ ,  $p 0.001$ ), with multivariate analysis suggesting that this was due to their lower clinical severity. In the LCDH group, TPT babies reached total tube enteral feeding earlier ( $18 \pm 8$  vs  $27 \pm 15$  days,  $p 0.007$ ), in spite of being more severely ill, and they suffered less feeding-associated complications (17% vs 38%,  $p 0.036$ ).

## Conclusions

Our results suggest that placing a TPT in patients with LCDH shortens the time to full enteral feedings, and this could lower the incidence of complications. Babies with RCDH usually have a more benign course and good digestive tolerance even through a GT.

## Epidemiology / Nosocomial infection and colonization

### HEALTHCARE-ASSOCIATED CONJUNCTIVITIS IN NEONATES: AN EPIDEMIOLOGICAL STUDY OF INCIDENCE, ETIOLOGY AND RISK FACTORS FROM A TERTIARY CARE HOSPITAL IN INDIA (012)

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#### Introduction /Case Report

Healthcare-associated conjunctivitis (HAC) is one of the commonest healthcare-associated infections in neonates. It is known to be associated with serious sequelae; both local such as blindness, and systemic such as meningitis. The absence of neonate specific diagnostic criteria, administration of empirical antibiotics without undertaking cultures and general ignorance about the possible serious sequelae has resulted in very few comprehensive studies describing the disease entity. We conducted this one-year prospective study at Lady Hardinge Medical College, New Delhi, India to determine the incidence, the etiological profile and the risk factors associated with neonatal HAC.

#### Patients and Methods

Study inclusion criteria included age 0-28 days, hospital stay >48 hours, no signs of sepsis at the time of admission, and no prior hospitalization. Diagnosis of HAC was established based on the CDC guidelines. Conjunctival swabs were obtained on all neonates that showed suggestive clinical signs such as redness or discharge from the eye; and were processed for the detection of bacterial, viral and fungal pathogens using standard protocols. Antimicrobial sensitivity was tested using CLSI disc diffusion method. Twenty-eight potential risk factors were evaluated to determine if they were associated with the development of neonatal HAC in our study. The outcome of neonatal HAC was compared in aspects of mortality rate and length of hospital stay.

#### Results

We detected 24 cases of neonatal HAC among 591 eligible neonates in our study (incidence: 4.1 per 100 admissions). 71% (17/24) of the cases occurred during days 3-7 of hospitalization. Of the 20 culture positive cases, *Escherichia coli* (35%) and *Staphylococcus aureus* (25%) were the most commonly isolated pathogens. Gram-negative bacteria (GNB) predominated (71%; 10/14) in the first 7 days of hospitalization; with most isolates after day 7 being gram-positive (67%; 4/6). Viral or fungal etiology was not established in any case. On multivariate analysis, intubation at birth ( $P=0.046$ ; 95% confidence interval {CI}, 1.02-7.37) and orogastric feeding ( $P=0.029$ ; 95% CI, 1.11-6.78) were found to have a statistically significant association with the development of neonatal HAC. Average length of hospital stay increased from 9.6 to 20.8 days for neonates diagnosed with HAC ( $P<0.001$ ).

#### Conclusions

Neonatal HAC is a common entity especially during first week of hospital stay. Predominance of GNBs during early hospitalization suggests a possible maternal birth canal origin. Local insults such as intubation

and orogastric tube insertion probably contribute to the development of neonatal HAC, warranting extra eye care. Standardized case definition and awareness of the possible complex outcomes are required for better future surveillance.

## Brain & Development / Early developmental care

Prediction of cognitive and language impairment in children born very preterm: Two decades of research - what do we know? (139)

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## Introduction /Case Report

Surviving children born very preterm (VPT;  $\leq 32$  weeks gestation) or with very low birth weight (VLBW;  $\leq 1250$ g) are at high risk of neurodevelopmental problems, including cognitive and language impairment. There is a large literature reporting risk factor analyses for poor long term outcome in this population, which to date has not been formally summarised.

## Patients and Methods

We performed a systematic review of multivariable risk prediction models for cognitive and language impairment in children born VPT or with VLBW after 1990 using the Medline, Embase and Pyscinfo databases. We extracted key information on study design, outcome definition, risk factor selection, model development and reporting, and conducted a risk of bias assessment. The strength of evidence for the prognostic value of risk factors identified was summarised graphically. The methods have previously been published in a review protocol (<http://www.crd.york.ac.uk/PROSPERO/>), registration number CRD42014006943. Results were reported according the PRISMA guidelines.

## Results

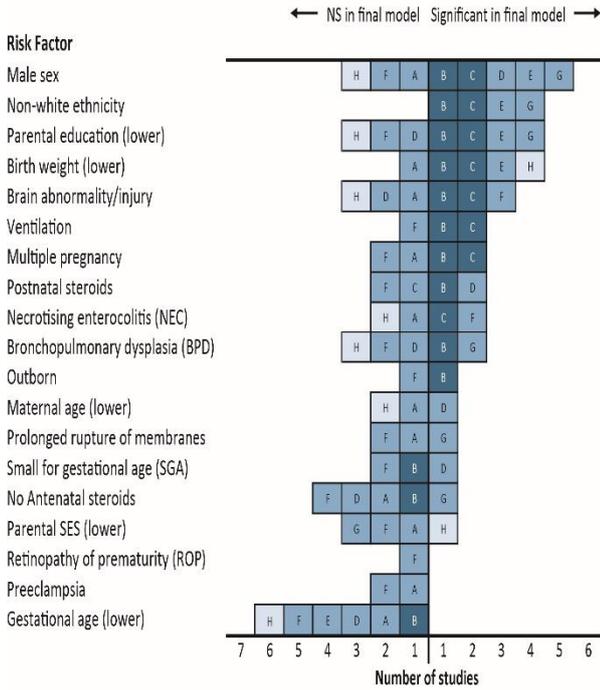
31 studies comprising 98 risk factor models were included. There was evidence that male sex, non-white race, lower parental education, lower birth weight and brain injury during the neonatal period were predictive of global cognitive dysfunction in infants under 5 years. In older children, only the influence of parental education was sustained. Male sex was also predictive of language development in early infancy, but not in middle childhood. Gestational age was a poor predictor of cognitive outcome in this population with restricted gestational age range of  $\leq 32$  weeks.

## Conclusions

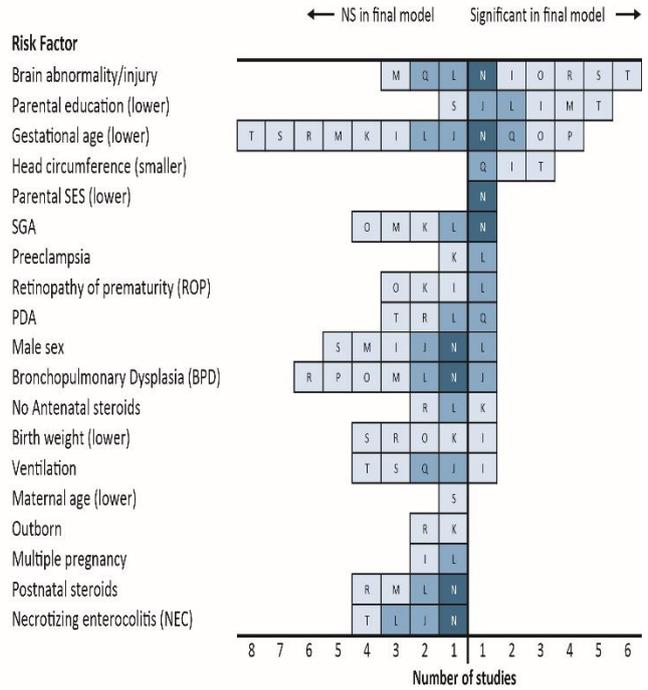
The findings suggest that the influence of perinatal risk factors diminish over time and that environmental factors become more important. It is difficult to isolate cognitive outcomes from motor and neurosensory impairments, and the strategy used for dealing with children who are too low functioning to be tested has implications for risk prediction.

# Picture

Age at assessment <5 years (n=8 studies)



Age at assessment ≥5 years (n=12 studies)



## Brain & Development / Neonatal Brain Injury and Neuroprotection

Neonatal Cerebral Function Monitoring (CFM): A survey of its provision and usage in practice throughout the East of England Neonatal Network (132)

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### Introduction /Case Report

Cerebral Function Monitoring (CFM) provides useful information to assess seizure activity in neonates and monitor severity of encephalopathy. CFM can also help guide management of babies in whom there is evidence of perinatal distress, but where a diagnosis of Hypoxic Ischaemic Encephalopathy (HIE) is uncertain. A regional guideline exists for the use of CFM in the East of England Neonatal network. Our objectives were to 1) survey the provision and practical use of CFM in neonatal units in the region, 2) audit usage of the regional guideline 3) Identify variations in practice and barriers to CFM use.

### Patients and Methods

Nursing and Consultant leads in all neonatal units in the region (n=17) were sent an online survey. The key questions included: a) whether their unit had CFM, b) whether CFM was used in clinical practice c) whether regional guidelines were used, d) indications for CFM use, e) the availability of staff competent in setting-up and interpreting CFM and f) barriers impeding the use of CFM.

### Results

All 17 neonatal units in the region provided at least one completed survey, 59% (n=10) contributing both consultant and nurse responses.

35% (n=6) of units did not have a CFM. A commonly cited reason (fig 1) was insufficient patient numbers to justify clinical need - 67% (n=4).

Of the 65%(n=11) units that possess a CFM, 90% (10/11) report using it regularly. One unit used CFM rarely - citing lack of trained medical and nursing staff. Of the 10 units that use CFM, 60% (6/10) use the regional guideline, 10%(1/10) use a local CFM guideline and 30% (3/10) had no guideline.

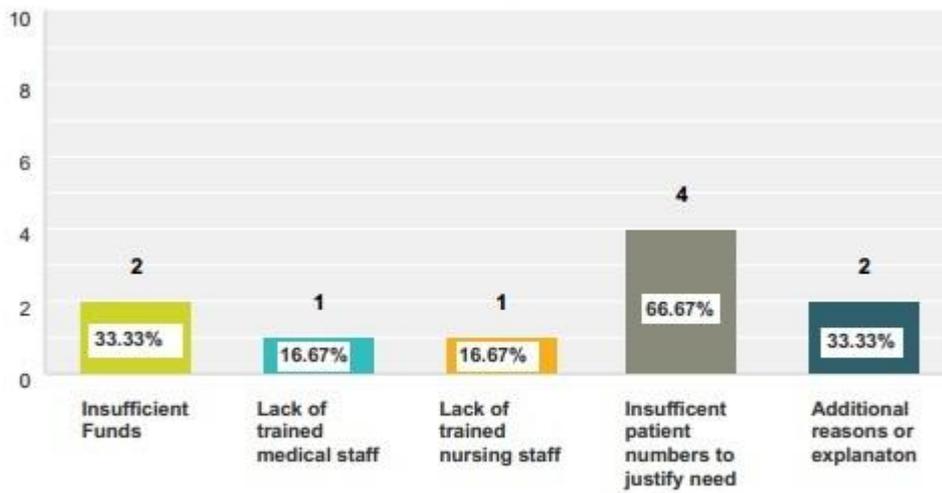
Only 20% (2/10) of units using CFM regularly reported no difficulties. 40%(4/10) of units using CFM reported that they do not have 24 hour availability of staff at any level who are able to either set up or interpret CFM. 40% of units reported nursing and clinical staff were not confident with CFM.

### Conclusions

The majority of neonatal units in the region either do not use CFM or cannot provide a 24 hour service. Staff confidence in setting up and interpreting CFM was cited as a barrier to its use. We propose a regional education programme to raise awareness of the utility of CFM in the neurological assessment of neonates, to increase awareness of regional guidelines and provide training of the practicalities of setting up and interpreting CFM.

Picture

### 35% of units without CFM (n=6): reasons given



#### Additional reasons or explanation

Awaiting Funding

Not all clinicians convinced of clinical need Babies get transferred out for cooling

Epidemiology / Host responses and early diagnosis of infection

DOES NEWBORNS WITH FEVER SHOULD ALWAYS BE HOSPITALIZED? NEW PROTOCOL FOR MANAGEMENT OF OUTPATIENT FOLLOW-UP OF NEWBORN WITH FEVER (312)

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### Introduction /Case Report

Febrile infants younger than 28 days are at risk for serious bacterial infections and often undergo extensive laboratory investigation and hospitalization. There was no protocol has been universally adopted in outpatient follow-up of newborn with fever. The aim of the study is to analyze effectiveness of new protocol for identifying serious bacterial infection (SBI) in newborns and compare our protocol with Boston, Rochester and Philadelphia protocols.

### Patients and Methods

The study was designed as prospective and observational. The neonate admitted with fever (rectal T.  $\geq 38$  0C) and  $\geq 35$  gestational weeks without any chronic illness were included study. All patients were hospitalized and prophylactic antibiotherapy were started and discharged after 72 hours if cultures were negative.

### Results

Out of the 165 patients included in the study, 64 of them ( %37,8) were diagnosed with Serious Bacterial Infection. 69 of the patients (%41,8) could not be classified, 24 of the patients (%14,5) were diagnosed with dehydration and 26 of the patients (%15,7) were diagnosed with urinary tract infection. While the negative predictive value of Boston, Philadelphia and Rochester protocols were %80,9, %83,1 and %75,5. The negative predictive value of Şişli Etfal protocol turned out to be %83,8. The Philadelphia protocol had highest value when all protocols were evaluated from the LR(+) aspect. In identifying of serious bacterial infections the highest sensitivity and highest negative predictive value and lowest LR (-) values were observed in the Sisli Etfal protocol.

### Conclusions

In conclusion we identified Sisli Etfal protocol had the highest negative predictive value among the other protocols. This data shows that %83,8 of the patients that are identified with a low risk of SBI do not have SBI according to the Sisli Etfal protocol.

Circulation, O<sub>2</sub> Transport and Haematology / Placenta and prenatal factors

## OXIDATIVE STRESS IN UMBILICAL VEIN AND ARTERY OF HEALTHY NEWBORNS . (685)

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### Introduction /Case Report

With advancing gestation, Po<sub>2</sub> and pH fell significantly, while Pco<sub>2</sub> concentration increases in both umbilical artery and vein blood. The etiology of these physiological changes is still unknown. Likely they may be the consequence of the fast growth of fetal tissues and the progressive decline in uterine and umbilical blood flows when normalized to fetal weight . The anaerobic metabolism enhanced by fetal hypoxia increases lactate production, decreases pH value and generates free radicals.[1]. We test the hypothesis that an oxidative stress (OS) occurs as physiological event in normal pregnancies.

### Patients and Methods

Umbilical artery and vein plasma samples were collected from 35 healthy term newborns born at A.O.R.N. Santobono di Napoli from healthy mothers with normal gestational course, by elective cesarean section due to maternal anxiety. Parent consent was obtained. Blood gas analysis was carried out immediately after delivery. Samples aliquotes were added with butylated hydroxytoluene and stored at -80°C until analysis.

Plasma F<sub>2</sub>-Isoprostanes (F<sub>2</sub>-Isops), recognized biomarkers of OS, were measured according to the methods previously reported by Casetta B. et al. This method is based on a light deproteinization with acetonitril followed by an LC-MS/MS analysis. Statistical analysis was performed using IBM SPSS Statistic 20.

### Results

There was no differences between cord artery and vein regarding F<sub>2</sub>-Isops levels (34,4±21,1 vs 33,9±18,6 micromol/L p=0.813). Statistically significant correlations were found between F<sub>2</sub>-Isops levels and pCO<sub>2</sub> values (r<sup>2</sup>=0.148; p=0.025) and between F<sub>2</sub>-Isops levels and pH values in the umbilical vein blood (r<sup>2</sup>= -0.144; p=0.027). F<sub>2</sub>-Isops levels correlated positively with pCO<sub>2</sub> values (r<sup>2</sup>=0.205; p=0.007) and negatively with pO<sub>2</sub> values (r<sup>2</sup>= -0.264; p=0.005) in umbilical artery blood.

### Conclusions

The lack of changes in OS values in fetal circulation of term newborns from normal pregnancy suggest that a physiological OS exists during pregnancy likely useful for the fetal growth in normal conditions. The several correlations found between pO<sub>2</sub>, pCO<sub>2</sub>, pH and F<sub>2</sub>-Isops indicates that blood gas changes may modify OS. Low oxygen, low ph and high CO<sub>2</sub> increase OS in cord blood . The role of placenta in modulating OS needs to be clarified in pathological pregnancies.

Circulation, O<sub>2</sub> Transport and Haematology / Placenta and prenatal factors

## A NEW CLASSIFICATION FOR METHODS OF REDISTRIBUTION OF PLACENTAL BLOOD AT BIRTH (593)

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### Introduction /Case Report

Redistribution of placental blood at birth has been the subject of many studies in the past decades. Benefits include better postpartum adaptation, higher haemoglobin values and improved iron storage at 3-6 months in term babies, less IVH and NEC in preterm babies. Redistribution is achieved by a variety of methods including delayed cord clamping, milking of the cord before and after cutting the cord or a combination. Often the methods used are only referred to as “delay” in cord clamping or “milking” of the cord without precisely recognizing the potential differences between the exact modes. The aim of our study was to develop a classification system to precisely describe the mode used.

### Patients and Methods

A retrospective analysis of randomized studies describing different ways of redistributions of placental blood to the baby at birth was performed. Published studies were included if they met the quality criteria to be included into two recently published Cochrane Reviews (McDonald 2013, Rabe 2012) and one meta-analysis on umbilical cord milking (Al-Waissa 2015) describing the effects of placental redistribution of blood on preterm and term babies. Items to be considered were position of baby in regard to level of placenta (P), immediate (C) or delay in cutting the cord (D), time delay in seconds (s), number of times (x) milking the cord (M) and resuscitation with the cord intact (R).

### Results

36 trials met the inclusion criteria for meta-analysis. A five item score system was developed (see table 1). In a second step the scoring system was tested on published studies to check on its applicability (see table 2).

### Conclusions

The new classification system will provide a useful and structured description tool to researchers and clinicians who are studying or implementing a mode of redistribution of blood. It will enable to compare the different methods used in research studies in a precise way.

Table

**Table 1:** Suggested Classification of Redistribution of Placental Blood at Birth

Category Abbreviation	Explanation	Comment
<b>Cxs</b>	Clamping the cord immediately (within 20 seconds of delivering the baby)	The time frame of 20 seconds was defined as “Immediate” in the Cochrane reviews
<b>xM</b>	x number of times the umbilical cord Milking from the placenta towards the baby was performed	Umbilical cord milking has been described between one and five times
<b>Dxs</b>	Delay/Deferred clamping of the cord with times (x) in seconds	Times range from 30 seconds in preterm babies to 300 seconds in term babies. A delay of 60 seconds would be coded as <b>D60s</b> . Time to cord stops pulsating is sometimes observed.
<b>P a, b, l</b>	Position of the baby in relation to the Placenta, <b>a</b> above, <b>b</b> below, <b>l</b> at level	Discussion is ongoing about the effects of gravity in delayed cord clamping
<b>R</b>	Resuscitation of the baby started before clamping the cord	Only a few studies have looked into this so far but interest is increasing

**Table 2:** Examples of applying the Classification to published studies

Study	Study groups	Coding
<b>Rabe 2011</b>	Control group 30 seconds cord clamping time, preterm baby held below level of placenta	D30sPb
	Milking group four times towards baby with cord intact, preterm baby held below level of placenta	D4MPb
<b>Al-Tawil 2012</b>	Control group term babies immediate cord clamping within 15 seconds, babies held on mothers abdomen	C15sPa
	Delayed group had cord clamped after 3 minutes, babies placed on mothers abdomen	D180sPa
<b>Andersson 2011</b>	Control group term infants early cord clamping within 10 seconds	C15sPb
	Delayed group had cord clamped after 180 seconds, baby was held below level of placenta for 30 seconds, then placed on mothers abdomen	D180sP30sb150sa
<b>Upadhyay 2013</b>	Control group of infants > 34 weeks gestation, immediate clamping within 30 seconds, position with regard to placenta not mentioned	C30s
	Milking group cord clamped within 30 seconds like control group and cord length of 20 cm milked 3 times towards infant on the resuscitaire	C30s3M

## Epidemiology

### ADRENAL HAEMORRHAGE IN TERM NEONATES: A RETROSPECTIVE STUDY FROM THE PERIOD 2001-2013 (304)

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## Introduction /Case Report

The aim of our study was to assess the incidence, risk factors and clinical presentations of neonatal adrenal haemorrhage (NAH) in uncomplicated, singleton, term deliveries.

## Patients and Methods

A retrospective analysis of 26,416 term neonates delivered between 2001 and 2013, and screened with abdominal ultrasonography.

## Results

Of the 26,416 neonates, 74 (0.28%) displayed NAH; the male/female ratio was 1.55:1. Vaginal delivery was significantly more frequent than caesarean section among them (71 vs. 3; 95.9% vs. 4.1%). Unilateral bleeding occurred on the right side in 36 (48.7%), and on the left in 34 (45.9%), without a significant difference; bilateral haematomas were found in 4 cases (5.4%). The most common risk factors were macrosomia (16, 21.6%) and fetal acidaemia (23, 31%), while 4 (5.4%) neonates exhibited pathological acidaemia. Clinical presentations included jaundice in 37 (50%), anaemia in 6 (8.1%) and an adrenal insufficiency in only 1 (1.3%) case. In 3 cases, neuroblastoma was diagnosed.

## Conclusions

Vaginal delivery, macrosomia and fetal acidaemia are the most important risk factors for NAH. The adrenal glands on both sides were similarly involved. In the healthy neonates with NAH, the clinical presentations were mild, with spontaneous regression. Differentiation of NAH from tumours is of considerable importance.

## Brain & Development / Neurodevelopmental Outcome

### ASSESSMENT OF ASSOCIATION BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LOW BIRTH WEIGHT IN 5 TO 10\_ YEAR OLD CHILDREN (118)

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#### Introduction /Case Report

ADHD is one of the most common childhood-onset psychiatric disorders that probably have relation with perinatal and postnatal complications.

Objective: to Assessment of association between ADHD and Low Birth Weight among 5-10\_ year old children.

#### Patients and Methods

this study is a cross-sectional study that was performed on 700 children at the age of 5 to 10 years selected through convenient sampling in pediatrics clinic of Dr. Sheikh hospital in 2009-2010.

Data were collected using 10-item parent Canners questionnaire and semi structural diagnostic interviews based on DMS-IV diagnostic criteria of ADHD in two group A and B (A: birth weight  $\leq$  2500gr and B:birth weight  $>$  2500gr ). Each group contains 350 children.

#### Results

700 cases (364 male & 336 female) were included. the number of low birth weight cases who had ADHD was 1.3 times the number of control cases who had birth weight upper 2500gr but it wasn't statistically significant ( $P=0.058$ ). The prevalence of ADHD according to the parents report was 17.3% (68.6% male, 31.4% female). Factor such as gender, history of admission to neonatal intensive care unit (NICU) and history of head trauma in infancy were shown to act as associated factor for ADHD( $P=0.0001$  ,  $P=0.002$ ,  $P=0.031$  respectively). Other risk factors didn't associate with ADHD.

#### Conclusions

according to our findings low birth weight is not a significant risk factor for ADHD, but there is an association between Male sex, history of admission to NICU, history of head trauma in infancy and ADHD.

Keywords: ADHD, LBW, prematurity

## Epidemiology / Host responses and early diagnosis of infection

Integrin CD11b plus IL-8 as early inflammatory markers in group B streptococcal neonatal sepsis. A bench study of stimulated human umbilical cord blood (420)

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### Introduction /Case Report

Non-specific signs of neonatal group B streptococcal (GBS) sepsis can quickly proceed to a life-threatening condition, and many newborn infants are being treated with antibiotics albeit microbiological evidence of infection is absent and clinical signs are obscure. Better diagnostic tools are warranted.

### Patients and Methods

We included 21 umbilical cord blood samples from healthy term pregnancies without signs or risk factors for infection. Whole blood samples were separately stimulated for 2h with a GBS isolate from a patient (GBS III) and a GBS type strain (GBS Ia). Non-stimulated blood samples served as controls. Leukocytes were analysed for inflammatory surface markers (CD11b, CD64, TLR2, TLR4 and TLR6) by flow cytometry. Soluble markers in plasma (interleukin (IL) -6 and -8; interferon- $\gamma$ -inducing protein (IP) -10 and procalcitonin) were analyzed with enzyme-linked immunosorbent assay. The Area Under the Curve (AUC) with 95% confidence interval (CI) was estimated for each of the markers.

### Results

GBS stimulated samples had marked increases in their surface receptors and cytokine responses compared with the non-stimulated controls. Procalcitonin was not higher than in control samples. The AUC was generally higher for GBS III stimulated than GBS Ia stimulated samples. Only IL-6 and IL-8 displayed an AUC approaching 0.8 for both GBS serotypes with a  $p < 0.001$ . CD11b and TLR2 was the leukocyte surface markers with the highest AUC-values for both GBS serotypes.

### Conclusions

Our findings underscore the complex role of inflammation in GBS infection, and confirm the predictive value of elevated IL-6 and IL-8. CD11b and TLR2 may also be useful indicators of early GBS-infection in the newborn infant.

Circulation, O<sub>2</sub> Transport and Haematology / Systemic circulation and cardiac output

## FEASIBILITY OF PULSE OXIMETRY SCREENING FOR CRITICAL CONGENITAL HEART DEFECTS AFTER HOME BIRTHS AND EARLY DISCHARGE IN THE NETHERLANDS (471)

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### Introduction /Case Report

Pulse oximetry (PO) screening for critical congenital heart defects (CCHD) has been proven to be accurate and cost-effectiveness and is being increasingly implemented worldwide. Feasibility, accuracy, and cost-effectiveness of the screening in the unique Dutch healthcare system with homebirths and early discharge is unknown. We aimed to assess the feasibility of PO screening for CCHD in the Netherlands.

### Patients and Methods

From October 2013 a feasibility study was performed in the Leiden region. At home or in hospital pre and post ductal SpO<sub>2</sub> are measured  $\geq 1$  hour after birth in term low-risk infants using Nellcor PO [figure 1]. The measurement is repeated at day 2 or 3. Infants with positive screenings were assessed at the pediatric department and echocardiography was performed in case of persistent abnormal SpO<sub>2</sub>. Screening percentage in infants with obtained parental consent, median SpO<sub>2</sub> in the first 3 hours, and false positive (FP) rate were calculated.

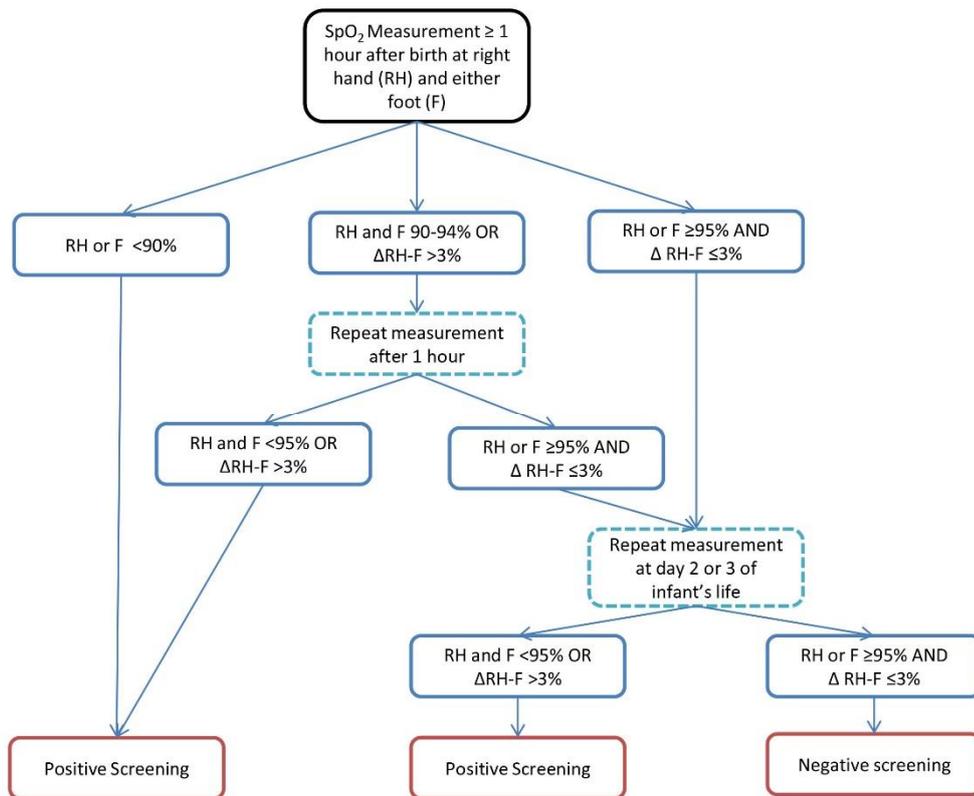
### Results

In a one-year period 3059 infants were screened, accounting for 99% of the infants with parental consent. Median (IQR) time points of the measurements were 1.8 (1.3-2.8) hours and 37 (27-47) hours after birth. Median pre- and post-ductal SpO<sub>2</sub> within the first hour after birth were both 99% (98-100% resp. 97-100%). No CCHD was detected. FP rate was 1.1% overall and 0.6% in the first hours after birth. Significant pathology was found in 48% of FP screenings (78% of FP in first hours, 13% at day 2 or 3).

### Conclusions

This is the first European pilot study assessing CCHD screening in a country with home birth and early discharge from hospital. In this setting CCHD screening is feasible and detects potential life-threatening pathology in newborns. Median pre and post ductal SpO<sub>2</sub> in the first hour of life is already 99%

Picture



Nutrition and gastroenterology / Obesity and risk factors for cardiovascular diseases

## PRENATAL MARKERS OF NEOANTAL FAT MASS, A SYSTEMATIC REVIEW (141)

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### Introduction /Case Report

The worldwide increasing prevalence of obesity and features of metabolic syndrome in children leads to higher morbidity and mortality rates at early ages. The 'fetal origins hypothesis' postulates that environmental influences during conception and pregnancy are able to affect offspring phenotype with lifelong effects. Recognition of fetuses at risk for neonatal adiposity may enable early interventions to improve long-term health. The aim of this study is to: 1) provide a systematic review of the literature on studies on prenatal markers of neonatal fat mass, and 2) appraise the clinical applicability of the assessed markers.

### Patients and Methods

A systematic literature search was conducted to identify studies on prenatal markers of neonatal fat mass. Inclusion criteria were 1) original research papers, written in English, 2) variable, measurable prenatal markers (no static parameters such as parity and age) and 3) neonatal fat mass measurement within one month after birth, using the four-compartment model, MRI, DXA or air displacement plethysmography. Two reviewers independently performed study selection, assessment of methodological (QUADAS-II) and statistical quality and appraisal of clinical applicability. Disagreements were solved by discussion and consensus. Potential relevant markers were defined as markers assessed in more than one study of moderate or high methodological and statistical quality in a sample size above 50.

### Results

Of 2333 studies identified by the search strategy, 16 studies were included. All studies were published between 2008-2015. Only four studies were of both methodological and statistical moderate or high quality. Due to substantial heterogeneity meta-analysis of the data was not possible. Prenatal markers investigated include maternal characteristics, ultrasound measurements and biochemical markers, all assessed in the second and third trimester of pregnancy. Markers of interest were maternal BMI, fasting glucose and HbA1c, all with conflicting results. Interpretation of these results was difficult because of major differences in timing of measurements and statistical analysis. Clinical applicability was appraised poor for all parameters, due to small differences detected using these parameters compared to wide distribution of normal neonatal fat mass.

### Conclusions

Although significant associations were found, no useful marker has been identified to date, due to poor methodological and statistical quality, inconsistent results and poor appraisal of clinical applicability. Remarkably, no markers in the periconceptional period have been studied. More research is warranted for

development and validation of clinical applicable techniques for early identification of fetuses at risk for chronic diseases.

## Brain & Development / Neonatal Brain Injury and Neuroprotection

### IN PRESENCE OF DEHYDROEPIANDROSTERONE, 17 $\beta$ -ESTRADIOL HAS NO ADDITIONAL NEUROPROTECTIVE EFFECTS IN HYPEROXIA-INDUCED CELL DAMAGE OF IMMATURE GLIAL CELLS (135)

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#### Introduction /Case Report

Hypoxia/ischemia, inflammation, prematurity itself, and particularly hyperoxia contribute to the extent of impaired neurodevelopment in preterm infants.

Preterm birth leads to disruption of the placental supply of 17 $\beta$ -estradiol (E2) and progesterone. This led to the idea to replace both steroids for mimicking intrauterine conditions to improve neurodevelopmental outcome and to protect in case of complications. However, preliminary clinical studies did not find improved neurological outcome. We hypothesize that the reason is the persistent high postnatal production of fetal zone steroids (mainly dehydroepiandrosterone (DHEA)) until term, which serve as ligands for estrogen receptors.

#### Patients and Methods

Primary immature oligodendrocytes (PDGFR $\alpha$ +MBP-; OL) were pretreated with in DMSO dissolved E2, DHEA, estrogen receptor (ER)-  $\alpha$  and - $\beta$  antagonist ICI 182,780 (ICI), the non-classical ER G protein-coupled estrogen receptor (GPER) agonist G1 and its antagonist G36 for 12 hours (h) (Table). Afterwards cells were exposed to hyperoxia (80% O<sub>2</sub>/ 5% CO<sub>2</sub>) for 12h. The immature astroglial cell line C6 (S100 $\beta$ +GFAP-) was preincubated 2h with the indicated compounds and afterwards exposed to hyperoxia for 48h.

To assess viability, the MTT assay was used for C6 cells. In this assay MTT, a yellow tetrazole, is reduced to purple formazan in living cells. For OLs the LDH assay was used. It measures the release of the enzyme lactate dehydrogenase (LDH) of dead cells.

#### Results

E2 prevented hyperoxia-induced apoptotic cell death in OLs and C6 cells (A+B). In OLs protection is mediated by classical ER- $\alpha$  and/ or - $\beta$  (A). In C6 cells protective effects were mediated via classical ERs as well as the non-classical ER GPER, being the most effective if both types of receptors mediating its effects (B).

DHEA was able to prevent cell death in OLs and C6 cells, but to a lower magnitude as E2 (A+C). In C6 cells, most of the protection was blocked with ICI pointing towards classical ERs (C).

When E2 and DHEA were added at the same time point, we found protection but no synergistic effects. With ICI the protection was blocked accounting for classical ERs (D).

Difference from controls (DMSO) were indicated by \* P<0.05, \*\* P<0.01 or \*\*\* P<0.001; difference from (A+B) E2-treated (C) DHEA-treated or (D) DHEA + E2-treated cells were indicated by # P<0.05 or ### P<0.001; (n $\geq$ 3).

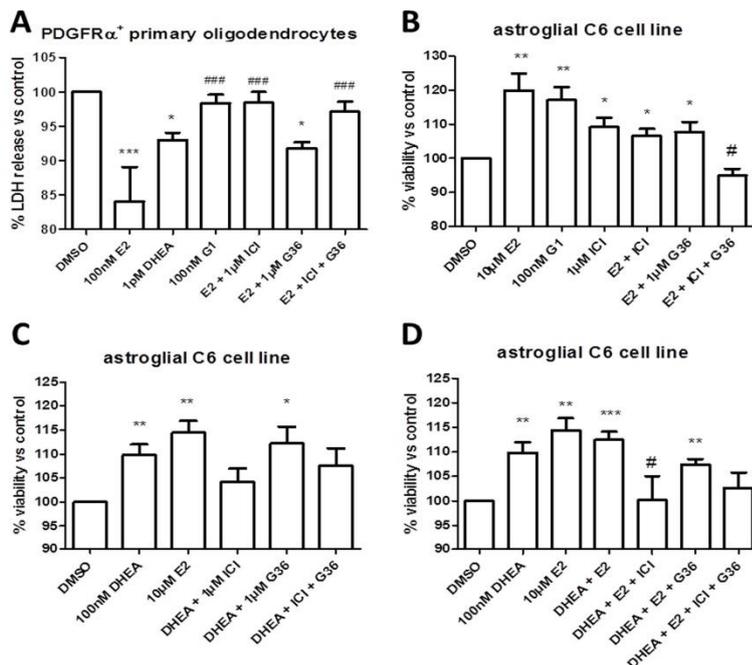
## Conclusions

E2 and DHEA were neuroprotective in hyperoxia-induced cell damage in both immature cell types. Co-treatment did not increase protection, presumably because DHEA activated predominantly classical ERs. Therefore, E2 supplementation may not be beneficial with respect to neuroprotection because fetal zone steroids are circulating in the  $\mu\text{M}$ -range until term in preterm infants. Further investigations are required before clinical studies get started.

Table

compound	abbreviation	concentration	effect on specific receptors
17 $\beta$ -estradiol	E2	as indicated	ER- $\alpha$ , - $\beta$ and GPER agonist
dehydroepiandrosterone	DHEA	as indicated	
ICI 182,780	ICI	1 $\mu\text{M}$	ER- $\alpha$ and - $\beta$ antagonist, but GPER agonist
G1	G1	100nM	selective GPER agonist
G36	G36	1 $\mu\text{M}$	selective GPER antagonist

Picture



### Determining the necessity of estrogen receptors (ER) for 17 $\beta$ -estradiol (E2) and dehydroepiandrosterone (DHEA)-mediated cytoprotection.

(A) PDGFR $\alpha^+$  primary oligodendrocytes were preincubated 12h with the indicated compounds and afterwards exposed to hyperoxia for 12h. Cells were examined for survival using LDH-Assay. Treatment with ICI or G36 alone did not influence survival (data not shown). (B, C, D) Astroglial C6 cells were preincubated 2h as indicated and afterwards exposed to hyperoxia for 48h. Viability was assessed using a MTT assay. Treatment with G36 alone did not influence survival (data not shown). For co-treatment, E2 and DHEA were added at the same time point.

Significant difference from control values (DMSO) were indicated by \*  $P < 0.05$ , \*\*  $P < 0.01$  or \*\*\*  $P < 0.001$ ; significant difference from (A+B) E2-treated (C) DHEA-treated or (D) DHEA + E2-treated cells were indicated by #  $P < 0.05$ , ##  $P < 0.001$  or ###  $P < 0.001$ ; (n $\geq$ 3).

## Brain & Development / Early developmental care

MORBIDITY AND NEURODEVELOPMENTAL PROGNOSIS IN A PROSPECTIVE SAMPLE OF 10140 NEAR TERM PREMATURE INFANTS (34 0/7 TO 36 6/7 WEEKS) FOLLOWED UP TO 1 YEAR OF CORRECTED AGE IN AN OUTPATIENT KANGAROO MOTHER CARE PROGRAM (KMCP) AT BOGOTA, COLOMBIA. (254)

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## Introduction /Case Report

Low birth weight (LBW) deliveries are highly prevalent, particularly in middle and low income countries (12% in Colombia). Since 1993 The Kangaroo Foundation is monitoring around 1000 LBW infants per year in the outpatient KMCPs.

## Patients and Methods

Design: prospective cohort of 20.835 premature (<37 weeks) and/or LBW (<2500 g) infants followed up to one year of corrected age in the outpatient Kangaroo Mother Care Programs at Bogotá, Colombia, between 2001 and 2014. 48,7% was near term infants.

Study Variables: Weight and gestational age at birth, acute fetal distress, anoxia, stay in NICU, any grade of interventricular hemorrhage, type of ventilation, seizures, bronchopulmonary dysplasia, neurologic exam at 3, 6, 9 and 12 months of corrected age; Somatic growth and breastfeeding rate; psychomotor development at 6 and 12 months of corrected age; neurosensory sequel and mortality rate at one year of corrected age.

## Results

Near term infants represented 48,7% of the total cohort. 43,5% received prenatal corticoids for lung maturation, 33% required immediate resuscitation, and 79% had IUGR. During hospital stay, 26,7% presented pathologic jaundice, 6,9% had symptomatic hypoglycemia, 2% had IVH and 20% were discharged with ambulatory oxygen. 35% were NICU graduates, 27% of them had been ventilated. 5,2% had history of nosocomial infection. Overall mortality was 0,6 % up to one year, 83% of deaths occurring between discharge and 3 months. 33,8% of patients were readmitted at least once up to one year. 1,4 % had retinopathy, 0,3% ophthalmic surgery with laser and 0,04% blindness. At 12 months, diagnosis of high risk of cerebral palsy was 3,1%, neurological exam was not normal in 5% and mean developmental coefficient was 100,7 with 12,8% borderline or less. Lost to follow up was 13,5 %.

## Conclusions

KMCP is a good strategy and unique opportunity in Colombia. One year of corrected age is the minimum acceptable follow up for these children, taking into account the data obtained from our 20 years quality monitoring, that demonstrate they cannot be assimilate to term infants. The opportunity for close monitoring and intervention is essential to detect and reduce reversible alterations in growth and development.

## Epidemiology

### PERINATAL OUTCOME IN RELATION TO CHORIONICITY (292)

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## Introduction /Case Report

The incidence of multiple gestation is increasing worldwide, mostly due to delayed childbearing and the use of assisted reproductive technology. Monochorionic (MC) twinning is remarkably constant (3-5:1000 pregnancies), unlike the Dichorionic (DC). Many studies have shown higher perinatal morbidity and mortality rates in MC twins compared to DC.

The purpose of this study was to evaluate the impact of chorionicity on perinatal outcomes of twin pregnancies.

## Patients and Methods

Retrospective study of all twins born in a tertiary center from January 2004 to December 2013. Twin pregnancies were classified as MC or DC by ultrasonographic criteria and confirmed histologically by placenta examination after delivery. Exclusion criterion: MC monoamniotic gestation.

Demographic data, delivery variables and perinatal morbidity and mortality were studied.

Statistical analysis was performed by  $\chi^2$  and t Student tests. A p value of  $<0,05$  was considered statistically significant.

## Results

In this period, 1051 twins were born, related to 540 gestations (26,7% MC; 73,3% DC).

There were no statistical significant differences between the groups concerning obstetric complications: preterm delivery threat, oligo/hydramnios and intrauterine discordant growth.

The MC group had a higher incidence of intrauterine growth restriction (20,5% vs 11,3%,  $p<0,001$ ), lower mean maternal age (29,9 vs 31,9 years,  $p<0,001$ ), lower mean gestational age (33,4 vs 34,3 weeks,  $p<0,05$ ) and lower mean birth weight (1943g vs 2147g,  $p<0,001$ ).

MC twins had a higher incidence of hyaline membrane disease (7% vs 4,2%,  $p<0,05$ ), sepsis (10,3% vs 5,8%,  $p<0,05$ ) and anemia (9,5% vs 5,4%,  $p<0,05$ ). There were no statistical significant differences concerning necrotizing enterocolitis, intraventricular hemorrhage or retinopathy of prematurity. Perinatal mortality was higher in the MC group (7,3% vs 3,3%,  $p<0,05$ ).

## Conclusions

Although our twin pregnancies had similar obstetric complication rates, the MC group was associated with greater morbidity and mortality rates than the DC group, as previous studies have reported. Therefore, MC twins represent considerable challenges to both obstetricians and neonatologists and should be monitored and delivered at tertiary centers to minimize perinatal morbidity and early adverse neonatal outcomes.

## Brain & Development / Placenta and prenatal factors

### ANTIDEPRESSANT MEDICATION DURING PREGNANCY AND EPIGENETIC CHANGES IN THE NEWBORN: A REVIEW OF THE LITERATURE. (127)

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#### Introduction /Case Report

Epigenetic mechanisms are important for regulating gene expression and differentiation during fetal and early life. These mechanisms are influenced by external factors and epigenetic changes might have life-long consequences on child health. Up to 20% of pregnant women experience symptoms of depression or anxiety and 3-8% of pregnant women are treated with antidepressant medication. These exposures are associated with adverse neonatal and long term developmental outcomes. Epigenetic changes may partly explain this. The aim of this study is to investigate whether there is an association between exposure to maternal antidepressant use during pregnancy and epigenetic changes in the newborn.

#### Patients and Methods

Systematic literature searches were performed in MEDLINE and EMBASE combining MESH-terms covering epigenetic changes, use of antidepressant medication, pregnancy and newborns. A keyword search was also performed. We included original studies on pregnant women and their children where there was a history of maternal depressed mood or anxiety and a reported use of antidepressant medication, and with measurements of epigenetic changes in the umbilical cord. Studies using genome-wide epigenetic analyzes or specific gene epigenetic analyzes were included. Citations and references from the included articles were investigated to locate further relevant articles. The completeness of reporting as well as the risk of bias and confounding was assessed.

#### Results

Six studies were included. One study found an association between antidepressant use and differential methylation at CpG sites in TNFRSF21 and CHRNA2 (FDR<0.05). Alterations in methylation of the first, also known as the death receptor 6 (DR6) on chromosome 8 has been associated with psychiatric and neurodegenerative disorders. Another study found an association between the use of antidepressants in pregnant African-American women and the methylation status in the IGF2 gene (H19 DMR) (p=0.01). A third study found an association between increased methylation levels at 3 CpG-sites and SRI exposure (CYP2E1, EVA1 and SLMAP (FDR=0)). CYP2E1 methylation status was also in turn associated birth weight. The other three included studies found an association between maternal mood and epigenetic changes but no association between epigenetic changes and the use of antidepressant medication.

#### Conclusions

Prenatal antidepressant exposure might influence epigenetic expression and hereby possibly the health of the child. Genome-wide epigenetic changes in 166 SSRI exposed children were examined. The methylation status in specific genes was examined in 97 SSRI exposed children. Future studies with larger sample sizes

are warranted in order to adjust for potential confounders that might influence epigenetic expression, such as maternal age and race.

IMPROVED EARLY NUTRITIONAL CARE OF VERY LOW BIRTH WEIGHT INFANTS – WHAT WAS THE IMPACT ON GROWTH? (681)

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Introduction /Case Report

Introduction: Following preterm birth, the newborn infant is acutely deprived of nutrition. This initial nutritional deficit may influence growth throughout the neonatal period resulting in extra-uterine growth restriction – a common complication in very low birth weight (VLBW) infants. Therefore, earlier and increased nutritional intakes have been recommended in a series of guideline updates. It is uncertain, however, if implementation of these guidelines in routine clinical practice has improved growth of the VLBW infants. The study aimed to compare nutritional guidelines, feeding practices, and growth in VLBW infants born in 1996/97 and in 2012.

Patients and Methods

Methods: The study was designed as a retrospective cohort study of 114 surviving VLBW infants (BW<1500g) at Copenhagen University Hospital, Rigshospitalet: 57 born in 1996/97 and 57 born in 2012. The infants were matched by birth weight and gestational age. Data was collected through chart reviews. Growth was expressed as changes in weight standard deviation scores over time using a fetal growth standard as reference. The change in standard deviation scores (deltaSDS) from birth to 7 days and from 7 to 28 days was compared between the groups. Clinical guidelines were retrieved from archives and reviewed to compare feeding practices (administration and daily advancement) and nutritional guidelines (caloric, protein and lipid intake and use of fortification) between the two groups.

Results

Results: The 1996 guidelines recommended parenteral nutrition – if needed – from day 3-5 and fortification of maternal milk only if the infant's weight gain did not satisfy predetermined growth goals after full enteral feedings were obtained. The 2012 guidelines recommended enteral and parenteral nutrition from day 1, a higher protein intake, and fortification of maternal milk once 160ml/kg/day was reached. The chart review showed that the guidelines were well implemented in clinical practice. A significant difference between 1996/97 and 2012 was detected in growth during the first week of life (deltaSDS +0.55, 95% CI +0.33 to +0.77,  $p<0.001$ ), whereas there was no statistically significant difference in growth from day 7 to 28 (deltaSDS +0.07, 95% CI -0.23 to +0.37,  $p=0.6$ ).

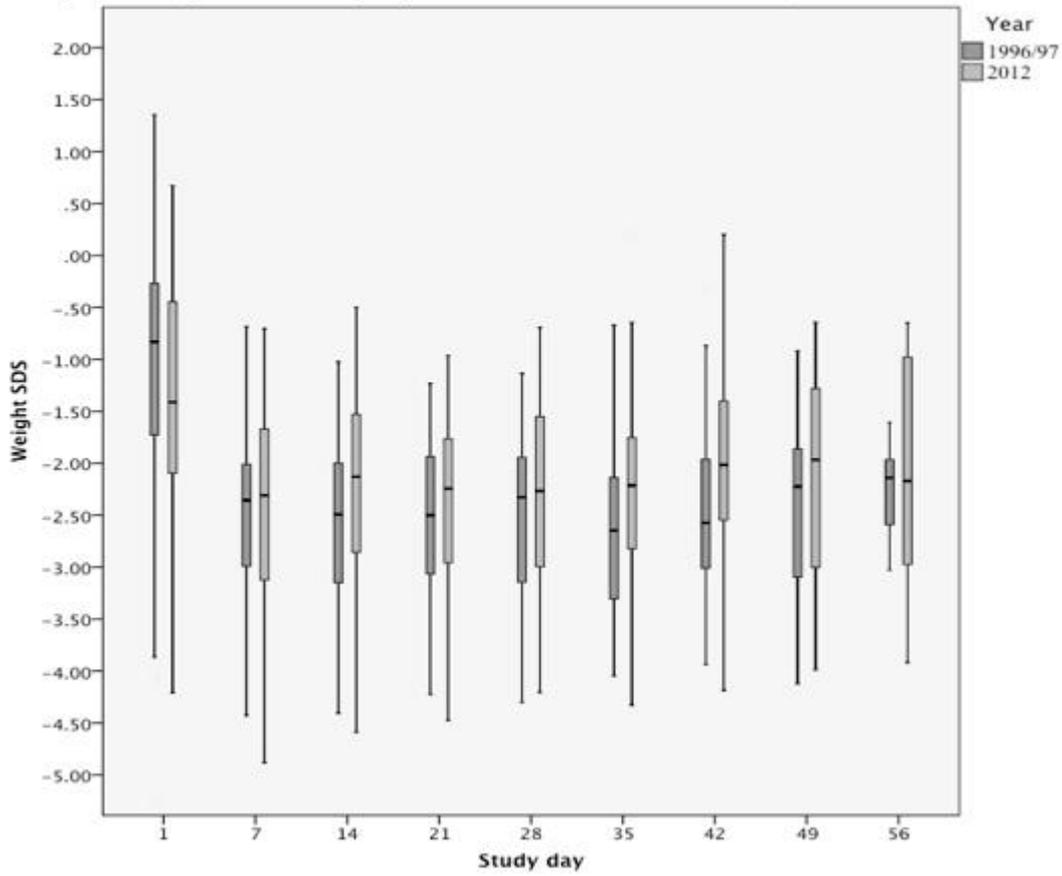
Conclusions

Conclusion: Updates of guidelines led to an increased use of parenteral nutrition and milk fortification. The improvement in growth from birth to 7 days may represent a reduced loss of lean body mass due to increased early protein intake from parenteral nutrition or represent reduced water loss – or both. The

improvement of growth from day seven to 28 in VLBW infants appeared to be limited in spite of routine fortification of mother's milk.

Picture

Figure 1: Weight SDS at study day 1 to 56 for infants born in 1996/97 and 2012.



Circulation, O2 Transport and Haematology / Placenta and prenatal factors

## THROMBOCYTOPENIA IN SMALL-FOR-GESTATIONAL-AGE NEONATES: A RETROSPECTIVE COHORT STUDY (661)

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### Introduction /Case Report

Intra-uterine growth restriction can lead to dysmaturity, or 'small for gestational age' (SGA). SGA neonates are at increased risk of thrombocytopenia, but little is known about the severity of and risk factors for thrombocytopenia in this high risk group. Our aim was to estimate the incidence and severity of early-onset thrombocytopenia in SGA neonates, and to identify risk factors. Bleeding risk was also assessed.

### Patients and Methods

Retrospective cohort study in SGA neonates (study group) and appropriate for gestational age (AGA) neonates (control group) matched for gestational age at birth. The following variables were recorded: platelet counts, other hematologic parameters, clinical risk factors and the occurrence of major bleeding in the first 3 days of life.

### Results

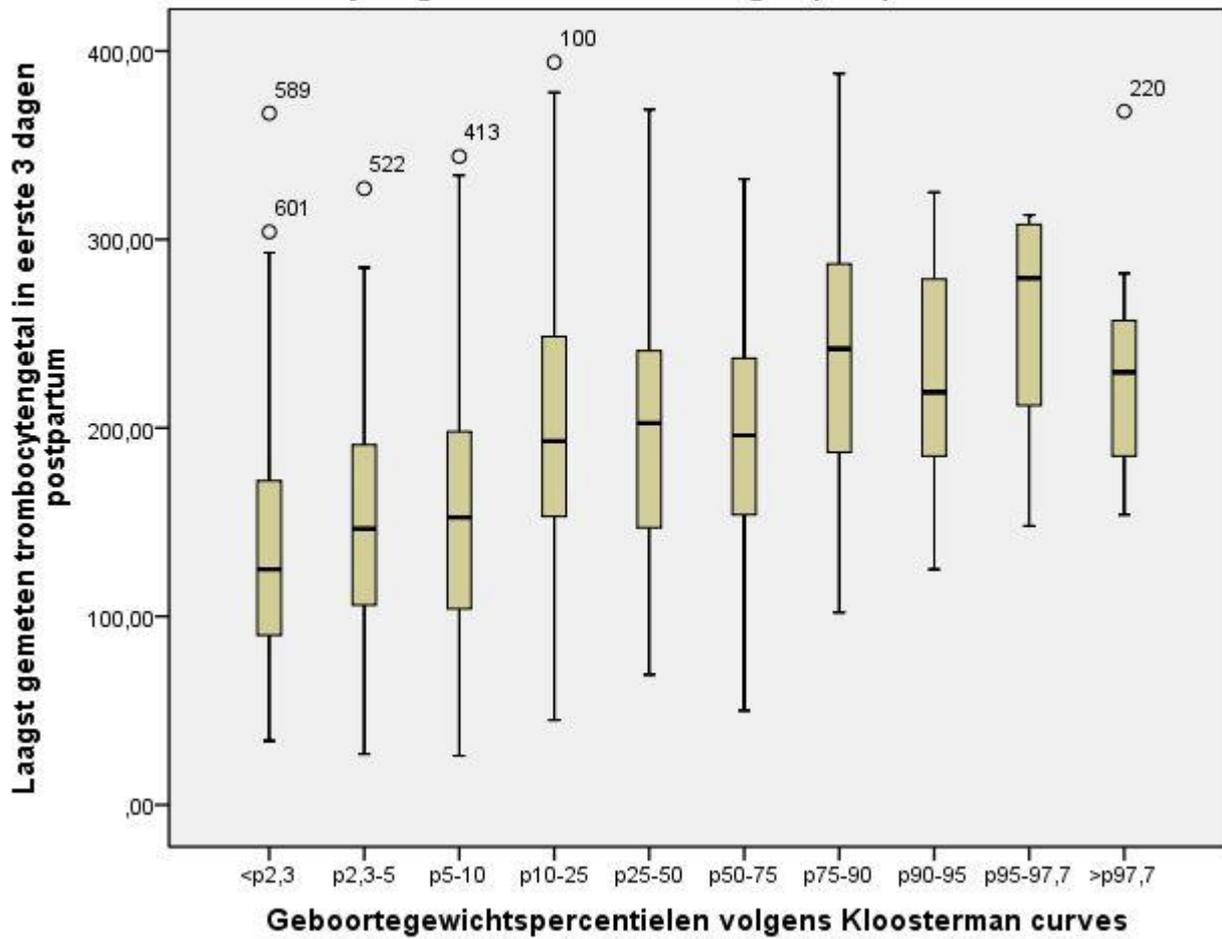
330 SGA neonates and 330 matched AGA neonates were included, with a mean gestational age at birth of  $32.9 \pm 4$  weeks. Thrombocytopenia ( $<150 \times 10^9/L$ ) was found in 53% (175/329) of SGA neonates and 20% (67/330) of AGA neonates ( $p=0.00$ , relative risk: 2.6). There were no neonates with very severe thrombocytopenia ( $<20 \times 10^9/L$ ), the number of neonates with severe thrombocytopenia ( $21-50 \times 10^9/L$ ) was 25 (8%) in the SGA and 2 (1%) in the AGA group. The risk of severe intraventricular hemorrhage (IVH grade  $\geq 3$ ) was not significantly different between the SGA (3%) and AGA (6%) group ( $p=0.35$ ), and was not increased in the subgroup of neonates with thrombocytopenia. Of the 22 neonates with severe IVH, 1 (5%) had severe thrombocytopenia. In the SGA subgroup, lower gestational age at birth ( $p=0.02$ ) and erythroblastosis ( $p=0.00$ ) were independently associated with thrombocytopenia.

### Conclusions

Early-onset thrombocytopenia occurs in over 50% of SGA neonates and occurs 2.6 times more frequently than in AGA neonates, but it is not associated with increased bleeding risk. Thrombocytopenia in SGA neonates is associated with lower gestational age at birth and erythroblastosis.

Picture

**Associatie tussen geboortegewichtpercentielen en het laagst gemeten trombocytengetal in de eerste 3 dagen postpartum.**



Circulation, O2 Transport and Haematology

Platelet mass index in very preterm infants: Can we use it as a marker for morbidities? (675)

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### Introduction /Case Report

Preterm birth is a leading cause of neonatal morbidity and mortality. Platelet count alone may be a poor predictor of bleeding in preterm infants. Assuming normal function of PLTs and endothelium, the hemostatic efficacy of PLT plug formation may be influenced more by the PLT mass than by the PLT count. The aim of this study was to evaluate the correlation between platelet mass index (PMI) on third day of life and the occurrence of various morbidities of prematurity such as necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), sepsis, retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), pulmonary hemorrhage and patent ductus arteriosus (PDA) in preterm infants.

### Patients and Methods

This retrospective study was conducted at Zekai Tahir Burak Maternity Teaching Hospital situated in Ankara. PMI was calculated from complete blood counts (CBCs) obtained for routine patient care as the product of the platelet number and the MPV ( $PMI = \text{Mean platelet volume} \times \text{platelet count} / 1000$ ). CBCs were obtained on NICU admission (first measure) and third to seventh day (second measure) for each patient. The average MPV over the first 48 h was used, because the MPV did not change over this time and not every CBC had a reported MPV value. Platelet mass was compared with clinical variables.

### Results

Premature infants (n=379) born at gestation of less than 32 weeks were enrolled in the study. Patients completed the entire study (n = 330) and the patients were excluded for major congenital malformations (n=36), neonatal alloimmune thrombocytopenia (n=5), neonatal immune thrombocytopenia (n=8). The demographic and clinical characteristics of the preterm infants are summarized in Table 1. BPD was diagnosed in 97 (29.3%) of the infants, 133 (40.3%) had severe IVH, 30 (9%) had NEC (grade >II), 55 (16.6%) had ROP (grade >III), 105 (31.8%) had EOS, 184 (55.7%) had LOS, 27 (8.2%) had pulmonary hemorrhage and 111 (33.6%) had PDA. Preterm morbidities (PDA, ROP, moderate-severe BPD, IVH, NEC) associated with platelet count, MPV, PMI in the first and second measurement are summarized in Table 2.

### Conclusions

Our data suggest that platelet mass index may be an important clinical indicator of some morbidities in VLBW infants. Platelet mass seems to be a marker of some preterm morbidities such as ROP, BPD, NEC, RDS, PDA, EOS, LOS, PH. But it is not sufficiently sensitive and specific for this disease, though it can be used to predict the severity of morbidities of VLBW infants.

Table

**Table 1.** The demographic and clinical characteristics of the patients

Variables	n=330
Gestational age (week) (mean± SD)	28±2.3
Birth weight (g) (median±SD)	994±212
Gender (male/female)	168/162
Apgar score 1 min, median (min-max)	5 (1-8)
Apgar score 5 min, median (min-max)	8 (1-10)
CRIB II scores, median (min-max)	3 (1-14)
Antenatal steroid (%)	224 (67.8)
Maternal hypertension (%)	32 (9.7)
Maternal diabetes (%)	14 (4.2)
Maternal preeclampsia (%)	57 (17.2)

**Table 2.** Preterm morbidities associated with platelet count, MPV, PMI in the first and second measure

	PDA (n=111)	Without PDA (n=219)	ROP (n=55)	Without ROP (n=275)	BPD (n=97)	Without BPD (n=233)	IVH (n=133)	Without IVH (n=197)	NEC (n=30)	Without NEC (n=300)	p-values
Platelet count in first measure (x1000/mm <sup>3</sup> )	222±83	213±80	195±71	221±82	202±64	223±86	212±74	220±85	202±70	217±82	<i>P</i> <sup>1</sup> 0.248 <i>P</i> <sup>2</sup> 0.033 * <i>P</i> <sup>3</sup> 0.034 * <i>P</i> <sup>4</sup> 0.392 <i>P</i> <sup>5</sup> 0.276
MPV in first measure (fl)	8.0±0.9	8.2±1.0	8.4±1.0	8.1±0.9	8.3±0.9	8.1±1.0	8.1±0.9	8.2±1.0	8.3±0.8	8.1±1.0	<i>P</i> <sup>1</sup> 0.123 <i>P</i> <sup>2</sup> 0.062 <i>P</i> <sup>3</sup> 0.210 <i>P</i> <sup>4</sup> 0.554 <i>P</i> <sup>5</sup> 0.421
PMI in first measure (fl nl <sup>-1</sup> )	1777±701	1727±589	1618±551	1774±641	1657±497	1788±673	1706±563	1777±668	1665±525	1751±637	<i>P</i> <sup>1</sup> 0.501 <i>P</i> <sup>2</sup> 0.094 <i>P</i> <sup>3</sup> 0.086 <i>P</i> <sup>4</sup> 0.316 <i>P</i> <sup>5</sup> 0.434
Platelet count in second measure (x1000/mm <sup>3</sup> )	219±119	264±142	210±121	258±138	214±119	264±140	228±132	264±137	195±94	255±139	<i>P</i> <sup>1</sup> 0.005 * <i>P</i> <sup>2</sup> 0.017 * <i>P</i> <sup>3</sup> 0.002 * <i>P</i> <sup>4</sup> 0.020 * <i>P</i> <sup>5</sup> 0.022 *
MPV in second measure (fl)	8.7±1.2	8.8±1.1	8.9±1.2	8.8±1.1	8.9±1.1	8.8±1.2	8.8±1.1	8.8±1.2	8.9±1.0	8.8±1.2	<i>P</i> <sup>1</sup> 0.426 <i>P</i> <sup>2</sup> 0.579 <i>P</i> <sup>3</sup> 0.553 <i>P</i> <sup>4</sup> 0.967 <i>P</i> <sup>5</sup> 0.623
PMI in second measure (fl nl <sup>-1</sup> )	1871±965	2318±1246	1828±1023	2249±1197	1861±990	2308±1226	1987±113	2301±118	1752±879	2216±1196	<i>P</i> <sup>1</sup> 0.001 * <i>P</i> <sup>2</sup> 0.016 * <i>P</i> <sup>3</sup> 0.002 * <i>P</i> <sup>4</sup> 0.018 * <i>P</i> <sup>5</sup> 0.011 *

\*p value is statistically significant, *p*<sup>1</sup> for PDA vs without PDA, *p*<sup>2</sup> ROP vs without ROP, *p*<sup>3</sup> BPD vs without BPD, *p*<sup>4</sup> IVH vs without IVH, *p*<sup>5</sup> NEC vs without NEC

Epidemiology / Host responses and early diagnosis of infection

#### DIAGNOSTIC VALUE OF ELEVATED CXCR4 AND CXCL12 IN NEONATAL SEPSIS (205)

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#### Introduction /Case Report

Neonatal sepsis remains a major cause of morbidity and mortality in newborns. The chemokine CXCL12 and its receptor CXCR4 are now known to play an important role in inflammatory states. However, it's unclear how chemokines respond to late-onset neonatal sepsis.

#### Patients and Methods

Patients were classified into the groups of septic and nonseptic ones. Samples of venous blood were obtained from all septic and nonseptic newborns at the beginning and within 48-72 hours after initiation of treatment. Serum levels of CXCR4 and CXCL12 were measured.

#### Results

Concentrations of IL-6, CXCR4, and CXCL12 at the time of diagnosis were significantly higher in the septic neonates compared with the nonseptic ones. Additionally, there were statistically significant differences in septic neonates between the first and the second levels of IL-6, CXCR4, CXCL12, and I/T ratio. ROC curve analyses revealed that IL-6, CXCR4, CXCL12, and I/T ratio resulted in significant AUC with respect to early identification of septic neonates. Univariate logistic regression analysis showed that increased IL-6, CXCR4 and CXCL12 were strong predictors of neonatal LOS.

#### Conclusions

Serum CXCR4 and CXCL12 levels increase in septic neonates and that both chemokines decrease within 48-72 hours of treatment. Serum concentrations of both chemokines represent promising novel biomarkers for neonatal sepsis.

Table

**Table.** Diagnostic accuracy of serum IL-6, CXCR4, CXCL12, and I/T ratio in septic neonates.

Diagnostic parameters	Cut-off point	ROC AUC (95%-CI)	<i>p</i> value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR	NLR
Biomarkers									
IL-6 (pg/ml)	7	0.97 (0.918-0.998)	<0.001	96.7	95	96.7	95.0	19.3	0.04
CXCR4 (pg/ml)	185	0.95 (0.885-0.998)	<0.001	86.7	95	96.3	82.6	17.3	0.14
CXCL12 (pg/ml)	200	0.94 (0.877-0.998)	<0.001	83.3	95	96.2	79.2	16.7	0.18
I/T ratio	0.19	0.91 (0.833-0.991)	<0.001	80.0	90	92.3	75.0	8.0	0.22

ROC AUC: receiver-operating characteristic area under the curve, PPV: positive predictive value, NPV: negative predictive value, PLR: positive likelihood ratio, NLR: negative likelihood ratio, IL-6: interleukin-6, I/T ratio: immature by total ratio.

Circulation, O<sub>2</sub> Transport and Haematology / Organ blood flow and autoregulation

Measuring the effect of breathing on ductus arteriosus blood flow at birth (042)

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### Introduction /Case Report

During neonatal transition, flow in the ductus arteriosus (DA) changes from right-to-left to left-to-right and contributes considerably to the increase in pulmonary blood flow. Large trans pulmonary pressures generated by crying at birth can influence DA shunting. This study aimed to quantify the effect of individual breaths on DA shunting during the first 12 minutes after birth.

### Patients and Methods

In healthy term infants born by caesarean section, DA shunting and tidal volume were measured simultaneously at 2-5, 5-8 and 10-13 minutes after birth. Echocardiography with pulsed wave Doppler was used to assess DA blood flow using the velocity time integral (VTI) function. VTI of left-to-right and right-to-left flow during inspiration and expiration, measured using a hot-wire anemometer, were assessed and compared between time points.

### Results

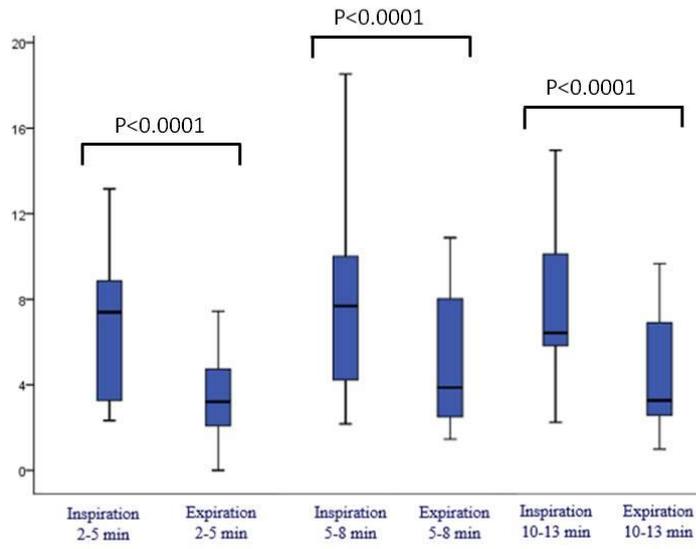
Nine infants with a mean (SD) gestational age of 40 (1) weeks and 3005 (697) grams were studied. The VTI of left-to-right shunting was significantly larger during inspiration when compared to expiration (7.7 (5.0) vs. 3.8 (2.3) cm, 7.8 (4.1) vs. 5.1 (2.8) cm and 7.7 (3.1) vs. 4.4 (2.4) cm  $p < 0.05$ ) at 2, 5 and 10 minutes respectively. Inspiratory tidal volume was 5.4 (2.9) mL/kg, 5.7 (2.6) mL/kg and 5.6 (1.8) mL/kg at 2-5, 5-8 and 10-13 minutes respectively. VTI left-to-right shunting was not correlated with inspiratory tidal volume at 2-5 minutes ( $-0.270$ ;  $p > 0.05$ ) but showed a moderate correlation at 5-8 and 10-12 minutes (0.538;  $p = 0.001$ , 0.478;  $p = 0.01$ ).

### Conclusions

Left-to-right DA shunting significantly increases during inspiration, which implies that breathing effort can contribute to the increase in pulmonary blood flow at birth.

Picture

Figure 1, VTI left-to-right shunting during inspiration and expiration at 2-5, 5-8 and 10-13 minutes after birth



## Epidemiology

### BIRTHMARKS AND NEONATAL SKIN DISORDERS: FROM ANGEL KISS TO EPIDERMOLYSIS BULLOSA (213)

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## Introduction /Case Report

At present there are no exact epidemiologic data on the prevalence of neonatal skin disorders and birthmarks in Hungary. The aim of our prospective, cohort study was to investigate the prevalence of skin disorders in mature healthy neonates during a 1-year examination period.

## Patients and Methods

Our survey was carried out in the Neonatal Care Unit at the Department of Obstetrics and Gynaecology at the University of Szeged, between April, 2012 and May, 2013. A total of 2289 newborn infants underwent whole-body screening skin examinations within the first 72 hours of extrauterine life. All of them belonged to the Caucasian race; the non-Caucasian neonates born in the department were excluded from the study.

## Results

At least one skin manifestation was found in 63% of the neonates. The major diagnosis groups were transient benign cutaneous lesions (43,16%), vascular lesions (34,08%), traumatic, iatrogenic, congenital or acquired disorders with skin injuries (4,02%), pigmented lesions (3,28%), and developmental abnormalities or benign skin tumours (0,83%). The most frequent lesions were nevus simplex (31,24%), erythema toxicum neonatorum (22,15%) and sebaceous gland hyperplasia (17,47%). We found a significantly higher prevalence of vascular lesions and nevus simplex in females, while developmental abnormalities and benign tumors, transient, benign cutaneous lesions, and, within the latter diagnostic group sebaceous gland hyperplasia and dry, desquamating skin occurred significantly more commonly among males.

## Conclusions

Our results confirm that cutaneous lesions are very common in neonates, therefore a good working knowledge of them is very important for dermatologist and pediatricians (and often parents). Fortunately, in the vast majority of cases, special treatment was not necessary, but 5.27% of the neonates required particular dermatological therapy, and in 9.21% of them close observation was indicated.

## Epidemiology

Improved neonatal care dramatically reduces the risk for severe ROP in a Mexican population (430)

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## Introduction /Case Report

To assess retinopathy of prematurity (ROP) frequency in a Mexican preterm population after implementations of reduced oxygen saturation target levels and to retrospectively revalidate WINROP, an online surveillance system for identifying infants at risk of ROP type 1, ROP fulfilling treatment criteria.

## Patients and Methods

Included in this study were preterm infants born at gestational age (GA)  $\leq 34$  weeks and/or with birth weight (BW)  $\leq 1750$  g who were screened for ROP between November 4, 2012 and March 8, 2014 at the Hospital Civil de Guadalajara, Mexico (n=151). Maximal ROP stage and ROP treatment were recorded. For WINROP analyses infants were qualified if born with GA  $< 32$  weeks (n=85), their GA, BW, and weekly weights were recorded in WINROP. The results of this study were compared to those of a previously performed WINROP study at the same hospital in 2005–2010 (n=362).

## Results

The frequency of ROP type 1 in the whole cohort was 9.3% (14/151). No infant born at GA  $\geq 32$  weeks or BW  $\geq 1540$  g required ROP treatment. WINROP correctly identified 80.0% (8/10) of the infants with GA  $\leq 32$  weeks who required treatment for ROP type 1. The median time from birth to alarm was 1 week (range 0 to 6 weeks). In the former cohort (2005–2010), 46.4% (168/362) of the infants developed ROP type 1 and received treatment. The sensitivity of WINROP was 84.7% in the former cohort.

## Conclusions

A previously performed WINROP study alerted the need of controlling risk factors for ROP at Hospital Civil de Guadalajara, Mexico. Improved oxygen supplementation control was implemented and ROP treatment frequency was reduced with 80% from 46.5% (2005 to 2010) to 9.3% (2012–2014). WINROP sensitivity in the present study was 80.0% compared to 84.7% in the former. Uncertainties in dating of pregnancies and differences in pre- and neonatal care might contribute to the lower sensibility of WINROP.

Nutrition and gastroenterology / Nutrition of the Very Preterm

ADIPONECTIN AND INSULIN LEVELS IN CORD BLOOD AND AT TERM EQUIVALENT AGE OF VERY LOW BIRTH WEIGHT PRETERMS AND TERM NEWBORNS (080)

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### Introduction /Case Report

Adiponectin and insulin levels in cord blood of preterm and term newborns have been described. Patterns of secretion of those hormones and weight gain during neonatal period are scarce. The objective was to compare adiponectin and insulin levels in cord blood and at term equivalent age of very low birth weight preterms, and of a control group at term.

### Patients and Methods

Cohort of preterm newborns with gestational age < 32 weeks and birth weight < 1500 grams was studied. Exclusion criteria: congenital malformations, inborn errors of metabolism, gestational diabetes. Adiponectin and insulin levels were measured in umbilical cord blood of preterm infants and term newborns and in venous blood sample at 38 – 40 weeks of preterm infants. Adiponectin was measured by ELISA and insulin by chemiluminescence. The study was approved by Ethical Committee of our Institution. Students' t, chi-square, Mann-Whitney, ANOVA one way tests and Spearman correlation were used.

### Results

127 newborns were studied: 55 preterm and 72 term. At birth preterm infants had significantly lower levels of adiponectin and similar insulin levels in comparison to term infants. At term equivalent age preterm infants had higher adiponectin and insulin levels than term newborns [adiponectin:  $2.5 \pm 0.035$  pg/mL and  $2.4 \pm 0.027$  pg/mL  $p=0.037$ ; insulin:  $0.82$  (0.3-1.15) U/mL and  $0.37$  (0 – 0.6) U/mL  $p<0.001$ ]. At term equivalent age preterm weight was lower than term newborn infants ( $2438 \pm 578$  grams and  $3230 \pm 448$ ,  $p<0.001$ ). There was a negative correlation between weight gain of preterm infants and adiponectin levels at term equivalent age ( $r=-0.65$ ,  $p=0.013$ ).

### Conclusions

Patterns of adiponectin and insulin secretions are different in preterm and term infants. The increase in adiponectin levels from birth to term equivalent age reflects the weight gain. Those hormones may have an epigenetic effect on prematurity programming a metabolic response in those newborns.

## Epidemiology

### COMPARISON OF KLIMEK METHOD VERSUS BALLARD METHOD IN DETERMINING GESTATIONAL AGE IN IMAM REZA AND QUAEM HOSPITAL OF MASHHAD UNIVERSITY OF SCIENCES (121)

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## Introduction /Case Report

Severe prematurity is responsible for 60-80% of mortality in neonates without abnormalities.

Objective: to define the exact time of fetus maturity, complications and side effects could be predicted and best decisions could be made

## Patients and Methods

This study is a descriptive cross sectional research in which 229 neonates, who were admitted in the post partum department in Qaem and Imam Reza Hospital in Mashhad. The neonate's maturity was determined according to Ballard and Klimek method.

The examination was in the first 6-12 hours after birth. Analysis of data was by the SPSS soft ware, Mann Whitney test and Kappa agreement value.

## Results

In this study determination of gestational age in the 2 methods N. Ballard and first day of LMP was not statistically significant and 74.6%(171 case) had the same gestational age in both methods ( $p=0.664$ ). Also determination of gestational age by klimek method and the first day of LMP was not statistically significant and 75.9 % ( 174 case) had the same gestational age in both methods ( $p=0.943$ ) and in 51.5 % ( 118 case) both methods detected mature neonates

## Conclusions

For the determination of neonatal maturity, the results of klimek method, Ballard method, and last day of LMP (negel law) were completely compatible.

KEY WORDS: Gestational age, Neonatal maturity, premature birth, Fetus maturity.

Epidemiology / Host responses and early diagnosis of infection

EFFECTIVE BIOMARKERS FOR DIAGNOSIS OF EARLY ONSET SEPSIS (EOS) IN NEONATES IN CONJUNCTION WITH C-REACTIVE PROTEIN (CRP) MEASUREMENT: A LITERATURE REVIEW (605)

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## Introduction /Case Report

Accurate and timely diagnosis of early onset sepsis(EOS) remains challenging and encourages clinical practice based on the fear of missing a treatable infection in a timely fashion.The current practice of starting empirical antibiotic therapy in all neonates showing infection-like symptoms results in their exposure to adverse drug effects, nosocomial complications, and in the emergence of resistant strains.CRP which is the most widely used test for neonates has diagnostic weakness during the early phases of EOS . This review investigates whether combination of CRP with new biomarkers compensates for its diagnostic weakness and provides reliable sensitivity during the early phases of EOS

## Patients and Methods

Literature search:Medline using Ovid interface (1946 to present /no limits set).Inclusion criteria:1) The diagnostic tests being evaluated were considered to be "new" tests (i.e., excluding haematological parameters, such as WCC, ANC, immature-total neutrophil ratio(IT Ratio) or thrombocytopenia)2)The postnatal age of the infants studied was less than 72 hrs 3) Studies were focused on serious bacterial infections, and true infections were proven by a criterion standard and 4)The diagnostic tests are evaluated in combination with CRP.Exclusion criteria:1)Studies that examined antenatal tests, including amniotic fluid tests and cord blood tests, and 2)Studies in which data for early and late onset neonatal infection could not be separated.

## Results

6 articles were relevant for inclusion based on a review of the abstract and full text. There were 2 articles each of Procalcitonin and Interleukin-8 and one each of Interleukin – 6 and CD-64 studied in combination with CRP. There is no standard definition of clinical sepsis in neonates and this inconsistency is a major confounding variable when assessing biomarker studies in neonatal sepsis. PCT, IL-6, IL-8 and CD64 are sensitive markers when compared to CRP during the early phase of the sepsis.Serial measurement of infection markers as well as the use of multiple markers improve the diagnostic sensitivity of these tests.Judicious use of diagnostic algorithm makes it possible to withhold or discontinue antibiotic therapy while being confident that the infant is not infected and no adverse outcome was reported due to delayed onset of antibiotics in babies in the initially missed group.

## Conclusions

CRP has the best diagnostic accuracy when combined with 'early sensitive' markers like PCT, IL-6, IL-8 and CD64 during the early phases of EOS.Serial measurement of infection markers improves the diagnostic sensitivity of these tests. These markers in conjunction with CRP may be used for early termination of

antibiotic treatment in non-infected infants and to safely withhold antimicrobial treatment in babies with suspected EOS infection.

Table

**Table 1: Diagnostic accuracy of CRP (mg/L) in combination with Interleukin 6 (IL-6 ,pg/ml), Interleukin 6 ( IL-8 ,pg/ml), Procalcitonin (PCT ,ng/ml), and CD64 (antibody-phycoerythrin molecules bound/cell)**

Source	Diagnostic test	Sens %	Spec %	PPV %	NPV %
Resch et al. <sup>5</sup>	PCT $\leq$ 6*	77	91	93	72
	CRP $\leq$ 8*	49	100	100	58
	CRP $\leq$ 2.5*	69	96	96	67
	PCT $\leq$ 6 and CRP $\leq$ 8*	83			
	IL-6 $\leq$ 60*	54	100	100	59
Abdollahi et al. <sup>6</sup>	PCT > 1.7*	76.6	78.2	93	72
	CRP >8*	49	100	100	58
	CRP >2.5*	69	96	96	67
	PCT > 1.7 & CRP > 8*	82			
	IL-6 > 60*	54	100	100	59
	IL-6 > 60 & PCT > 1.7*	88			
Franz et al. <sup>7</sup>	IL-8 $\leq$ 70*	44	90	58	83
	CRP >10*	54	100	100	86
	IL-8 $\leq$ 70* and /or CRP >10*	80	87	68	93
#Franz et al. <sup>8</sup>	IL-8 $\leq$ 70*	82	79	67	90
	CRP >10*	28	98	86	87
	IL-8 $\leq$ 70* and /or CRP >10*	92	77	67	95
	IT ratio >0.20*	70	51	45	75
	IT ratio >0.20* and /or CRP >10*	73	49	45	76
	IL-8 $\leq$ 70*	80	76	43	94
	CRP >10*	34	95	63	94
	IL-8 $\leq$ 70* and /or CRP >10*	92	74	44	97
	IT ratio >0.20*	81	42	24	91
	IT ratio >0.20* and /or CRP >10*	91	41	26	95
Rego et al. <sup>9</sup>	IL-6 $\leq$ 36*	82	44	40	85
	CRP >0.6 mg/dL**	76	70	52	87
	IL-6 $\leq$ 36* and /or CRP > 0.6 mg/dL**	93	37	41	92
Ng et al. <sup>10</sup>	CD64 $\leq$ 6136*	79	89	78	89
	CRP $\leq$ 10.0*	49	91	73	77
	CD64 $\leq$ 6136**	96	81	71	97
	CRP $\leq$ 10.0**	60	83	64	80
	CD64 $\leq$ 6136* or CRP $\leq$ 10.0*	81	82	69	89
	CD64 $\leq$ 6136** or CRP $\leq$ 10.0**	97	71	63	98

\* At the time of evaluation; \*\* at 24 h after onset.

# The study included two study periods

DEHYDROEPIANDROSTERONE AND ITS SULFATE ESTER PROTECT PRE-MYELINATING OLIGODENDROGLIAL CELLS AGAINST OXYGEN-GLUCOSE DEPRIVATION - A PILOT STUDY (114)

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Introduction /Case Report

Neonatal hypoxic-ischemic brain injury is a problem of great global and national importance. Improvements in perinatal care have increased survival rates of affected infants, but the risk of long-term morbidity is still substantial. To date, causal therapeutic strategies are not available. An experimental substance class with considerable promise as a future treatment option are so-called sigma-1 receptor agonists. The aim of the current pilot study was to assess the therapeutic potential of the endogenous sigma-1 receptor agonists dehydroepiandrosterone (DHEA) and dehydroepiandrosterone-sulfate (DHEAS) in an in vitro model of hypoxic-ischemic injury in developing white matter.

Patients and Methods

The permanent oligodendroglial cell line OLN-93, which corresponds to an intermediate stage between pre- and immature oligodendrocytes, was subjected to oxygen-glucose deprivation by switching cells to a glucose-free medium and exposing them to anoxic conditions (95% N<sub>2</sub>/5% CO<sub>2</sub> at 37 °C) for 4 hours. Cells were co-treated with i) 0.1 μM, 1 μM or 10 μM DHEA, ii) 0.1 μM, 1 μM or 10 μM DHEAS, or iii) vehicle. Control cells were kept in standard medium under normoxic conditions. After a reoxygenation period of 20 hours, cell viability was assessed by means of a colorimetric assay (CCK-8, Dojindo). Findings were confirmed in four independent subsets of experiments.

Results

Cell viability was significantly increased in cells treated with 0.1 μM (mean cell viability +/- standard deviation: 80 +/- 11%, p<0,01), 1 μM (76 +/- 15%, p<0,01) and 10 μM DHEA (78 +/- 3%, p<0,01) as well as 0.1 μM (70 +/- 7%, p<0,01) and 1 μM DHEAS (71 +/- 11%, p<0,01) during oxygen-glucose deprivation in comparison to vehicle (44 +/- 3%). A concentration of 10 μM DHEAS had no statistically significant effect (40 +/- 7%).

Conclusions

In this pilot study using an in vitro model of neonatal hypoxic-ischemic brain injury, DHEA and DHEAS significantly increased viability in premyelinating oligodendroglial cells. The underlying mechanisms of action as well as their effect on neuronal structures are currently being investigated.

Epidemiology / Host responses and early diagnosis of infection

HIV VERTICAL TRANSMISSION IN A TERTIARY CENTRE: 2000-2014 – HOW ARE WE? (294)

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## Introduction /Case Report

Nowadays, the majority of Human Immunodeficiency Virus (HIV) infections in children results from mother-to-child transmission. In the absence of intervention, the rates of HIV transmission during pregnancy, labor or breastfeeding vary from 15 to 45%. Vertical HIV transmission rates can be substantially reduced to levels below 2% with combined antepartum and intrapartum antiretroviral (ARV) therapy and infant ARV prophylaxis. Prevention of vertical HIV transmission has evolved significantly in Portugal over the last decades.

The aim of our study was to analyze the risk factors associated with vertical transmission of HIV-infected pregnant women in a tertiary maternity center in Portugal.

## Patients and Methods

Retrospective study of children born to HIV-infected mothers whose birth occurred in a Portuguese tertiary maternity center from January 2000 to December 2014.

Several parameters were analyzed: demographic data, route and timing of maternal infection, delivery variables, antepartum and intrapartum ARV therapy, infant ARV prophylaxis and rate of vertical transmission.

## Results

A total of 95 newborns from HIV-infected women were delivered in our center in this 15-year period. Most women were caucasian (72,6%). Sexual contact was the most common risk category for maternal infection (63,2%), followed by injection drug use (24,2%).

Co-infection occurred in 26,3% of the cases (25/95), mostly with Hepatitis C Virus - HCV (19/25). HIV infection was diagnosed during pregnancy in 57,9% of the cases.

Membrane rupture occurred less than 4 hours before birth in 88,4% of the cases. Type of delivery was elective cesarean section in 89,5% of the cases. Only 3 women (3,2%) did not receive intrapartum zidovudine.

Status of viral infection in the newborn was determined by Polymerase Chain Reaction in the first 48 hours, at 4 weeks and 4 to 6 months after birth. All newborn had ARV prophylaxis during the first 4 to 6 weeks of life. Two newborns became infected (2,1%).

## Conclusions

HIV mother-to-child transmission has improved considerably due to adequate prenatal care and the introduction of ARV therapy/prophylaxis.

Our low vertical transmission rate (similar to national rate) represents an important public health achievement, which contrasts with the situation in poorer countries, particularly those where health-care services are not universally granted.

## Brain & Development / Neonatal Brain Injury and Neuroprotection

SERUM LEVELS OF MANNOSE BINDING LECTIN (MBL) AND S100 PROTEIN B AS BIOMARKERS OF NEUROLOGICAL DAMAGE IN ASPHYXIATED NEWBORN: POSSIBLE EFFECTS OF THERAPEUTIC HYPOTERMIA. PRELIMINARY DATA FROM A PROSPECTIVE STUDY. (158)

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### Introduction /Case Report

Hypothermia is the standard of care in at term infants with hypoxic-ischaemic encephalopathy (HIE). MBL initiates lectin complement pathway. In animal models MBL-mRNA is expressed in brain and play a role in tissue alteration due to ischemia-reperfusion injury because of complement activation. Genetic or pharmacological inhibition of brain complement components reduces brain tissue and blood-brain barrier damage, neutrophil accumulation and apoptosis. As an astrocytic protein, S100B is a potentially useful biomarker of brain injury in HIE, but there is no evidence on its prognostic value. Our hypothesis is that hypothermia could influence the release of MBL and of S100B in HIE.

### Patients and Methods

Prospective study on asphyxiated infants, 25 cooled within 6 hours of age [group A: Gestational Age (GA)  $38.49 \pm 2.5$  ws, Birthweight (BW)  $3,229 \pm 565$ g] and 13 uncooled (group B: GA  $39.45 \pm 1.6$  ws, BW  $3,331 \pm 548$  g). MBL and S100B were measured on plasma samples collected on admission in NICU (T1) and at 7 days (T2) in both groups by immunoassay (MBL oligomer ELISA, Antibody Shop, Copenhagen, DK; LIA-mat Sangtec 100 kit, Bromma, SE). 750 ng/ml was the cut-off to discriminate MBL deficiency in neonates and 50 pg/ml for S100B. All neonates were examined by MRI between 7-10 days from admission and after 6 months. MRI brain damage was defined by the Barkovic score. MBL and S100 B plasma levels have been correlated with brain MRI score. Statistically significant p value  $< 0.05$ , by SPSS.

### Results

Mean serum levels of MBL and of S100B compared at T1 and at T2 were similar in the two groups ( $p=0.30$  and  $p=0.88$  for MBL;  $p=0.83$  and  $p=0.65$  for S100B). The mean level of MBL was significantly increased from T1 to T2 in the group A ( $1373.3 \pm 866.36$  vs  $2554.36 \pm 1430.55$  ng/ml,  $p=0.01$ ). On the contrary, S100B was significantly reduced ( $5638.53 \pm 5878.91$  pg/ml vs  $411.24 \pm 470.70$  pg/ml,  $p=0.001$ ). In the group B there was a similar significant increase of MBL from T1 to T2 ( $1621.3 \pm 338.3$  vs  $2654.2 \pm 1148$  ng/ml  $p=0.04$ ), but no significant differences in S100B variations at the same time points ( $5085.79 \pm 6146.13$  vs  $327.91 \pm 121.38$  pg/ml,  $p=0.067$ ). No association were present between MBL levels and a Barkovich score  $> 0$  in cooled and uncooled babies. Brain MRI at 6 months showed no significant differences between the two groups of patients ( $p=0.44$ ).

## Conclusions

MBL serum level significantly increases in asphyxiated infants, without relationship with hypothermia, in response to inflammation. We detect no association between MBL plasmatic increase and the brain MRI parenchymal damage at one week of life and at 6 months in both the groups of patients. On the contrary S100B significantly decrease in cooled infants, probably due to a more quick resolution of the astrocytic damage due to hypothermia.

## Table

**Table 1:** GA: Gestational Age (weeks); BW: Birth Weighth (grams); BE: Base Excess (mEq/L)

	<b>Cooled (Group A)</b>	<b>Uncooled (Group B)</b>	
<b>GA</b>	38.49±2.5	39.45±1.6	p=0.45
<b>BW</b>	3229±565	3331±548	p=0.87
<b>APGAR 1 min</b>	3.7±1.6	4.5±2.7	p=0.016
<b>pH 1 min</b>	6.98±0.17	7.17±0.19	p=0.02
<b>BE 1 min</b>	-18.24±5.12	-14.48±10.32	p=0.18

Circulation, O<sub>2</sub> Transport and Haematology / Organ blood flow and autoregulation

## CEREBROVASCULAR AUTOREGULATION IN PRETERM INFANTS DURING AND AFTER SURGICAL LIGATION OF THE DUCTUS ARTERIOSUS, COMPARING TWO SURGICAL APPROACHES (072)

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### Introduction /Case Report

During ligation of a hemodynamically significant patent ductus arteriosus, cerebrovascular autoregulation (CAR) may deteriorate, possibly inducing hypoxic-ischemic cerebral damage. CAR can be estimated continuously using Near-infrared Spectroscopy (NIRS). Impaired CAR has been described in preterm infants undergoing posterolateral thoracotomy, a procedure after which a reduction in cardiac output and an increased systemic vascular resistance have been observed. It is unknown whether CAR is also impaired after ductal ligation using sternotomy. The aim of this observational study was to compare CAR in preterm infants during and after ductal ligation between the two surgical approaches.

### Patients and Methods

Infants born <32wks requiring ductal ligation between July 2011 and September 2014 with regional cerebral tissue oxygen saturation (rcSO<sub>2</sub>) and invasive mean arterial blood pressure (MABP) measurements before, during and after ligation were included. Halfway this timeframe the standard surgical approach changed from posterolateral thoracotomy to sternotomy. Data were collected at 0.2Hz. Dynamic CAR was quantified using the tissue oxygenation index (TOx), a moving correlation coefficient between 10sec averaged values of rcSO<sub>2</sub> and MABP in a 5min window. TOx values were averaged over the following epochs: pre-ligation, during ligation, 0-4, 4-8, and 8-12hrs post-ligation. Changes in TOx over time and between surgical approaches were evaluated using repeated measurements ANOVA.

### Results

Data were complete for nine infants with both NIRS and invasive MABP measurements. The first four were approached by posterolateral thoracotomy, the latter five by sternotomy. Median GA was 26 weeks (range:24.9-27.9), BW 800 grams (640-960) and PNA 18 days (15-30). We did not observe changes in MABP ( $p=0.24$ ) or rcSO<sub>2</sub> ( $p=0.09$ ) during the study periods. TOx changed significantly over time ( $F=9.95;p=0.024$ ), with higher TOx values during and after surgery for all defined epochs. Although the two surgical groups differed in baseline TOx, the posterolateral thoracotomy group showed more increase in TOx from baseline (surgery:0.32, 4h:0.36, 8h:0.32,12h:0.31) compared to the sternotomy group (surgery:0.20, 4h:0.05, 8h:0.15, 12h:0.11) ( $F=6.50;p=0.038$ ).

## Conclusions

In preterm infants, CAR capacity was reduced during and up to 12 hours after ductal ligation, significantly more so when using posterolateral thoracotomy, compared to sternotomy.

## Epidemiology

### EVALUATING CONTRIBUTION OF INFANT CRY ANALYSIS TO THE NEW BALLARD SCORING SYSTEM IN DETERMINATION OF GESTATIONAL AGE (671)

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## Introduction /Case Report

If adequate and regular follow-up is not done prenatally, new Ballard score (BS) is a commonly used scoring method in estimation of gestational age (GA). Data investigating cry analysis parameters with development and weight of the babies in neonatal period are currently investigated. This study was performed to demonstrate the usability of audio analysis parameters in the estimation of gestational age of healthy babies in the neonatal period and to benefit from objective data obtained from separate usage of audio analysis separately or with new BS.

## Patients and Methods

Newborn babies who were admitted to our NICU were eligible for this prospective study. Exclusion criteria were as follows; presence of major congenital anomalies, previous intubation history, Grade  $\geq 3$  periventricular haemorrhage and no parental consent. Voices of the babies were recorded while crying during the routine blood sampling procedures at the early hours of hospitalisation. Voice samples were recorded in a sound insulated room with a high quality omnidirectional microphone. Samples were captured on hard disk at a 44.100-Hz sampling rate and a 16-bit resolution. Computerized Speech Lab was used to analyze the samples. Acoustic parameters of voice samples were: fundamental frequency (Fo), intensity (Int), jitter percent (Jitt), shimmer percent (Shim), Noise-to-Harmonic ratio (NHR).

## Results

The mean birth weights, GA, new BS values, estimated gestational age regarding to BS and infant cry analysis parameters were presented in Table 1. Among the parameters of infant cry analysis; Intensity showed a medium-level correlation with new BS and GA ( $p=0.02$ ,  $r=0.543$ ). Results of the correlation analysis and the significance values between total new Ballard score with estimated GA according to BS and cry analysis parameters with real GA were presented in Table 3. Regression analysis exposed that real GA can be predicted via the new BS with a high power of correlation (89%). Additionally, intensity value of the infant cry which showed a significant statistical relationship with the GA, elevated the percentage of estimation of GA model as 93%. Estimation formula for the real gestational age of the aforementioned acquired model was: Estimated GA =  $0.820 \times$  GA according to BS +  $0.165 \times$  Intensity.

## Conclusions

As one of the parameters obtained by the analysis of the sound of crying, intensity may contribute as an objective parameter to the subjective estimation of gestational age with new Ballard score.

Table

Table 1. Basic demographic characteristics of the babies

		Birth weight (gram)	Gestational age (week)
<b>Girl</b>	18	2313±736	35.1± <b>2.8</b>
<b>Boy</b>	30	2451±887	35.1± <b>4.1</b>
<b>Total</b>	48	2399±828	35.2±3.6

Values are presented as mean ±SD

Table 2. New Ballard scores, estimated gestational age regarding to Ballard score and parameters of infant cry analysis according to the gender.

GENDER		TOTAL	ESTIMATED	Fo	Int	Jitt	Shimm	NHR
		BALLARD SCORE	GESTATIONAL AGE					
Female	Mean Value	29,61	35,72	460,61	58,33	2,611	9,44	,427222
	Std. Deviation	8,001	3,322	50,203	5,434	1,2433	3,792	,1366320
Male	Mean Value	30,27	36,00	425,33	57,40	2,267	8,27	,482667
	Std. Deviation	10,593	4,169	57,618	4,938	1,4126	3,493	,1954823
<b>Total</b>	<b>Mean Value</b>	<b>30,02</b>	<b>35,90</b>	<b>438,56</b>	<b>57,75</b>	<b>2,396</b>	<b>8,71</b>	<b>,461875</b>
	<b>Std. Deviation</b>	<b>9,617</b>	<b>3,838</b>	<b>57,078</b>	<b>5,093</b>	<b>1,3486</b>	<b>3,614</b>	<b>,1762573</b>

F<sub>0</sub>: Fundamental frequency, Int: Intensity, Jitt: Jitter%, Shimm: Shimmer%, NHR: Noise to Harmonic ratio.

Table 3. Correlation analysis and the significancy values between total new Ballard score with estimated gestational age according to Ballard score and cry analysis parameters with real gestational age

	<b>REAL GESTATION AGE</b>	<b>TOTAL BALLARD SCORE</b>	<b>ESTIMATED GESTATION AGE<sup>Ä</sup></b>	<b>Font</b>	<b>Jitt</b>	<b>Shimm</b>	<b>NHR</b>
<b>Pearson</b>							
<b>Correlation</b>	1	,885**	,887**	-,236	,543**	,049	,103
<b>Coefficient</b>							
<b>p value</b>		,000*	,000*	,107	,002*	,740	,488

<sup>Ä</sup>Regarding to new Ballard score.

\*Parameters with <0.05 asymptotic significant level.

\*\*Pearson Correlation Coefficient >0.05, values shown in red, presented medium and high level correlation.

Circulation, O2 Transport and Haematology / Transfusion and volume therapy

## MEASURING UMBILICAL FLOW AND PLACENTAL TRANSFUSION FOR PRETERM BIRTHS: WEIGHING BABIES AT 33-36 WEEKS GESTATION WITH CORD INTACT (878)

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### Introduction /Case Report

If the umbilical cord is not clamped immediately at birth, blood flow between placenta and baby continues for a few minutes. The physiological role of this continued flow ('placental transfusion') is poorly understood. It may be part of the physiological mechanisms supporting neonatal transition, potentially providing a reservoir for the expanding pulmonary circulation. This may be particularly important for very premature infants, and better understanding of the physiology may help determine optimal timing for cord clamping.

Little is known about umbilical flow at preterm birth. The aim of this study was to assess continued umbilical flow and placental transfusion at preterm birth.

### Patients and Methods

Placental transfusion can be measured by weighing babies before cord clamping: 1ml of blood weighs 1gm. At a tertiary referral centre in India, women with a singleton pregnancy giving birth between 33 and 36 weeks were eligible. At birth, the baby was placed onto digital scales, and wrapped with towels to prevent heat loss. The scales calculated weight twice every second, with recordings stored electronically. Weighing continued for up to three minutes, the cord was then clamped.

### Results

To date, eighteen babies have been weighed; 8 vaginal births, 10 caesarean. Uterotonic was given after cord clamping for all. Twelve infants were 33-34 weeks, and six 35-36 weeks. Gestation assessment was based on ultrasound for 11. The pattern of flow varied, and was often continuing to change at three minutes. For 2 babies there was no net change in weight between birth and cord clamping; for 1 weight change was minus 30g; for the remainder weight increase was between 15-100g. There were no clear differences between vaginal and caesarean births.

### Conclusions

Data for the full study will be presented and discussed. Results so far suggest that for preterm births, umbilical flow often continues for at least three minutes for both vaginal and caesarean births. As at term births, the volume of placental transfusion varies. Further research is needed to understand umbilical flow after very premature birth if the cord is not clamped immediately.

PREDICTION VALUE OF EARLY ULTRASOUND EXAMINATION IN VLBW INFANTS WITH SUSPECTED NEC—  
PRELIMINARY REPORT (454)

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Introduction /Case Report

Necrotizing enterocolitis (NEC) is the most common severe gastrointestinal emergency in neonates that predominantly affects premature infants. There is inverse relationship between gestational age and prevalence rate of NEC. The incidence of disease is estimated for 6-10% among infants with birthweight <1500g. The mortality rate of NEC ranges between 10-30%. Nowadays, when there is direct access to ultrasound in NICU, it can play role of useful tool in monitoring of NEC's clinical course in order to improve the infants' survival rate. The aim of the study was the evaluation of abdominal US specific markers in assessment of clinical course of NEC and qualification for surgical treatment.

Patients and Methods

Twenty-nine children with mean birthweight of 1038 g (SD 343g) and with gestational age equalled to 27.7 weeks (SD: 2.8) were evaluated at the day of the suspicion of NEC and 24 and 48 hours later. The children were examined using the custom-made protocol of US abdominal scans composed of: 2D-evaluation for the presence of pneumoperitoneum, hydroperitoneum, gas in the portal vein system, pneumatosis interstitialis, bowel movements and Doppler examination for blood flow in the SMA and CT. Based on the follow-up assessment, the children were divided into two groups: group A – no progression of the NEC signs (NEC stage I or suspected NEC only) (n=18) and group B – developed NEC (NEC stage II (n=6) or stage III (n=5)).

Results

There were no differences regarding the gestational age (27.8±3.2 vs. 27.5±2.6 weeks) birthweight (1053±381 vs. 1017±295g) and postmenstrual age (30.6±4 vs. 30.4±3.6 weeks) between the groups. Signs like gas in the portal vein or pneumatosis interstitialis were found only in 3 future proved cases of NEC. The values of systolic and diastolic blood velocity measured in the SMA were significantly higher in the group of future NEC cases (PSV: 86±34 vs. 71±21 cm/s; p=0.1; EDV: 21±12 vs. 14±6 cm/s; p=0.05). Interestingly, there were no differences regarding blood flow pattern in the CT (PSV: 77±20 vs. 82±30 cm/s; p=0.8; EDV: 22±11 vs. 22±11 cm/s; p=1.0). In the group of NEC cases the second evaluation revealed further aggravation of SMA blood flow (PSV increased up 94±24 cm/s p=0.1). In the control group the blood flow measurements performed 24 and 48 hours later did not change significantly.

Conclusions

Evaluation of the SMA (but not CT) blood flow can be useful marker of prediction in NEC's clinical course. Increased values of blood velocities in SMA helped to distinguish infants with higher risk for NEC development from the group of children with feeding intolerance (suspected NEC). Moreover, further aggravation of SMA blood flow was observed only for serious NEC cases.

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

## MANAGEMENT OF PATENT DUCTUS ARTERIOSUS IN VERY PRETERM INFANTS WITH A MORE CONSERVATIVE APPROACH. COMPARISON OF TWO PERIODS IN A LEVEL III NEONATAL UNIT (664)

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### Introduction /Case Report

The management of patent ductus arteriosus (PDA) in the very preterm infant has been controversial in recent years. Different authors suggest a more conservative approach.

In our Neonatal Unit, a new and more conservative protocol for the diagnosis and treatment of preterm babies under 30 weeks gestational age (GA) with PDA, was implemented in 2013.

Our goal was to minimize the side effects of the pharmacological or surgical closure, restricting both to those patients with clinical and echocardiographic criteria of hemodynamically significant ductus.

### Patients and Methods

A cohort study was performed. Preterm babies under 30 weeks of gestational age in two different periods were enrolled: 2009-2010 before the introduction of the new protocol, and 2013-2014.

Different items were compared: number of performed echocardiographies, persistence of ductus, pharmacological treatment with ibuprofen/indomethacin, surgical closure, global rate of patients receiving any intervention (medical or surgical ligation), morbidity (necrotising enterocolitis-NEC-, bronchopulmonary dysplasia- BPD-, intraventricular haemorrhage- IVH- , retinopathy of prematurity – ROP-) and mortality.

### Results

- 2009 to 2010:

80 babies under 30 weeks GA were attended. Echocardiography was carried out at 71.3% of the infants; PDA was diagnosed in 42.5% of them.

22% of the patients received pharmacological treatment, while 7.5% required surgical ligation. The global percentage of intervention (ibuprofen or surgery) was 30%.

NEC (>stage II) was observed in 10%, IVH (>stage III) in 15%, BPD in 17.5% and finally ROP in 7.5% of the patients. The mortality rate was 20%.

- 2013 to 2014:

61 babies under 30 weeks gestation were attended. Echocardiography was carried out at 63.9% of the infants; PDA was diagnosed in 44.3% of them.

14% of the patients were treated with ibuprofen, and only 1.6% received surgical treatment. The total percentage of intervention was 16.4%.

NEC was observed in 9.8%, IVH in 4.9%, BPD in 18% and finally ROP in 11% of the patients. The mortality rate was 13.1%.

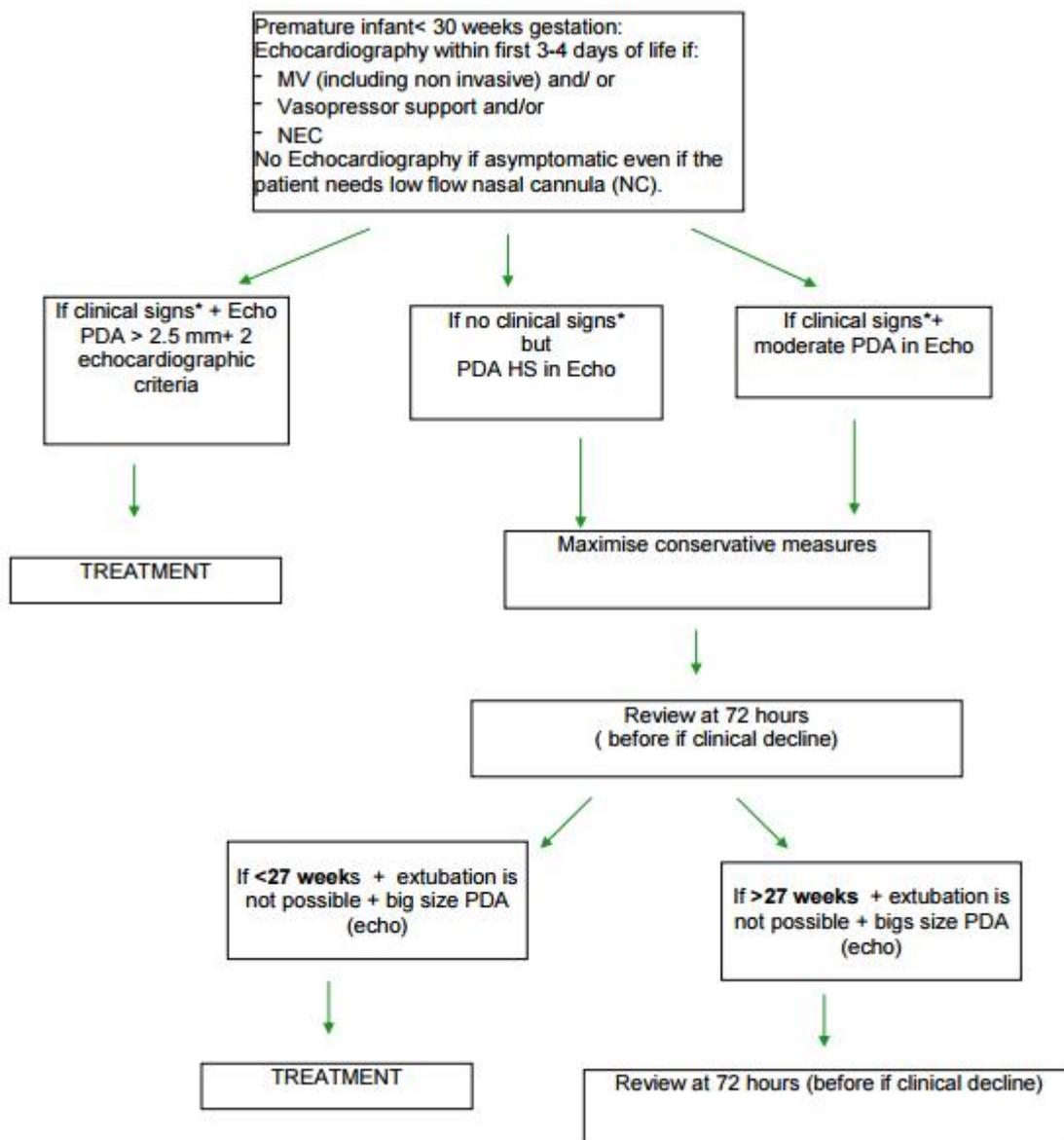
Conclusions

With our new protocol, the intervention rate halved (from 30% to 16%). Our strategy facilitated a high percentage of spontaneous closure, without an increase of associated morbidity.

According to our experience, a more conservative approach in the management of PDA may be adequate, as the possible side effects of any treatment are reduced without an increase of morbidities related to prematurity.

Further studies with larger sample should be performed.

Table



\* Clinical criteria of hemodynamically significant (HS) ductus arteriosus - Pulmonary hemorrhage - Hypotension not caused by an identifiable cause other than PDA requiring vasopressor dose >8 mg/kg/min - Respiratory failure (not caused by an identifiable cause other than PDA) defined as the presence of FIO2 >

0.4, peak inspiratory pressure > 20 cm H<sub>2</sub>O, or high frequency ventilation with Paw > 10. These settings were required to maintain O<sub>2</sub> saturation between 88 and 95% and PaCO<sub>2</sub> < 65 mm Hg.

	<b>No HS SIGNIFICANT</b>	<b>HS SIGNIFICANT Size criteria + 2</b>	
<b>PDA SIZE</b>	<b>&lt; 1,5 mm</b>	<b>&gt;2.5 mm</b>	
<b>DUCTAL FLOW</b>	<b>Restrictive continuous transductal flow (V<sub>max</sub> &gt;2.0 cm/s)</b>	<b>Unrestrictive pulsatile transductal flow</b>	} <b>Unrestrictive Flow</b>
<b>LA: Ao ratio</b>	<b>&lt; 1,4-1,5:1</b>	<b>&gt;2:1</b>	
<b>Decreased or absent diastolic flow in Desc Ao at diafractamic level</b>	<b>NO</b>	<b>YES</b>	} <b>Systemic hypoperfusion</b>
<b>Diastolic flow in superior mesenteric artery</b>	<b>Normal</b>	<b>Absent or reversal</b>	
<b>Diastolic flow in middle cerebral artery</b>	<b>Normal</b>	<b>Absent or reversal</b>	
<b>LPA diastolic flow</b>	<b>&lt; 0,3 m/seg</b>	<b>&gt;0,3 m/seg</b>	} <b>Pulmonary overcirculation</b>

Moderate HS:  
 Size between 1.5-2.5 mm + 1 criteria or  
 >2.5mm + 1 criteria

Epidemiology / Nosocomial infection and colonization

Screening of intestinal carriage of ESBL producing bacteria in neonatal patients (771)

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Ist Department of Pediatrics Semmelweis University Budapest

#### Introduction /Case Report

Major factors influencing postnatal intestinal bacterial colonisation are gestational age, weight, mode of delivery, hospitalisation and antibiotic therapy. NICU patients are at high risk for pathologic gastrointestinal bacterial colonisation, and increased risk for systemic infection.

#### Patients and Methods

The aim of our investigation was to establish intestinal carrier stage of ESBL producing bacteria in neonatal patients in the I.st Department of Pediatrics Semmelweis University Budapest Hungary in years 2010-2014. Perianal swab samples were collected at admission and thereafter weekly until discharge of patients. Samples were culturing on ESBL selective chromogen medium, identified and antibiotic sensitivity performed.

#### Results

During the 5 years period 7642 sample were performed and ESBL producing bacteria were demonstrated in 270 patients. The most common strain was *Klebsiella* spp.(55%), *E. coli* (24%), *Enterobacter* spp. (17%) and *Serratia* spp.(less than 1%). During the investigational period no epidemic causing by ESBL producing bacteria was observed.

#### Conclusions

Prior known antibiotic resistance of cultured bacteria help to start appropriate and more successful empiric antibiotic therapy in case of late onset infections in NICU patients. Monitoring ESBL bacteria carrier stage permit of the isolation and cohort care of carrier patients.

Nutrition and gastroenterology / Nutrition of the Very Preterm

## NUTRIENT INTAKES DURING INTENSIVE CARE UNIT STAY AND THE RISK OF CHRONIC LUNG DISEASE IN PRETERM INFANTS (701)

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### Introduction /Case Report

It is likely that the nutritional status of preterm infants impacts on their risk of chronic lung disease (CLD). For instance, a recognised strategy for improving the lung function of preterm infants is to ensure they grow adequately, increasing their lung size and therefore capacity. Furthermore, specific nutrients have been associated with the development of CLD, including sodium and vitamins A and E. There is also experimental evidence linking specific nutrient to lung development, such as choline. We aimed to use existing nutrient intake data in a large cohort of preterm infants to look at the associations between nutrient intakes and the risk of developing CLD.

### Patients and Methods

We carried out a secondary analysis of detailed data on the daily intake of 33 different nutrients (see table 1) during stay collected on a cohort of preterm infants born and cared for on our neonatal unit between 2009 and 2013 as part of another interventional study. CLD was defined according to the Vermont Oxford Definition of a need for oxygen at 36 weeks post-conception age. To look at the association between the intake of different nutrients and the risk of CLD, multivariate logistic regression analysis was carried out with adjustment for sex, gestational age (GA) and weight standard deviation score (SDS) at birth. All 33 nutrients were entered into the model in order to adjust for the association of different nutrients together in various feeding solutions.

### Results

263 infants were included in the analysis, with a mean (SD) gestational age of 28.7 (2.8) weeks, a mean (SD) weight of 1.03 (0.28) at birth. Table 1 shows the results of multivariate logistic regression, with the odds ratios for the risk of CLD for each nutrient after adjustment for the other nutrients in the model, together with sex, GA age and weight SDS at birth. It can be seen that higher mean relative intakes of protein, sodium, thiamine, riboflavin and inositol across stay were associated with a decreased risk of CLD. Higher mean intakes of fat, chloride, calcium, phosphorous, manganese, biotin and vitamins A and C were associated with increased risk of CLD. In particular, high protein and sodium intakes had a strongly protective effect, whilst high fat and phosphorous intakes massively increased the risk of CLD. The whole model accounted for 64% of the variability in CLD.

## Conclusions

This study supports the idea that the risk of CLD is strongly influenced by nutrition. In addition, it seems that relatively high protein and sodium intakes across stay offer a protective effect, whilst high fat and phosphorous intakes in the face of static provision of other nutrients should be avoided. This secondary analysis of observational data is subject to limitations, and the hypotheses generated here warrant testing in formal trials.

Table

Nutrient	Odds Ratio (95% Confidence Interval)	p Value
Energy (kcal/kg)	0.814 (0.367 - 1.801)	0,611
Protein (g/kg)	0.0000002 (0 - 0.007)	<b>0,004</b>
Carbohydrate (g/kg)	7.517 (0.164 - 344.499)	0,301
Fat (g/kg)	156903.4 (2.562 – 9.61E+9)	<b>0,033</b>
Sodium (mmol/kg)	0.003 (0 - 0.156)	<b>0,004</b>
Chloride (mmol/kg)	499.798 (9.036 - 27644.65)	<b>0,002</b>
Potassium (mmol/kg)	0.027 (0 - 2.343)	0,112
Calcium (mmol/kg)	109.417 (0.101 - 119058.8)	0,188
Phosphorous (mmol/kg)	151248.7 (26.351 – 8.68E+8)	<b>0,007</b>
Magnesium (mmol/kg)	1.68E+17 (0 - 1.51E+44)	0,255
Iron (µmol/kg)	0.993 (0.919 - 1.072)	0,854
Zinc (µmol/kg)	0.639 (0.043 - 9.377)	0,744
Copper (µmol/kg)	0.0000001 (0 – 260E+19)	0,592
Selenium (nmol/kg)	0.958 (0.504 - 1.823)	0,896
Iodine (nmol/kg)	1.073 (0.949 - 1.214)	0,26
Manganese (nmol/kg)	1.012 (1.004 - 1.02)	<b>0,004</b>
Vitamin A (IU/kg)	1.027 (1.002 - 1.052)	<b>0,034</b>
Vitamin D (IU/kg)	0.997 (0.954 - 1.042)	0,884
Vitamin E (IU/kg)	0.428 (0.038 - 4.833)	0,493
Vitamin K (µg/kg)	1.003 (0.939 - 1.072)	0,922
Thiamin (µg/kg)	0.8 (0.675 - 0.949)	<b>0,01</b>
Riboflavin (µg/kg)	0.702 (0.518 - 0.952)	<b>0,023</b>
Vitamin B6 (µg/kg)	1.496 (1.076 - 2.079)	<b>0,017</b>
Folate (µg/kg)	0.883 (0.621 - 1.255)	0,487
Vitamin B12 (µg/kg)	5.946 (0 - 238288.4)	0,742
Biotin (µg/kg)	19.177 (1.904 - 193.203)	<b>0,012</b>
Pantothenic Acid (mg/kg)	0.605 (0.31 - 1.18)	0,14
Niacin (mg/kg)	12.125 (0.039 - 3768.027)	0,394
Vitamin C (mg/kg)	1.301 (1.088 - 1.555)	<b>0,004</b>
Taurine (mg/kg)	2.04 (0.916 - 4.543)	0,081
Choline (mg/kg)	0.379 (0.046 - 3.111)	0,367
Carnitine (mg/kg)	2594.132 (0.033 – 2.05E+8)	0,172
Inositol (mg/kg)	0.73 (0.555 - 0.96)	<b>0,024</b>
Birth weight SDS	0.356 (0.17 - 0.745)	<b>0,006</b>
Gestational Age at Birth	0.297 (0.178 - 0.495)	<b>&lt;0.001</b>

Sex	0.398 (0.136 - 1.159)	0,091
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Table 1: Multivariate logistic regression model of mean daily nutrient intakes across entire stay for risk of CLD, with adjustment for gestational age, weight and sex at birth. Significant ( $p < 0.05$ ) factors are highlighted in bold

## Nutrition and gastroenterology / Breast feeding

### MATERNAL EDUCATION AND BREASTFEEDING OF VERY PRETERM INFANTS IN NICUS: RESULTS FROM THE ITALIAN AREA-BASED EPICE STUDY (328)

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#### Introduction /Case Report

Maternal education has been linked to several perinatal outcomes, including breastfeeding<sup>1,2</sup>. In very preterm infants, maternal milk confers protection against neonatal sepsis and necrotizing enterocolitis and possibly contributes to neurodevelopment<sup>3</sup>; however immaturity, morbidities and prolonged hospitalization interfere with breastfeeding. This study uses the data collected in three Italian regions (Lazio, Emilia Romagna and Marche) for the European area-based project EPICE (Effective Perinatal Intensive Care in Europe) on use of evidence-based care in 11 EU Member States. The aim is to explore the impact of maternal education on breastfeeding for very preterm infants in NICUs.

#### Patients and Methods

All births at 22-31 weeks gestation in the three regions were recruited over 12 months in 2011/12. Use of maternal milk was assessed both at initiation of enteral feeding (time of first feed and milk type in the subsequent 24h) and at discharge (any maternal milk, exclusive maternal milk, and any feeding directly from the breast). Information on maternal education (university, upper secondary, lower secondary or less) was also collected.

Multivariable logistic modelling was used to explore the relation between maternal education and outcomes adjusting for potential confounders (mother age, parity, country of birth, gestational age, multiplicity, infant sex, congenital malformations, inborn status). Multilevel analysis accounted for the clustering of observations within regions and NICUs.

#### Results

Type of first enteral feed was recorded for 1031 of the 1114 infants admitted to neonatal intensive care; 259 babies (25.1 %) received only maternal milk at initial feedings, that started within the first 3 days of life for 159 babies (15.4%). At discharge, 62.7% of 975 babies received any, and 17.6% exclusive maternal milk feedings; 198 infants (21.1%) were fed at the breast, either exclusively or not.

There was no association between maternal education and type of early feeding. However, upper secondary and university education significantly increased the odds of exclusive maternal feeding at discharge (OR 2.6 and 3.3 respectively,  $p < 0.001$ ), and this applied also to any maternal milk and to feeding at the breast. Associations remained statistically significant after adjusting for potential confounders.

## Conclusions

Maternal education is strongly associated with maternal milk feeding at discharge, but has no effect on enteral feeding initiation. Better access to health care knowledge and increased awareness of the benefits of breastfeeding may lead more educated mothers to a positive decision to breastfeed their very preterm infants, while early use of maternal milk may be more dependent on NICUs policies and staff beliefs regarding value of breast milk.

## Nutrition and gastroenterology / Breast feeding

Exclusive human breast milk versus bovine milk-based formula in the feeding of very low birth weight infants (876)

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### Introduction /Case Report

We aimed to compare the duration of parenteral nutrition, hospital length of stay, incidence of nosocomial sepsis, necrotizing enterocolitis (NEC) and feeding intolerance in very low birth weight infants (VLBWIs) fed either bovine milk-based formula (BOV) or exclusively human breast milk (eBM).

### Patients and Methods

VLBWIs (gestation age : 25 – 30 weeks) who were born and admitted to Keimyung University Dongsan Medical Center, Daegu, South Korea, were enrolled. Infants born from March to August 2014 (N = 28) fed BOV. Infants born from September to December 2014 (N = 18) fed eBM. Pasteurized (heating at 62.5°C for 30 minutes) donor human milk was used if mother's own milk was not available due to insufficient breast milk production. Feeding intolerance was defined as the presence of gastric residual volume more than 50% of previous feeding; emesis or abdominal distension or both; and the decrease, delay, or discontinuation of enteral feedings. We studied infants with feeding intolerance fed hydrolyzed protein formula (HPF) or amino acid formula(AAF).

### Results

Gestational age ( $28.0 \pm 1.7$  vs  $27.8 \pm 1.4$ ) and birth weight ( $1055.0 \pm 265.9$  vs  $1175.6 \pm 187.5$ ), in BOV and eBM, respectively, were similar. Other demographic variables between two groups were similar, too. There was a significant difference in duration of parenteral nutrition ( $36.4$  vs  $24.1$ ,  $p = 0.038$ ), hospital length of stay ( $74.3$  vs  $61.2$ ,  $p = 0.037$ ), incidence of nosocomial sepsis ( $53.6\%$  vs  $22.2\%$ ,  $p = 0.035$ ), in BOV vs eBM, respectively. The incidence of NEC (stage  $\geq$  II) was decreased from  $21.4\%$  (6 cases) in BOV to  $5.6\%$  (1 case) in eBM, but not shown a significant difference ( $p = 0.144$ ). The incidence of feeding intolerance (feeding with HPF or AAF) was decreased from  $36.3\%$  (11 cases) in BOV to  $27.8\%$  (5 cases) in eBM, but not shown a significant difference ( $p = 0.424$ ). In all infants fed pasteurized donor human milk, perinatal cytomegalovirus infection was not found.

### Conclusions

An exclusively human-milk based diet is associated with a significant improvement in the incidence of nosocomial sepsis, duration of parenteral nutrition and hospital length of stay, but not in the incidence of NEC and feeding intolerance.

## Nutrition and gastroenterology / Metabolism

Insulin and glucagon levels of the cord blood between preterm infants with and without early hypoglycemia (Insulin, Glucagon, Cord blood, Hypoglycemia) (200)

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### Introduction /Case Report

Prematurity is a known risk factor for hypoglycemia, possibly associated with glucoregulatory hormone (insulin and glucagon) alterations. We aimed to determine whether insulin and glucagon levels of umbilical cord blood correlate with subsequent hypoglycemia after birth in preterm infants.

### Patients and Methods

98 preterm infants born at 23 to 34 weeks' gestation (mean gestational age  $30.5 \pm 3.3$  weeks, mean birth weight  $1,614 \pm 572$  g) were enrolled. The infants of diabetic mothers were excluded. Insulin and glucagon levels of the umbilical cord blood were measured by enzyme-linked immunosorbent assay. Preterm infants with hypoglycemia (blood glucose level  $\leq 40$  mg/dL) were compared with them without hypoglycemia during the first 2 hour after birth.

### Results

23 infants (23.6%) developed hypoglycemia. Gestational age, body weight, height, head circumference, ponderal index, gender, mode of delivery, Apgar score, incidence of small for gestational age and premature rupture of membrane were not different between infants with and without hypoglycemia. There was a significant difference in glucagon levels of the cord blood between infants with and without hypoglycemia ( $24 \pm 9$  vs.  $37 \pm 26$  pg/mL,  $p = 0.031$ ), but no difference in insulin levels ( $338 \pm 250$  vs.  $317 \pm 264$  pg/mL,  $p = 0.842$ ).

### Conclusions

Early hypoglycemia in preterm infants may be related to glucagon levels of the cord blood, but not insulin levels.

Circulation, O2 Transport and Haematology

NEONATAL PULSE OXIMETRY SCREENING: AN EVALUATION OF CURRENT CLINICAL PRACTICE (514)

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### Introduction /Case Report

Pulse oximetry screening has been well studied in research studies in over 250,000 children as a screening tool for detection of congenital heart disease. It has been reported to have high specificity and moderate sensitivity, fulfilling the criteria for universal screening too to detect critical congenital heart defects (CHDs) in neonates. Pulse oximetry screening was introduced as a neonatal screening tool in Jan 2014 in the Rosie hospital, Cambridge.

Aims:

1. To study the outcome of children with positive pulse oximetry test.
2. To assess adherence to the local guideline on pulse oximetry screening in neonates.

### Patients and Methods

A retrospective observational study and all the babies born in the Rosie Hospital between Nov 2014 and March 2015 were included in the study. Data were collected from the electronic patient records. Data analysed using Microsoft excel.

### Results

Pulse oximetry screening results were documented in 91% (1980 of the 2177) case notes studied.

47 of the 1980 neonates had low SpO<sub>2</sub> upon first measurement. Repeat pulse oximetry was documented in 27 out of these 47 neonates. 15 neonates had normal 2nd POS test result with an oxygen saturation of >95% on repeat while 12 had abnormal results (positivity 0.6%). More than half of babies had sepsis while one third of them had underlying congenital heart disease. Only one case needed medical treatment and none of them critical CHD. Table 1 shows details of all cases with positive results.

One child had false negative pulse oximetry screening, which was diagnosed with large VSD, ASD, PDA and persistent left superior vena cava at 2 weeks of age and needed surgical intervention for heart failure.

There was no reported case of neonatal collapse in the postnatal was during the study period.

### Conclusions

We found pulse oximetry screening to have high sensitivity and moderate specificity as reported in previous studies. Interestingly it was found to be an effective screening tool for detection of non-cardiac conditions in otherwise asymptomatic babies, which could potentially lead to significant illness in neonates.

No critical CHD case detected during the study period which could reflect high antenatal detection rate of CHDs in Cambridge.

Table

Table 1: Positive pulse oximetry screening cases

Sr number	Diagnosis	No of cases
1	Neonatal sepsis	5
2	Sepsis with mild PPHN	1
3	Congenital cystic adenomatoid malformation (CCAM)	1
4	Ventricular septal defect (VSD) with sepsis	1
5	Atrioventricular septal defect (AVSD)	1
6	Hypertrophic cardiomyopathy	1
7	Perimembranous VSD, atrial septal defect (ASD) and dysplastic aortic valves	1

Circulation, O2 Transport and Haematology

## DEVELOPMENT OF COAGULATION INDICES IN INFANTS LESS THAN 30 WEEKS WITH RESPECT TO GESTATIONAL AND POSTNATAL AGE (556)

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### Introduction /Case Report

Haemostasis of the newborn premature infant is poorly understood. How prematurity and postnatal transition affect the coagulation system is not well defined in infants before 30 weeks corrected gestation. We hypothesized that prospective characterization of coagulation tests in neonatal blood samples would provide information on the development of coagulation indices; prothrombin, activated partial thromboplastin time, and fibrinogen in relationship to both gestational and postnatal age.

### Patients and Methods

In a prospective observational study of infants up to 30 weeks corrected age, blood was drawn into citrated tubes on day 1 of life from non-heparinised lines and on day 3 and day 14 from peripheral phlebotomy if no plasma product had been administered. Vitamin K was administered at birth. Exclusion criteria included antenatal intraventricular haemorrhage or parental bleeding disorder. Preanalytical variables were controlled for by ensuring samples were correctly filled, not clotted, and majority drawn by lead investigator. Platelet poor plasma was obtained by centrifugation of whole blood at 3000rpm for 10 min. All samples were analysed for PT,APTT and Fibrinogen using ACL TOP 500 coagulometer using HemosIL APTT Iyophilized reagent, IL Clauss Fibrinogen and IL RecombiPlasTin reagent.

### Results

From a total of 137 neonates that were studied on one to 3 occasions, 127 neonatal samples were obtained on admission to NICU, 49 on day 3 of life and 25 at 2 weeks postnatal age. Attenuation reflected plasma product use and infants passing 30 weeks' corrected age. Serial paired samples were available in 17 infants. Gestation was inversely related with coagulation parameters with infants between 24-27/40 (n=70) having higher PT and APTT values compared to infants 28-29/40 (n=56),  $p=0.07$  and  $p=0.0002$  respectively. PT and APTT studied were higher on day 1 of life compared to matched corrected gestational age infant for all gestational ages.

### Conclusions

This study suggests that regulation of coagulation indices follows characteristic patterns relative to the gestation of the infant. Postnatal development was similar irrespective of initial gestational age suggesting that birth process initiates development of coagulation proteins.

Picture

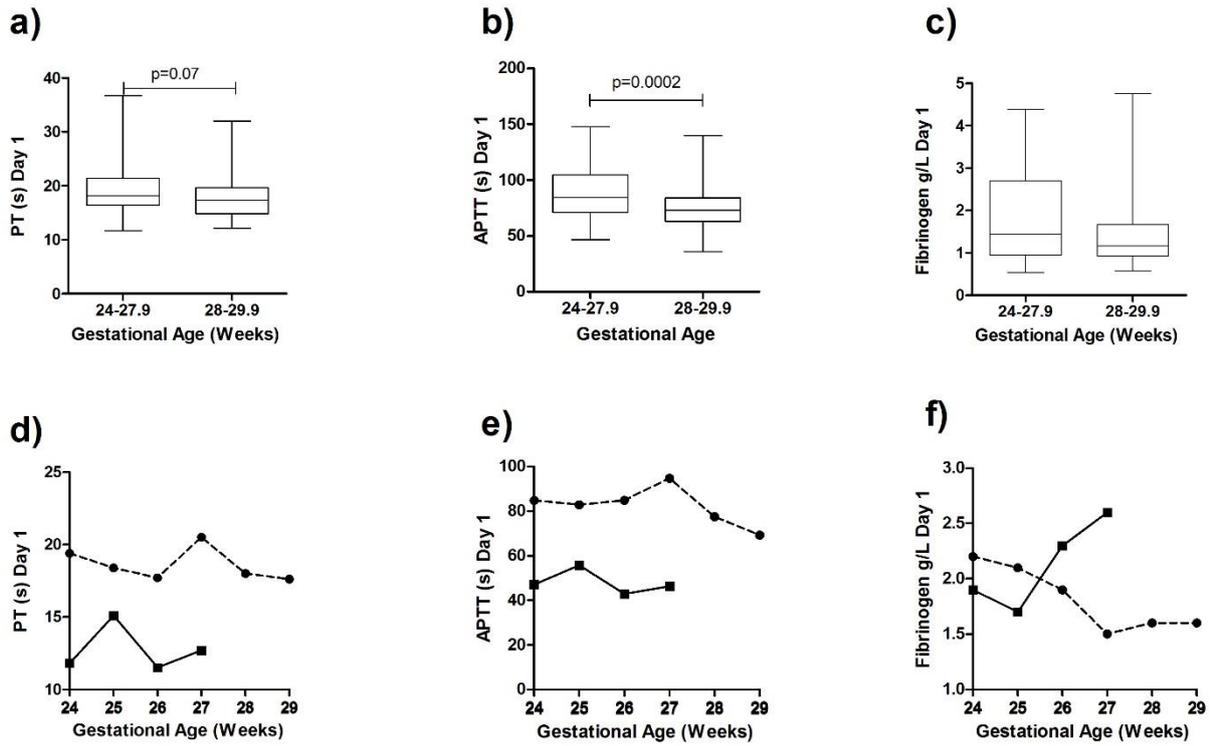


Figure: Coagulation parameters in preterm infants. PT (A), APTT (B) and fibrinogen (C) of peripheral blood drawn from non-heparinized lines on day 1 of life (preterm infants, n=127). Serial PT (D), APTT (E) and Fibrinogen of plasma prepared from peripheral blood drawn from peripheral lines on day 1(dashed line) and 14 of life (solid line) in extremely premature infants. \*PT=prothrombin time, APTT=activated partial thromboplastin time

Circulation, O2 Transport and Haematology / Placenta and prenatal factors

## CORD BLOOD INVESTIGATIONS IN PREMATURE NEONATES (543)

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### Introduction /Case Report

Very premature infants are at risk of bleeding complications and frequently coagulation profiles are performed at birth. However phlebotomy in extremely premature neonates is a major cause of blood loss leading to red cell transfusion, which is not without potential complications. The use of cord blood has been proposed as an alternative source of blood for baseline neonatal testing. Whether cord blood represents an accurate reflection of neonatal coagulation values is not determined. We hypothesized that prospective characterization of coagulation tests in cord blood alongside neonatal blood samples would provide information on feasibility of cord blood use for coagulation testing.

### Patients and Methods

In a prospective observational study, blood was drawn into citrated tubes from cord blood of neonates less than 30 weeks gestation and on day 1 from non-heparinised lines. Exclusion criteria included antenatal intraventricular haemorrhage or parental bleeding disorder. Preanalytical variables were controlled for by ensuring samples were correctly filled, not clotted, and majority drawn by lead investigator. Platelet poor plasma was obtained by centrifugation of whole blood at 3000rpm for 10 min. All samples were analysed for PT,APTT and Fibrinogen using ACL TOP500 coagulometer(Vendor Brennans,Dublin:Manufacturer Instrumentation Laboratory, Lexington,MA(IL) using HemosIL APTT lyophilized reagent, IL Clauss Fibrinogen and IL RecombiPlasTin reagent with analysers optical method of measurement.

### Results

Between April 2013-April 2015, 137 patients <30/40 were admitted, 11 excluded and 126 recruited. Median(25th-75th) gestational age and birth weight was 27.7(26.3-28.7)wks and 1020(818-1221)g respectively. 38 infants had paired cord and neonatal blood samples. Correlation of cord blood results to neonatal blood samples for PT, APTT and Fibrinogen was  $r=0.8, 0.6, 0.7$  respectively. Median (5th-95th percentile) cord PT of 15(11.9-21.5)s was observed vs. 15.8(12.4-32.2)s from neonatal samples. Mean cord APTT was 67.5(15.5)s vs. 73.4(18.4)s in neonatal samples and median cord fibrinogen was 1.2(0.6-4.2)g/L vs. 1.3(0.8-4.0)g/L. Preanalytical variables which led to difficulty in obtaining cord blood samples were due to coagulation( $n=40$ ), insufficient volume( $n=32$ ), haemolysis( $n=2$ ). Successful cord blood collection was associated with increasing gestational age and birthweight( $p=0.001$ ).

### Conclusions

In the largest prospective study to date of very preterm infants, we describe typical ranges for coagulation tests from neonatal and cord blood samples. Cord blood sampling offers an alternative to neonatal

sampling for coagulation testing. Further trials should examine needle free systems to minimise rates of coagulation in cord samples.

Picture

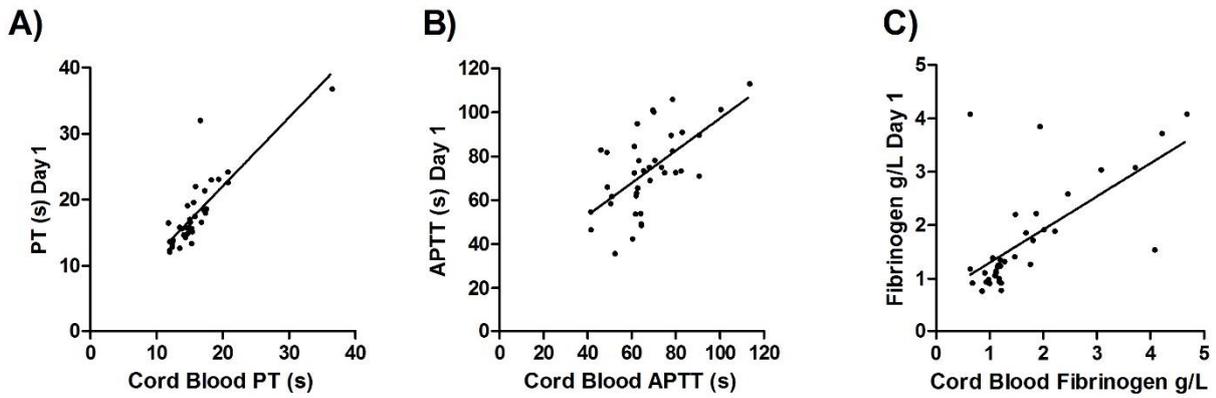


Figure: Scatterplot with least squared regression line for PT, APTT and Fibrinogen. Individual points represent the paired data of each individual patient (n=38). Correlation, Spearman R= 0.8 (A), Pearsons R= 0.6 (B), Spearman R= 0.7 (C).

## Brain & Development / Neonatal Brain Injury and Neuroprotection

### Levomepromazine reduces excitotoxic injury in HT-22 cells (394)

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#### Introduction /Case Report

Pain and stress cause high levels of excitotoxic glutamate and can lead to irreversible neuronal injury in preterm born infants. Thus a homeostasis of excitatory and inhibitory processes is of prime importance for this vulnerable system. Intensive care procedures need sedation and analgesia, therefore an advantageous substance should be chosen. A drug which could combine sedative, analgesic and anti-excitotoxic actions is the well-known atypical anti-psychotic phenothiazine levomepromazine. Of interest phenothiazines have been shown to be neuroprotective. We hypothesize that levomepromazine reduces excitotoxic injury in an in vitro model of excitotoxic brain injury.

#### Patients and Methods

We evaluated the effect of levomepromazine on cell death in a neuronal excitotoxic cell injury model in vitro. Therefore we used the glutamate-sensitive HT-22 neuronal cell line and applied glutamate to represent neonatal excitotoxic brain injury. Cells were preincubated with levomepromazine for thirty minutes before injury in a dosage of 0,5 $\mu$ M, 10 $\mu$ M, 20 $\mu$ M and 50 $\mu$ M or vehicle, respectively. Viability was evaluated after 17 hours of glutamate exposure using a colorimetric viability assay (CCK-8, Dojindo). Results were confirmed in four independent experiments.

#### Results

Pretreatment of HT-22 cells with levomepromazine before excitotoxic injury resulted in a significant increase in viability in the dosages 20 $\mu$ M (median 37,12%,  $p < 0,05$ ) and 50 $\mu$ M (median 41,9%,  $p < 0,05$ ) compared to control group (median 21,6%). Treatment with 0,5 $\mu$ M (median 17,9%) and 10 $\mu$ M (median 27,3%) did not significantly affect viability.

#### Conclusions

The application of the phenothiazine levomepromazine is neuroprotective in an in vitro model of excitotoxic brain injury. These results form the basis for further studies investigating underlying mechanisms in vitro and in vivo.

## Brain & Development / Structural and Functional Brain Imaging

### FULL NEONATAL EEG MONITORING: HOW WELL CAN NICU NURSES AND PHYSICIANS DETECT SEIZURES? AN EYE-TRACKER STUDY (335)

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#### Introduction /Case Report

Increasing evidence exists for the high likelihood of subclinical seizures in preterm and term neonates admitted to the intensive care. Since these epileptic foci can be highly focal, detection amplitude-integrated EEG can be missed. Hence full EEG is currently more often used as neuromonitoring tool in high risk infants on the NICU (neonatal intensive care unit). However, interpretation and seizure recognition can be difficult for non-trained physicians and nurses. Therefore, we want to compare full EEG assessment by NICU staff and NICU nurses, compared to trained EEG experts (child neurologists and clinical neurophysiologists), using a remote infrared eye-tracking device.

#### Patients and Methods

A pilot with an eye-tracker device (Tobii T60 XL, Tobii Corporation, Sweden) evaluated assessment of EEG images containing seizures and/or artifacts, by three participant groups: NICU physicians (n=8), NICU nurses (n=7) and EEG experts (n=8). Twenty-four EEG images were shown, each with a duration of 5 seconds. Three areas of interest (seizures, uncertain seizure activity and artifacts) were predefined and not visible for participants. With Tobii Studio Statistics, the total fixation duration, fixation count, total visit duration and visit count to the specific areas of interest, were calculated. To determine significant differences, we performed an unpaired Student's t-test, with 95% confidence interval by Graphpad. P values below 0,05 were considered significant.

#### Results

We found significant differences in mean total fixation duration (9,73 sec, SD=3,51 sec towards 16,14 sec, SD= 6,29 sec; p-value 0,0237), mean fixation count (32 sec, SD=11,31 sec towards 48 sec, SD=18,40 sec; p-value 0,0456) and total visit duration (9,78 sec, SD= 3,48 sec towards 16,26 sec, SD= 6,29 sec; p-value 0,0234) between respectively NICU physicians and EEG experts on uncertain seizure activity for all images together.

Also, the differences in mean total fixation duration (20,46 sec, SD= 5,32 sec towards 14,09 sec, SD=2,53 sec; p-value 0,0097) and mean total visit duration (20,73 sec, SD=5,50sec towards 14,16 sec, SD=2,57sec; p-value 0,0096) between NICU nurses and EEG experts on artifact were found to be significant.

## Conclusions

A significant difference was revealed in the visual assessment of uncertain seizures, seen less by NICU physicians compared to EEG experts. In contrast, NICU nurses were significantly more distracted by artifacts in EEG compared to EEG experts.

In order to obtain better interpretation of full EEG, future automated seizure detection systems are needed to improve the detection rate of uncertain seizures.

Nutrition and gastroenterology / Nutrition of the Very Preterm

NEOMUNE-NEONUTRINET: NUTRITION FOR PRETERM INFANTS AROUND THE WORLD DURING THE FIRST WEEKS AFTER BIRTH (676)

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## Introduction /Case Report

Poor nutrition and impaired growth is associated with adverse long-term consequences in very low birth weight (VLBW) infants. However, feeding these preterm infants is a challenge and the optimal timing, volume and diet remain controversial. The aim of the NeoNutriNet database is to give an overview of differences in feeding practice for VLBW infants around the world. This will help to identify optimal feeding regimens and design appropriate intervention studies.

## Patients and Methods

Fourteen hospitals in 'Western' (USA, Denmark, Netherlands, UK, Australia, New Zealand) and 'non-Western' (Mainland China, Taiwan, Nigeria) regions participated. Infants with a birth weight of 1500g or less were included. Collected data included timing and composition of (par)enteral nutrition and use of anti-/probiotics, anthropometrics and clinical outcomes from birth until a post-menstrual age of 37 weeks or discharge from hospital. Here we present preliminary results from all hospitals, eight non-Western (A-H) and six Western (I-N).

## Results

A total of 2905 infants were included. Gestational age (mean 29.6 wks), birth weight (median 1210g), gender distribution, and mortality differed significantly among hospitals (Table). Additionally nutritional regimes and outcomes, including time to full enteral feeding (150 ml/kg/day), incidence of necrotizing enterocolitis, growth velocity and probiotics use differed markedly. Infants from Western hospitals had lowest birth weight, but reached full enteral feeding earlier (median 14 vs. 31 days,  $p < 0.0001$ ).

## Conclusions

Nutritional practices and associated clinical outcomes in VLBW infants showed marked differences among hospitals. The variations may relate to differences in clinical practice, traditions or national

recommendations among hospitals. This is important to clarify because early enteral feeding is suggested to influence both short- and long-term outcomes. Results from the NeoNutriNet database will be a valuable tool to help design future intervention studies in this field.

Table

**Table: Baseline characteristics, nutritional and clinical outcomes**

<b>N<sup>1</sup></b>	<b>A</b>	<b>B</b>	<b>C</b>	<b>D</b>	<b>E</b>	<b>F</b>	<b>G</b>	<b>H</b>
<b>GA (wk), mean (SD)</b>	30.4 (2.2)	30.6 (2.0)	30.3 (2.2)	30.4 (2.0)	29.7 (2.0)	30.5 (2.1)	29.9 (2.6)	30.5 (2.4)
<b>BW (g), median (IQR)</b>	1275 (1120-1400)	1300 (1240-1430)	1300 (1150-1400)	1330 (1050-1450)	1300 (1150-1400)	1300 (1155-1410)	1199 (990-1363)	1250 (1100-1400)
<b>Male, n (%)</b>	234 (56.9)	13 (68.4)	231 (50.6)	43 (46.2)	108 (64.7)	153 (63.5)	117 (46.8)	65 (43.6)
<b>NEC, n (%)</b>	8 (1.9)	2 (10.5)	5 (1.1)	5 (5.4)	7 (4.2)	25 (10.4)	2 (0.8)	2 (1.3)
<b>Dead, n (%)</b>	44 (10.7)	0 (0)	7 (1.5)	3 (3.2)	14 (8.4)	8 (3.3)	0 (0.0)	26 (17.3)
<b>TFF 150<sup>2</sup>, d median (IQR)</b>	37 (33-41)	47 (38-54)	30 (29-31)	33 (28-42)	35 (32-42)	37 (34-40)	31 (28-36)	13 (12-14)
<b>Weight gain<sup>3</sup>, mean (SD)</b>	8.8 (4.3)	11.1 (3.2)	9.3 (2.4)	12.6 (3.0)	10.6 (3.4)	5.0 (3.5)	8.3 (4.4)	8.8 (5.5)
<b>Δ Z score<sup>3</sup>, mean (SD)</b>	-1.16 (0.50)	-0.75 (0.34)	-1.09 (0.33)	-0.70 (0.35)	-0.93 (0.40)	-1.55 (0.41)	-1.17 (0.42)	-1.22 (0.61)
<b>Probiotics, n (%)</b>	91 (22)	19 (100)	132 (29)	0 (0)	81 (49)	87 (37)	43 (17)	0 (0)

Epidemiology / Host responses and early diagnosis of infection

Review of fungal infections over a 6 year period (745)

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### Introduction /Case Report

Birmingham Women's Hospital is a busy Level 3 Neonatal Intensive Care Unit with over 1,000 admissions per year from >8,000 deliveries per year. We are currently reviewing our infection rates with regard to both bacterial and fungal infections. Over a period of 6.5 years, we have reviewed our positive blood cultures for candidal infection to see the numbers and the demographics of the babies. We also introduced Fluconazole prophylaxis in March 2010 for all babies > 26 weeks gestation.

### Patients and Methods

We reviewed all babies with candidaemia and there were a total of 6 babies over the 6.5 years. We carried out this review by using the Microbiology Department and reviewed the clinical episodes via our online database. We were interested in the gestation, what antibiotics they had been exposed to, whether they had required surgery and what their outcome was.

### Results

Gestation ranged from 24+0 to 29+6

50% of the babies were Outborn

100% of the babies had been exposed to broad spectrum antibiotics

33% of the babies had undergone surgery

33% of the babies died

33% of the babies had seizures

17% of the babies had fungal infection shown on ultrasound scan

### Conclusions

We have a strict antibiotics policy encouraging the use of narrow spectrum antibiotics for both our first and second line. Our rate of invasive fungal infection is very low, being less than 1 per 1,000 admissions. Of the babies who did have candidaemia, they were all complex, preterm neonates who had been exposed to broad spectrum antibiotics. Interestingly, the majority of the cases were in a cluster in 2011 and we have not had a case over the last 2 years.

Epidemiology / Host responses and early diagnosis of infection

## RELATION OF UMBILICAL CORD BLOOD IP-10 AND IL-6 LEVELS WITH CLINICAL AND LABORATORY PARAMETERS IN PRETERM INFANTS (196)

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### Introduction /Case Report

Umbilical cord blood cytokine levels, placental pathology, postnatal clinical evaluation and imaging modalities are used in assessment of fetal involvement in intrauterine inflammation. We aimed to investigate how umbilical cord blood IFN- $\gamma$ -inducible protein 10 (IP-10) and IL-6 levels are related to clinical and laboratory parameters in preterm infants.

### Patients and Methods

Preterm infants <37 weeks gestational age were included in the study. Infants with major congenital anomalies were excluded. Umbilical cord blood was obtained at the time of birth for IP-10 and IL-6 analysis. Antenatal, natal and postnatal characteristics of each infant and presence of morbidities related to prematurity were recorded. Fetal inflammatory response syndrome (FIRS) was defined as presence of chorioamnionitis or funisitis in pathologic examination of the placenta and/or high cord blood IL-6 levels.

### Results

Eighty five preterm infants were enrolled. Infants with preterm premature rupture of membranes (n=31) have significantly higher cord blood IP-10 and IL-6 levels (234 pg/ml vs.14.6 pg/ml,  $p<0.001$ ; 4.2 pg/ml vs. 1.6 pg/ml,  $p<0.001$ ). Infants with FIRS (n=37) have significantly higher cord blood IP-10 levels (472 pg/ml vs. 11,8pg/ml  $p<0.001$ ). Patients who were diagnosed with early (n=7) or late (n=8) neonatal sepsis had significantly higher cord blood IP-10 levels (359pg/ml, 620pg/ml vs 200pg/ml  $p<0.05$ ). There was no relationship between other morbidities and IP-10 levels.

### Conclusions

Umbilical cord blood IP-10 levels are related to fetal inflammation in preterm infants. IP-10 measurement in cord blood can be valuable in diagnosis of FIRS, and early prediction of neonatal sepsis.

Table

**Table 1:** IP-10 and IL-6 levels in infant born after preterm premature rupture of membranes

	PPROM (+) (n=31)	PPROM (-) (n=20)	p
IP-10 (pg/ml)	234 (4,8-1475)	4,2 (0,11-176)	<0,001
IL-6 (pg/ml)	14,6 (0,72-118)	1,6 (0,03-14,3)	<0,001

**Table 2:** IP-10 levels in infants with FIRS

	FIRS (+) n=37	FIRS (-) n=48	P
IP-10 (pg/ml)	472 (0,12-1475)	11,8 (0,11-274)	<0,001

**Table 3:** IP-10 and IL-6 levels in morbidities of prematurity

Neonatal Morbidities		IP-10 (pg/ml)	p	IL-6 (pg/ml)	p
RDS	(+)	188 ± 87	p=0.315	16.4 ± 25.3	p=0.133
	(-)	240 ± 45		6.98 ± 7.5	
BPD	(+)	190 ± 150	p=0.160	15.7 ± 24.9	p=0.313
	(-)	230 ± 43		6.6 ± 8.2	
Erken sepsis	(+)	359 ± 97	<b>p=0.009</b>	30.3 ± 14.4	<b>p=0.021</b>
	(-)	201 ± 40		12.7 ± 2.36	
Geç sepsis	(+)	620 ± 190	<b>p=0.013</b>	40.8 ± 17.0	<b>p=0.024</b>
	(-)	191 ± 40		11.4 ± 2.0	
NEK	(+)	55.4 ± 28	p=0.241	5.46 ± 2.6	p>0.05
	(-)	240 ± 43		14.9 ± 2.6	
İVK	(+)	329 ± 199	p=0.494	6.7 ± 2.7	p>0.05
	(-)	210 ± 40		15.4 ± 2.9	
ROP	(+)	243 ± 100	p=0.607	9.23 ± 2.57	p>0.05

Epidemiology / Host responses and early diagnosis of infection

## ENDOCAN AND SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS-1 AS NOVEL MARKERS FOR NEONATAL SEPSIS (204)

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### Introduction /Case Report

Neonatal sepsis is an important cause of neonatal morbidity and mortality in the neonatal intensive care unit. Soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) has been evaluated in sepsis and septic shock and it was found valuable in distinguishing septic ones from nonseptic ones. Endocan is constitutively expressed by endothelial cells and high levels of endocan may be of relevance for the promotion of systemic inflammation. The aim of this study was to investigate whether the levels of sTREM-1 and endocan are increased in late-onset neonatal sepsis.

### Patients and Methods

Patients were classified into the groups of septic and nonseptic ones. Blood was collected from a peripheral vein of all septic and healthy newborns at the time of initial laboratory evaluation before any treatment and within 48-72 hours after initiation of treatment. Serum sTREM-1 and endocan measurements were performed when the study was finished.

### Results

The study population comprised 50 neonates: 20 nonseptic and 30 septic. The groups were similar as regards baseline characteristics. The initial measurements of Interleukin-6 (IL-6), sTREM-1, endocan, and immature/total neutrophil ratio (I/T ratio) were significantly higher in septic neonates in comparison with nonseptic ones. Receiver operating characteristic (ROC) curve analyses revealed that IL-6, sTREM-1, endocan, and I/T ratio resulted in significant areas under the curve (AUC) with respect to early identification of septic neonates. Soluble TREM-1 and IL-6 performed the best to distinguish septic neonates from nonseptic ones. Univariate logistic regression analysis showed that increased IL-6 and sTREM-1 were strong predictors of neonatal LOS.

### Conclusions

Serum sTREM-1, IL-6, endocan levels and I/T ratio increase in septic neonates. However, diagnostic accuracy of circulating sTREM-1 seems to be better than endocan and I/T ratio, but less than IL-6.

Table

**Table 2.** Diagnostic accuracy of serum IL-6, sTREM-1, endocan, and I/T ratio in septic neonates

Diagnostic parameters	Cut-off point	ROC AUC (95%-CI)	p value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR	NLR
Biomarkers									
IL-6 (ng/ml)	7	0.96 (0.908-0.998)	<0.001	93.3	95	96.6	90.5	18.66	0.07
sTREM-1 (pg/ml)	450	0.97 (0.931-0.998)	<0.001	93.3	90	93.3	90	9.33	0.07
Endocan (ng/ml)	22.5	0.80 (0.674-0.923)	<0.001	76.7	70	79.3	66.7	2.56	0.33
I/T ratio	0.17	0.90 (0.826-0.987)	<0.001	83.3	80	86.2	85.7	4.17	0.21

ROC AUC: receiver-operating characteristic area under the curve, PPV: positive predictive value, NPV: negative predictive value, PLR: positive likelihood ratio, NLR: negative likelihood ratio, IL-6: interleukin-6, sTREM-1: soluble triggering receptor expressed on myeloid cells-1, I/T ratio: immature by total ratio.

Epidemiology / Host responses and early diagnosis of infection

THE INCIDENCE OF BACTERIAL INFECTIONS AMONG ELBW PRETERMS HOSPITALIZED AT THE NEONATAL INTENSIVE CARE UNIT (NICU) OF THE EMERGENCY COUNTY HOSPITAL OF TG-MURES (838)

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### Introduction /Case Report

Infections are an important source of morbidity and mortality among ELBW preterms. Prematurity comes with immature, ineffective and inadequate immune system, which leads to these three types of infection: early onset neonatal sepsis (EONS), late onset neonatal sepsis (LONS), nosocomial or healthcare associated neonatal infections(HCANI).The authors were interested to determine the incidence of bacterial infections/colonization, list the major micro-organisms responsible for each of these types of infections, understand the risk factors for NICU nosocomial infections and evaluate the antibiotic resistance pattern in our neonatal intensive care unit.

### Patients and Methods

This study was carried out on 190 ELBW premature newborns, born at or transferred to the Neonatology I Clinic of the Emergency County Hospital Tg-Mures, between 01.01.2009 and 31.12.2013. We examined blood culture, throat culture, gastric aspirate culture, coproculture and uroculture results, which were analyzed according to Gram stain, biochemical properties, and antimicrobial sensitivity testing using Gram positive and Gram negative antibiotic discs, based on the isolated species, then the results were reported as sensitive (S), intermediate (I) or resistant (R).

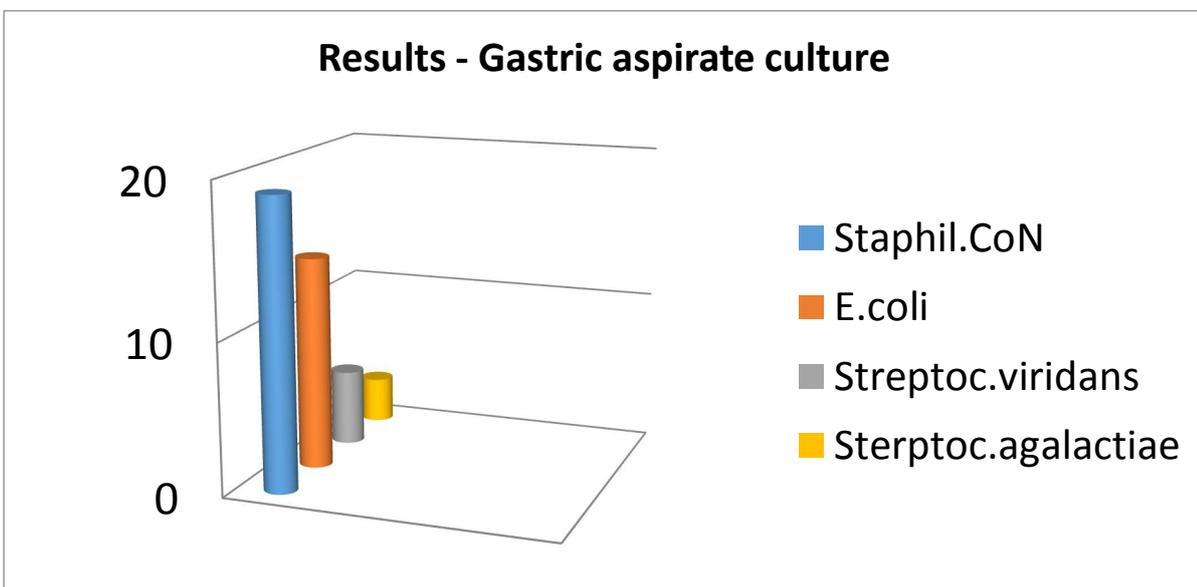
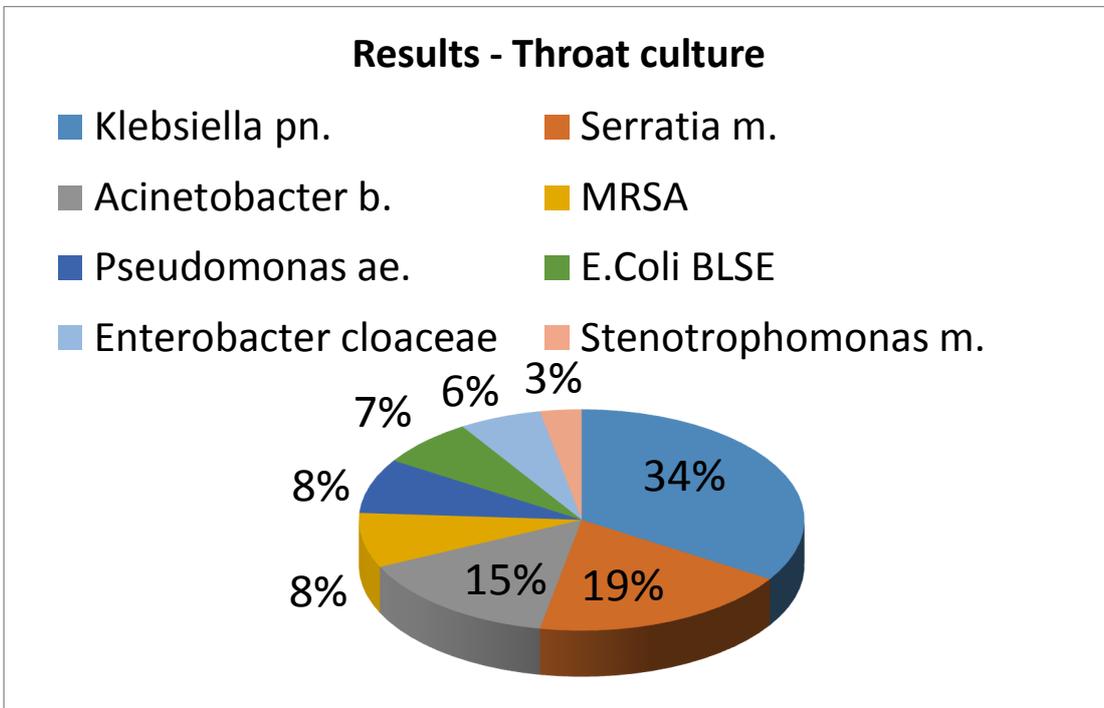
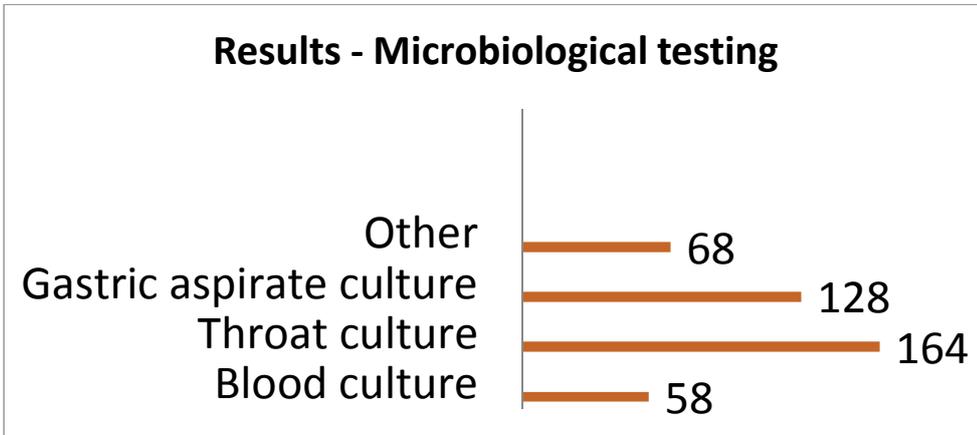
### Results

Out of the 190 cases we found microbiological records for 134 patients: Haemoculture was performed in 43.28% cases, and it was positive in 13.79%. The most commune species isolated from blood samples were *Serratia marcescens*, Coagulase-negative *Staphylococcus* and *Enterococcus faecium*, *Staphylococcus haemolyticus*, and *Acinetobacter baumannii*. *Candida albicans* occurred only in a few cases. Early onset neonatal sepsis is rare, but in case it occurs, it has a fulminating outcome. Late onset neonatal sepsis was caused by *Serratia marcescens*, *Acinetobacter baumannii*, CoN *Staphylococcus* and *Enterococcus faecium*. Nosocomial or healthcare associated infections are caused commonly by *Klebsiella pneumoniae*, *Serratia marcescens* and *Acinetobacter baumannii*. Treatment was administered according to the clinical symptoms and antibiotic susceptibility.

### Conclusions

Nosocomial colonization and/or infection are facts in the NICU. Clinical manifestation and outcome did not follow exactly the type of species detected. There is an urgent need of developing guidelines for antibiotic use and prevention measures especially for the high risk patients in the NICU, in order to stop the spread of multidrug resistance strains.

Table



## MODIFIED EDIN SCALE IMPLEMENTATION IN A NEONATAL INTENSIVE CARE UNIT (NICU): A PROSPECTIVE COHORT STUDY (287)

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### Introduction /Case Report

Chronic neonatal pain can lead to long-term adverse effects on the developing brain. Its proper recognition and treatment are recommended. Behavioural EDIN (Echelle Douleur Inconfort Nouveau-Né) scale for prolonged pain seems to be inaccurate for more premature babies, unable to express pain. Our aims were to test a modified EDIN scale (EDIN6), adding post-conceptual age (PCA) as a sixth item, and to collect nursing staff's perceptions of clinical utility of EDIN6 vs EDIN scale in neonatal prolonged pain assessment.

### Patients and Methods

In a two-phased (T1-T2) prospective study, pain was assessed at least once per 8h-shift in all neonates consecutively admitted in our NICU, for a 4-months period, from 24th November 2013 to 23rd March 2014. In T1 (from 24th November 2013 to 23rd January 2014) EDIN was applied; in T2 (from 24th January to 23rd March 2014) EDIN6 with an additional score of 2, 1, 0 respectively for 25-32, 33-37 and > 37 weeks PCA, was tested. Scores > 6 suggested pain. Nursing staff was administered a questionnaire, to compare their perceptions between EDIN and EDIN6, using a five-Likert scale (between 1: very low and 5: very high).

### Results

333 neonates were admitted and a total of 15960 scores were recorded. In T1 we evaluated 195 neonates (8693 scores: 1734 at PCA 25-32, 4335 at PCA 33-37, 2624 at PCA >37), while in T2 138 (7267 scores: 1472 at PCA 25-32, 2606 at PCA 33-37, 3189 at PCA >37). With EDIN6, cumulative detection of pain (score > 6) was 3-times (117/7267 vs 52/8693,  $p=0.001$ ), more premature babies being the main source of difference (50/1472 vs. 17/1734,  $p=0.001$  at PCA 25-32; 26/2606 vs. 10/4335,  $p=0.001$  at PCA 33-37; 41/3189 vs 25/2624,  $p=0.26$  at PCA > 37). Suitability of EDIN6 for the assessment of prolonged pain was perceived by the nursing staff as "very high" in 1% vs 0% if compared to EDIN, "high" in 12% vs 0%; "medium" in 37% vs 9%, "low" in 16% vs 21% and "very low" in 4% vs 40%. Overall adequacy ("medium to very high") perception was 71.4% for EDIN6 vs 13.4% for EDIN ( $p<0.001$ ).

### Conclusions

In T1 score>6 recurred in 0.6% of records vs 1,6% in T2. This difference was greater for the lowest PCAs. EDIN6 allowed us to better evaluate discomfort in preterm babies and could represent a more accurate tool to improve pain management in this population. These results are confirmed by nurses' subjective perception.

Table

<b>Pain detection = Score &gt; 6 / Total evaluation (%)</b>			
	EDIN	EDIN6	p (Fisher Exact T)
PCA < 33 wks	17/1734 (0,98%)	50/1472 (3,3%)	p < 0.001
PCA 33-37 wks	10/4335 (0,23%)	26/2606 (0,99%)	p < 0.001
PCA > 37 wks	25/2624 (0,95%)	41/3189 (1,28%)	p = 0,260
Total population	52/8693 (0,59%)	117/7267 (1,61%)	p < 0.001

Picture

Item	Description	Score
1. Facial activity	Relaxed facial activity	0
	Transient grimaces with frowning, lip purse and chin quiver	1
	Frequent grimaces, lasting grimaces	2
	Permanent grimaces resembling crying or blank face	3
2. Body movements	Relaxed body movements	0
	Transient agitation, often quiet	1
	Frequent agitation but can be calmed down	2
	Permanent agitation with contraction of fingers and toes and hypertonia of limbs or infrequent, slow movements and prostration	3
3. Quality of sleep	Falls asleep easily	0
	Falls asleep with difficulty	1
	Frequent, spontaneous arousals, independent of nursing, restless sleep	2
	Sleepless	3
4. Quality of contact with nurses	Smiles, attentive to voice	0
	Transient apprehension during interactions with nurses	1
	Difficulty communicating with nurses. Cries in response to minor stimulation	2
	Refuses to communicate with nurses. No interpersonal rapport. Moans without stimulation	3
5. Consolability	Quiet, total relaxation	0
	Calms down quickly in response to stroking or voice, or with sucking	1
	Calms down with difficulty	2
	Disconsolate. Sucks desperately	3
6. Post-conceptional age	> 37 wks	0
	33-37 wks	1
	< 33 wks	2

**Figure 1 : EDIN6 scale (modified Échelle Douleur Inconfort Nouveau-Né).**

Neonatal pain and discomfort scale integrated by gestational age as a sixth item.

Other / Involvement of parents in care

CO-RECRUITMENT IN NEONATAL RESEARCH; OUR EXPERIENCE OF ENROLLING MOTHERS AND BABIES IN MULTIPLE INTERVENTIONAL STUDIES. (526)

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### Introduction /Case Report

Seeking parental consent for participation in neonatal research has the potential to increase families' stress [1]. Early consent poses ethical and practical challenges. These are magnified when consent for multiple trials is sought [2,3,4].

Many parents welcome research participation, and some studies are suitable, or even designed with potential co-recruitment in mind. Three interventional RCTs recruited from almost identical patient groups over a 21 month period in our unit. We sought to describe levels of co-recruitment, and establish if parental decline of one study reduced the likelihood of participation in others. We also sought parental feedback on involvement in research.

### Patients and Methods

We reviewed approach and participation logs of three multicentre trials running concurrently over a 21 month period on our 32-bed tertiary neonatal unit. One RCT tested a perinatal intervention, and two trialled feeding related interventions. Clinicians were free not to approach families if they lacked clinical equipoise.

We assessed rates of approach, consent and randomization for the longest-running of the three studies and analysed reasons for non-recruitment.

We obtained additional data on eligibility from electronic records. A similar population of newborns was eligible for all three studies; those born at <32/40 or weighing <1500g with no significant congenital abnormalities. We limited our analysis to inborn infants.

### Results

Studies were well received on our unit. "We found reassurance that neonatal research would benefit both our little girl and many other babies in the future".

Over a period of 21 months, 145 babies were eligible for two studies and 21 for three. Recruited infants were less mature than those eligible overall (28 vs 29 weeks  $p<0.05$ ).

57% of parents were approached for consent to the longest-running trial. Reasons for not approaching included 'Time constraints' (40%), 'Clinical decision' (26%), 'Patient factors' (8%) and 'Staffing' (2%).

While three studies were open, 67% of 21 were recruited. 14% were in three, 43% in two, and 10% in only one trial.

Half those declining an initial trial participated in a second. More of those joining a first trial agreed to join a second (70% vs 48%  $p<0.05$ ).

Of parents consenting to a second trial, 64% had declined participation in a first trial.

## Conclusions

High levels of research participation and co-recruitment to RCTs, are possible in neonatal units. Whilst parents who had declined to participate in an initial study were less likely to consent to subsequent trials, the majority who joined a second had in fact declined a first.

Clinicians should not be dissuaded from seeking consent solely on the grounds of initial lack of participation and many parents appreciate being involved in research.

Nutrition and gastroenterology / Metabolism

## GLUCOSE LEVELS DURING METABOLIC TRANSITION IN THE HEALTHY TERM NEWBORN: A PILOT STUDY WITH CONTINUOUS GLUCOSE MONITORING (779)

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### Introduction /Case Report

There is ongoing controversy on the definition of normal blood glucose concentrations in the newborn, particularly during the transitional period. Immediately after birth, the infant undergoes an abrupt change from the continuous delivery of transplacental glucose to the alternation of intermittent fed and fasted states, requiring hormonal and metabolic adaptation. Current management of neonatal hypoglycaemia is based on safety thresholds established by pragmatic consensus of experts, based on a small number of studies from the last two decades. We aimed to investigate glucose levels during the transitional period in the healthy newborn by continuous glucose monitoring.

### Patients and Methods

Participants (n=6) were recruited among singleton uneventful pregnancies without risk factors for neonatal hypoglycaemia. After prenatal informed consent, a subcutaneous sensor was placed in the delivery room during the first hour of life, and connected to a continuous glucose monitor (CGM Gold® or iPro®, Minimed, Medtronic). The sensor measures interstitial glucose by an enzymatic reaction, and a concentration value is stored by the monitor every 5 minutes. Limits of detection are 40-430 mg/dL. Three capillary glucose measurements per day were used for calibration. The devices were removed after 48 hours and the information from the monitors and the capillary measurements were subsequently downloaded. Data were analyzed with SPSS® statistical package v17.0.

### Results

A total of 3142 interstitial glucose values (equivalent to 262 hours) and 41 capillary measurements were analyzed. There was a good correlation between methods ( $r= 0.782$ ,  $p<0.001$ ), with a Mean Absolute Relative Difference of  $8.0\pm 8.1\%$ . Mean glucose values were similar with both techniques (interstitial:  $55.3 \pm 9.0$  mg/dL; capillary:  $53.3 \pm 13.2$  mg/dL; paired values Student's t:  $p 0.462$ ). Due to inherent technical limitations of the CGM systems, the lowest extreme values were lower with point-of-care glucometers, but the interquartile ranges were similar (interstitial: IQR 49.0-62.0mg/dL; capillary: 45.0-60.0 mg/dL). Hypoglycaemia was defined as an interstitial glucose value of 40mg/dL for 20 minutes or longer. Five of the babies (80%) had episodes fulfilling this criterion (total of 14 episodes), with most (80%) appearing during the first 24 hours of monitoring.

### Conclusions

CGM systems were useful for a detailed evaluation of glucose values on the postnatal metabolic transitional period and acceptability was good. Correlation with capillary measurements was good. In spite

of a lower limit of detection of 40 mg/dL, probably overestimating nadir values, it allows for a more detailed picture of temporal evolution during the first 48 hours of life than intermittent methods.

Epidemiology / Nosocomial infection and colonization

## CAN A NETWORK-BASED SURVEILLANCE APPROACH ENHANCE KNOWLEDGE AND CONTROL OF MRSA SPREAD IN NICU? THE PALERMO (ITALY) EXPERIENCE (801)

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### Introduction /Case Report

Methicillin resistant *Staphylococcus aureus* (MRSA) is a major causal agent of infection in neonatal intensive care units (NICUs). Colonized neonates generally act as a reservoir and transmission between patients is the major driving force of MRSA spread. Referral NICUs frequently admit infants who previously stayed in other NICUs and can carry multidrug resistant pathogens, including MRSA.

The aim of our study was to assess MRSA colonization prevalence in five NICUs of Palermo area, Italy, which are connected by patient referrals, and to analyse each local epidemiology. An innovative network-based strategy has been tested in order to design targeted infection control strategies.

### Patients and Methods

Since February 2014 a network surveillance study is performed in five NICUs in Palermo area, Italy, including the University hospital NICU (NICU1), referral unit for pediatric surgery and genetic diseases, where a surveillance program on MRSA and multiresistant Gram negatives by universal weekly rectal and nasal sampling is in place since 2009.

Nasal swabs were collected in NICUs 2 to 5 at four week-intervals and cultured on selective culture media, according with previously described procedures. MRSA were typed by Multi Locus Variable Number Tandem Repeat Fingerprinting, PCR for *tst-1* and *pvl* genes, SCCmec characterization, MultiLocus Sequence Typing (MLST). Local epidemiology of each NICU has been studied and compared by statistical methods. MRSA transmission between NICU has been traced.

### Results

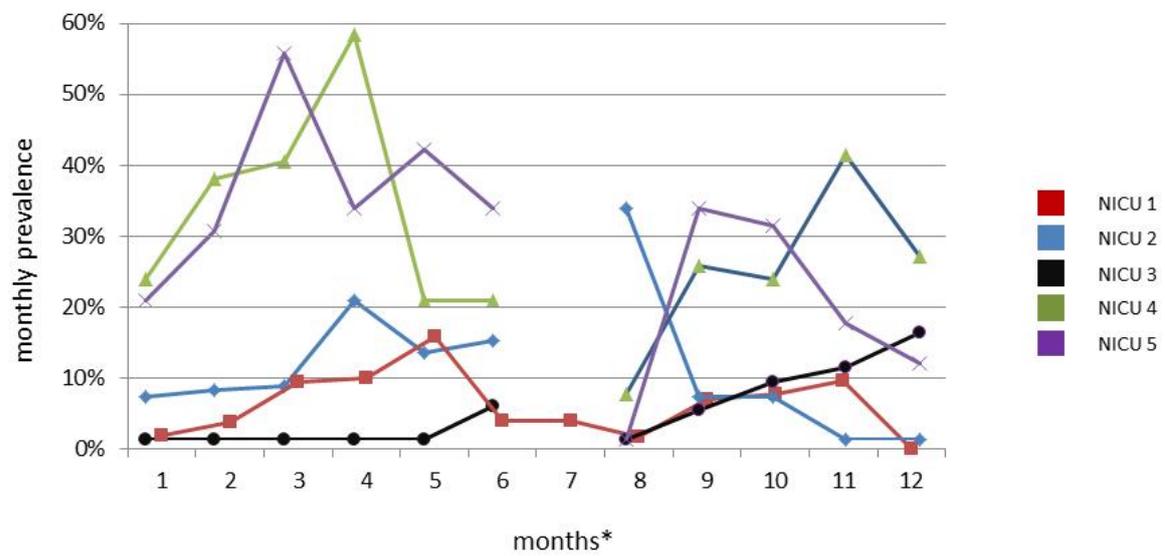
Mean yearly MRSA colonization prevalence significantly differed between the five NICUs, ranging from 3% to 26%. NICU1 had a mean yearly prevalence of 6%. All NICUs showed a decreasing trend of their MRSA colonization frequency in the second semester of surveillance, except for NICU3 which had the lowest monthly prevalence through the year. A *tst-1*- positive ST22-MRSA-IVa strain was predominant in all NICUs, accounting for 68% (NICU4) to 95% (NICU1) of MRSA isolates. Many epidemiologically relevant MRSA lineages, such as ST217-MRSA-IVh (an allelic variant of EMRSA-15), ST1-MRSA IVa, ST5-MRSA-IVg (Pediatric clone) and *pvl* positive ST80-MRSA-IVa (European clone) were also detected. Strain discrimination by molecular typing showed that most MRSA strains were shared between at least two NICUs. The *pvl* positive ST80 isolate was detected in NICU1 in a child born in Palermo from Tunisian parents.

## Conclusions

Prevalences of MRSA colonization in Palermo area NICUs were high and different. EMRSA-15/Middle Eastern Variant confirmed to be endemic in all NICUs. Transfer of neonates proved to be epidemiologically linked to trade of some MRSA isolates. A network-based surveillance approach can be a helpful tool to understand local epidemiology of MRSA, to clarify cross transmission routes between NICUs and to effectively prevent and control MRSA spreads.

## Picture

Figure. Monthly prevalence of MRSA colonization in the NICUs under surveillance, Palermo, Italy



\* In August, the active surveillance culture (ACS) program in the NICUs 2 to 5 was not carried out

Other / Involvement of parents in care

## PARENTING THE POST-NICU PREMATURE INFANTS: PROBLEMS AND INFORMATION NEEDS AFTER DISCHARGE (013)

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### Introduction /Case Report

The hospitalization of a critically ill infant to the neonatal intensive care unit can be very stressful for parents. Guidelines recommended that discharge planning begin upon admission. Parents' confidence and ability to care for their infants at home can be strengthened throughout the infants' hospitalization by offering them training and opportunities to participate in care giving activities. However, parent participation in care is often minimal during hospitalization because of their anxiety or insufficient support of health professionals. This situation may cause problems for the infant care and telephone counseling support needs (or home care services) after discharge.

### Patients and Methods

The sample of this descriptive study included 238 preterm infants and their parents. Data was collected by using High Risk Infant and Parent Information Form, Post-discharge Infant Following Form and Telephone Counseling Form. At 8 weeks post discharge from hospital, researchers administered a structured telephone interview that focused on problems of mothers for preterm infant's care. Researchers gave their mobile phones for helping the parents by the telephone support counseling that they need about their infants care. Information needs of parents during 8 weeks after discharge were recorded to Telephone Counseling Form. In the step of data evaluation; percentage, mean, standard deviation, were used.

### Results

More than half of mothers 70,2 % had problems about their preterm infants care after discharge. The subjects that mothers had problems were; recognizing the symptoms of the disease (%93,4), drug administration (%49,7), nutrition (%18,6), body care (%15,6) and sleeping (%4,2). More than half of mothers 62,2 % phoned researchers to obtain information on issues related to infant care. The subjects that mothers counseled were colic pain and constipation (%78,4), recognizing the symptoms of the disease (%39,9), how and how much the infant feed (%38,5), drug administration (%30,4) and vaccines (%13,5).

### Conclusions

High rate of mothers having problems of baby care after the discharge, indicate that the discharge services are not effective and sufficient. To support a family centered philosophy of care, parents must be welcomed as partners in the discharge process. Parents should be able to provide care to their infant as desired throughout the hospitalization to ensure ample opportunity to develop competence and confidence in care giving.

Circulation, O2 Transport and Haematology

## MEASUREMENT OF VITAMIN K METABOLITES IN NEONATAL STOOL SAMPLES ALLOWS NON-INVASIVE COMPARISON OF VITAMIN K METABOLISM IN TERM AND PRETERM NEONATES (522)

D.J. Card 1; P. Clarke 2; R. Huisjes 3; K. Deuchande 1; K. Few 2; M.J. Shearer 4 and D.J. Harrington 1.

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### Introduction /Case Report

Prophylactic phytomenadione (vitamin K1) effectively prevents vitamin K deficiency bleeding of the newborn. However there are currently insufficient data to inform further dose optimisation which may be desirable, particularly for preterm infants. A non-invasive method to assess vitamin K status would be preferable. Our aims were: i) to devise a novel method for the measurement of the two major metabolites of vitamin K (5-carbon and 7-carbon side chain aglycone metabolites) in neonatal faecal matter; ii) apply this method to the comparison of patterns of excretion in term and preterm neonates. We hypothesised that vitamin K metabolite excretion in stool would be lower in preterm infants.

### Patients and Methods

Meconium and subsequent stool samples were collected longitudinally from 21 infants (11 preterm, 10 term) during the first 6 months of life. All term neonates received 1 mg intramuscular (IM) vitamin K1, preterm neonates received ~0.4 mg/Kg IM. Data on type of milk feeding regimes were collected during the study. Vitamin K metabolites were measured in stool samples as detailed in figure 1.

### Results

Comparison of vitamin K metabolite excretion corrected for dry faecal mass (see table 1) indicated preterm neonates have a reduced rate of vitamin K metabolism compared to term neonates during the first 12 weeks of life, which reaches rates equivalent to term neonates between 5 and 12 weeks of life. There was no significant difference in the relative abundance of the two metabolites in the two groups (preterm mean 7C excretion = 35.2 % of total metabolite excretion, term = 36.0%). Mean faecal vitamin K metabolite excretion was markedly elevated in formula vs. breast milk fed neonates (table 1).

### Conclusions

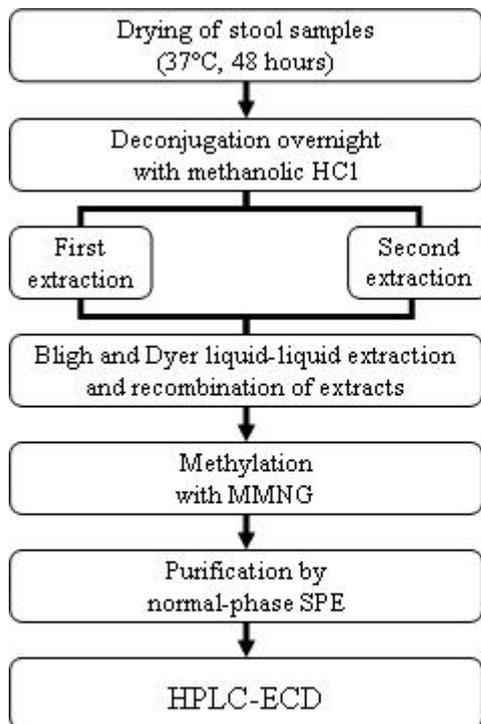
In this study faecal vitamin K metabolite excretion was consistent with data from previous studies indicating preterm neonates have a reduced rate of vitamin K metabolism compared to term neonates during the first 1-3 months of life. The assessment of vitamin K status by measurement of vitamin K metabolite excretion in stool samples may allow a non-invasive means to refine phytomenadione dosages in neonates.

Table

Table 1. Gestational age, vitamin K<sub>1</sub> dosage and comparison of metabolite excretion in term vs. preterm and breast fed vs. formula fed neonates. \*Not applicable as feeding regimes switched during the study. †Insufficient data, all neonates breast fed at this time point.

	n	Mean gestational age (range)	Mean vitamin K <sub>1</sub> dosage (range)	Mean 5C vitamin K metabolite excretion (µg/g dried stool sample)			
				9.9 h ± 2.4 h	31.6 h ± 9.0 h	4.5 weeks ± 4.4 days	12.6 weeks ± 8.0 days
Term neonates	10	39.3 weeks (37.0-40.8)	0.28 mg/Kg (0.23-.0.34)	16.3	19.4	37.0	61.7
Preterm neonates	11	31.7 weeks (27.2-36.2)	0.41 mg/Kg (0.38-5.0)	0.8	3.2	27.3	61.1
Breast fed	*	*	*	†	11.3	3.5	1.7
Formula fed	*	*	*	†	19.6	65.0	148.9

Picture



Epidemiology / Host responses and early diagnosis of infection

ASSOCIATION OF FGF21 PLASMA LEVELS WITH INFECTION IN NEONATES: PRELIMINARY RESULTS (347)

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### Introduction /Case Report

Experimental studies have shown that Fibroblast Growth Factor 21 (FGF21), a key regulator of glucose and lipid metabolism, is also a positive acute phase response protein that protects animals from the toxic effects of lipopolysaccharide and sepsis. The involvement of FGF21 in neonatal infection is not known.

### Patients and Methods

Plasma FGF21 levels upon admission were determined by an immunoenzymatic technique in 25 term neonates with febrile infection and also in 52 healthy term neonates, as controls. In neonates with infection, associations of FGF21 levels with glucose, lipid and CRP levels were assessed.

### Results

Plasma FGF21 levels were significantly higher in neonates with infection than controls ( $p < 0.001$ ). FGF21 levels on admission correlated significantly with serum CRP levels ( $r = 0.487$ ,  $p = 0.01$ ) and also with plasma glucose ( $r = 0.446$ ,  $p < 0.05$ ) and triglyceride levels ( $r = 0.419$ ,  $p < 0.05$ ). The correlation between FGF21 and CRP levels remained significant after adjustment for glucose or triglyceride levels. Receiver operating characteristic analysis of FGF21 levels resulted in significant areas under the curve (AUC) for detecting infected neonates on admission (AUC=0.965,  $p < 0.001$ ).

### Conclusions

Circulating FGF21 levels are increased at the acute phase of neonatal infection possibly reflecting and/or participating in the inflammatory process. FGF21 may be used as an early marker of neonatal infection.

## Brain & Development / Placenta and prenatal factors

Outcome in patients with placental pathologies on fetal MRI - a prospective long-term outcome study (380)

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### Introduction /Case Report

MRI studies have shown that placental lesions can clearly affect pregnancy outcomes. We performed a prospective cohort study to investigate the influence of placental lesions diagnosed in fetal MRI on perinatal outcome and long-term neurodevelopmental outcome.

### Patients and Methods

In our hospital-based, cross-sectional study all fetal MRI examinations (n=187) of pregnancies with vascular placental lesions (i.e. infarction with/without hemorrhage, subchorionic thrombi/hemorrhages, intervillous thrombi/hemorrhages, or retroplacental hematoma) between 2003-2007 were included. The extent of the pathology was expressed as the percentage of abnormality related to the whole placental volume (Figure 1). Gestational age at MRI and at birth and the occurrence of intrauterine growth restriction (IUGR) were noted. Pathohistological reports were correlated to MRI findings. Infants were prospectively investigated using Bayley developmental scales at the age of 2–3.5 years. Impairment was categorized as a Bayley scale two standard deviations (SD) below normal (<85 points).

### Results

Perinatal mortality rate in singleton pregnancies was 36%. Among the survivors, 87% were born before 37+0 gestational weeks and 50% suffered from IUGR. Mortality was predicted by earlier gestational age at fetal MRI for placental pathology ( $P < 0.05$ ) and increasing extent of the vascular lesion ( $P < 0.05$ ), but not by the presence of pathological Doppler ultrasound data. Accuracy of the prediction was 82%, sensitivity was 67% and specificity 89%.

In 56 patients long term neurodevelopmental follow up was investigated (Table 1+2). Impairment rates were 32.2% in singletons and 32.0% in multiple births. No correlation between neuro/motordevelopmental outcome at 2–3.5 years and the type, extent or gestational week at the time of diagnoses of placental vascular pathologies was found.

### Conclusions

Fetal MR can detect vascular placental pathologies and can predict perinatal mortality. The long-term outcome of children with vascular placental pathologies on fetal MRI was associated with a high impairment rate after 2–3.5 years, both on motor- and neurodevelopmental Bayley scales. Neurological impairment did not correlate with the extent of placental involvement, intrauterine growth restriction, gestational age at birth or multiple state.

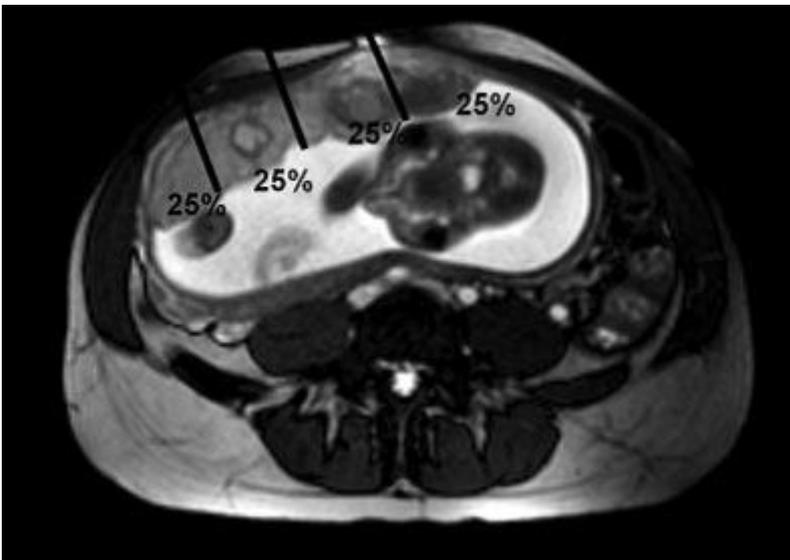
Table

**Table 1.** Outcome data

Singeltons <i>n</i> = 31	Impaired ( <i>n</i> = 10/32.2%)*	Not impaired ( <i>n</i> = 21/67.8%)	
GA at birth	31 + 1	30 + 4	<i>ns</i>
GA at MRI	27 + 1	27 + 6	<i>ns</i>
Extent of vascular lesion (%)	36.7	39.47	<i>ns</i>
IUGR ( <i>n</i> )	8	9	<i>ns</i>
Bayley >85 ( <i>n</i> )		21	
Bayley 50–85 ( <i>n</i> )	9	–	
Bayley <50 ( <i>n</i> )	1	–	
Multiples <i>n</i> = 25	Impaired ( <i>n</i> = 8/32%)*	Not impaired ( <i>n</i> = 17/68%)	
GA at birth	32 + 5	30 + 5	<i>ns</i>
GA at MRI	26 + 1	27 + 5	<i>ns</i>
Extent of vascular lesion (%)	51.4	60.9	<i>ns</i>
IUGR ( <i>n</i> )	8	3	<i>ns</i>
Bayley >85 ( <i>n</i> )		17	
Bayley 50–85 ( <i>n</i> )	6	–	
Bayley <50 ( <i>n</i> )	2	–	

\*Impaired = Bayley scale <85 (mental and/or motor).

Picture



Other / Involvement of parents in care

## VISCERAL FAT NECROSIS IN A NEWBORN AFTER THE WHOLE BODY HYPOTHERMIA (666)

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### Introduction /Case Report

Subcutaneous fat necrosis of the newborn (SCFN) is a condition characterized by inflammation of subcutaneous fat tissue in term and post-term newborns, mostly due to asphyxia and hypothermia. It is characterised as localized edema followed by subcutaneous firm nodules with surrounding erythema. We present here a case with a mild SCFN with accompanying widespread intraabdominal visceral fat necrosis after undergoing hypothermia due to perinatal asphyxia.

### Case Report

A 3,400-g female newborn was born at 38 weeks of gestation to a 40-year-old mother by spontaneous vaginal delivery. She was hospitalized after undergoing resuscitation in the delivery room. The newborn's 1. and 5. minute APGAR scores were three and four, respectively. She underwent resuscitation with intubation in the delivery room. With the present clinical and laboratory findings and the epileptic activity on amplitude-integrated electroencephalogram monitoring, the baby was diagnosed as perinatal asphyxia with left brachial plexus paralysis and then the whole body hypothermia was started at the first hour of her life. On the 17th day, the baby presented palpable subcutaneous nodules with erythema, limited to submandibular, brachial and gluteal regions. The first abdominal ultrasonography was completely normal but on the 28th day, confluent homogeneously increased reflectivity surrounding both kidneys (Figure 1), similar to the appearance of the subcutaneous nodules, was observed. MRI of the abdomen showed extensive peri-renal and peri-hepatic soft-tissue masses with increased signal intensity (Figure 2 and 3). This appearance was most consistent with fat necrosis. The baby is then discharged from the neonatology clinic on the 42nd day with the plan of further follow-up.

### Conclusions

To our knowledge, only one case with thoracic and abdominal involvement along with SCFN after asphyxia is described in the literature. This case is reported for its didactic radiological findings concordant with visceral fat necrosis besides a mild subcutaneous one, which was very rarely observed in such cases. We wanted to draw attention to the possible presence of visceral fat necrosis together with subcutaneous one, regardless of its severity.

Table



Picture



## Other / Miscellanea

### ARE EARLY POSTNATAL PROINFLAMMATORY CYTOKINE LEVELS, SNAPPE-II AND NTISS SCORES PREDICTIVE FOR MORBIDITY AND MORTALITY IN PRETERM NEONATES (161)

B. Dilac 1; N. Tekin 2; O Aydemir 2, E.C. Dinleyici 3; M.A. Aksit 2

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## Introduction /Case Report

Inflammation at fetomaternal interface is the main trigger of preterm birth. Fetal inflammatory response syndrome (FIRS) is related to increased neonatal morbidity and mortality. The Score for Neonatal Acute Physiology-Prenatal Extension-II (SNAPPE-II) is a scoring system designed to estimate mortality risk based on data obtained shortly after admission to neonatal intensive care unit (NICU). Neonatal Therapeutic Intervention Scoring System (NTISS) is a therapy-based index used as an indicator of neonatal illness severity. We aimed to assess whether proinflammatory cytokine levels early in the neonatal period, SNAPPE-II and NTISS can predict morbidity and mortality in preterm neonates.

## Patients and Methods

A prospective cohort study was conducted including inborn neonates <34 weeks gestational age (GA) who were admitted to NICU of Eskişehir Osmangazi University Hospital just after birth. IL-1 $\beta$ , IL-2, IL-6, IL-8, IL-10, TNF- $\alpha$ , and IFN- $\gamma$  levels were measured on 1st and 4th day of life (DOL) by Luminex method using "Human Ultrasensitif Cytokin 10-plex". Patient characteristics, SNAPPE-II, and NTISS on 1st, 7th and 14th DOL, neonatal morbidities such as bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), neonatal sepsis, necrotising enterocolitis (NEC) and mortality were recorded.

## Results

Birth weight and GA of the cohort (n=40) were 1430 $\pm$ 425g and 31.2 $\pm$ 2.3weeks, respectively (table 1). Neonates with BPD had higher SNAPPE-II (p=0.015), 1st(p=0.002), 7th(p=0.014), 14th(p<0.001) day NTISS. Cytokine levels were similar among neonates with and without BPD. First day IL-6 (p=0.037), SNAPPE-II (p=0.03) and 7th day NTISS (p=0.002) were higher in neonates with sepsis. Neonates with NEC had higher NTISS at 7th DOL (p=0.009). Neonates with and without ROP have similar cytokine levels, SNAPPE-II, and NTISS. Higher 1st day IL-6 (p=0.047), IL-10 (p=0.028) and SNAPPE-II (p=0.018) were associated with mortality (table 2 and table 3). SNAPPE-II was correlated with 1st day IL-6, IL-1 $\beta$ , IL-2 and IFN- $\gamma$ ; 1st day NTISS with 1st day IL-1 $\beta$ , IL-6, IL-8, and IL-10; 7th day NTISS with 1st day IL-6 and IL-10 and 14th day NTISS with 1st day IL-8 and IL-10.

## Conclusions

Proinflammatory cytokines were not predictive for BPD, ROP and NEC. High SNAPPE-II and NTISS were associated with BPD. IL-6 a proinflammatory cytokine associated with FIRS was higher in the first DOL in neonates who were later diagnosed with sepsis. FIRS might have continued as neonatal systemic

inflammatory response syndrome which had been recognised as sepsis. High IL-6 and IL-10 levels were associated with mortality.

Table

**Table 1: Patient Characteristics**

Gestational age (weeks) (mean±SD)	31.2 ± 2.3
Birth weight (gram) (mean±SD)	1430 ± 425
Male sex (%)	20 (50)
Antenatal steroids (%)	9 (22,5)
C/S (%)	36 (90)
Multiple gestation (%)	14 (35)
Resuscitation needed (%)	13 (32,5)
Preterm rupture of membranes (%)	4 (10)
RDS (%)	19 (47.5)

**Table 2: Cytokine levels**

	1 <sup>st</sup> day IL-1β (pg/ml)	4 <sup>th</sup> day IL β (pg/ml)	1 <sup>st</sup> day IL-2 (pg/ml)	4 <sup>th</sup> day IL-2 (pg/ml)	1 <sup>st</sup> day TNF α (pg/ml)	4 <sup>th</sup> day TNF α (pg/ml)	1 <sup>st</sup> day IFN γ (pg/ml)	4 <sup>th</sup> day IFN γ (pg/ml)	1 <sup>st</sup> day IL-6 (pg/ml)	4 <sup>th</sup> day IL-6 (pg/ml)	1 <sup>st</sup> day IL-8 (pg/ml)	4 <sup>th</sup> day IL-8 (pg/ml)	1 <sup>st</sup> day IL-10 (pg/ml)	4 <sup>th</sup> day IL-10 (pg/ml)
No BPD (n=28)	11.74	12.27	3.18	3.33	3.70	3.35	3.11	1.91	275.7	208.5	349.8	473.50	26.68	12.07
BPD (n= 12)	13.04	8.25	2.83	3.08	3.50	3.08	1.91	2.00	328.8	71.75	401.3	290.62	50.50	11.08
No sepsis (n= 11)	8.27	9.09	3.00	2.90	3.77	3.40	5.18	2.09	74.22	90.18	274.3	394.63	21.54	9.72
sepsis (n=29)	13.66	11.80	3.10	3.39	3.58	3.22	1.78	1.87	<b>377.6*</b>	196.3	401.6	427.74	38.91	12.57
No NEK (n= 32)	11.54	11.67	3.12	3.25	3.56	3.34	3.04	1.98	223.24	169.6	399.3	468.25	35.69	11.64
NEC (n= 8)	14.43	8.56	2.87	3.25	3.93	3.00	1.56	1.75	558.68	154.0	235.3	220.18	27.50	12.25
No ROP (n= 35)	12.41	11.47	3.08	3.29	3.67	3.37	2.91	1.92	314.13	174.5	372.0	445.35	36.60	12.33
ROP (n= 5)	10.30	8.1	3.00	3.00	3.40	2.60	1.60	2.00	141.90	111.3	322.7	231.60	16.4	7.9
Survivors (n= 34)	10.69	10.53	3.06	3.21	3.59	3.19	2.89	1.86	208.39	153.	362.0	404.36	34.40	10.3
Exitus (n=6)	20.08	13.83	3.16	3.50	3.91	3.75	1.91	2.33	752.16*	236.3*	385.6	499.50	31.83	19.8*

\*p<0.05

**Table 3: SNAPPE-II ve NTISS Scores**

	<b>SNAPPE-II</b>	<b>NTISS 1<sup>st</sup> day</b>	<b>NTISS 7<sup>th</sup> day</b>	<b>NTISS 14<sup>th</sup> day</b>
<b>No BPD (n=28)</b>	9.11	16.17	18.03	14.55
<b>BPD (n= 12)</b>	<b>21.16*</b>	<b>20.75*</b>	<b>23.25*</b>	<b>22.25#</b>
<b>No sepsis (n= 11)</b>	5.90	11.45	15.11	14.50
<b>Sepsis (n=29)</b>	<b>15.53*</b>	18.34	<b>21.27*</b>	17.96
<b>No NEC (n= 32)</b>	12.25	17.53	18.34	17.28
<b>NEC (n= 8)</b>	15.42	17.62	<b>24.62*</b>	18.00
<b>No ROP (n= 35)</b>	12.32	17.48	19.48	16.74
<b>ROP (n= 5)</b>	16.20	18.00	20.40	21.20
<b>Survivors (n=34)</b>	10.69	17.23	18.41	16.50
<b>Exitus (n=6)</b>	<b>24.50*</b>	19.33	26.33	24.00

\*p<0.05, #p<0.001

Circulation, O<sub>2</sub> Transport and Haematology / Organ blood flow and autoregulation

PRENATAL SMOKING, AS A POSSIBLE RISK FACTOR FOR RETINOPATHY OF PREMATURITY (406)

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## Introduction /Case Report

Exposure to maternal smoking during pregnancy is related to short and long-term health risks, ranging from intrauterine growth restriction to psychological problems. It is considered the most important determinant of decreased birth weight. The main risk factors of retinopathy of prematurity (ROP) are low gestational age and low birth weight, which are mainly caused by preterm birth. As the role of prenatal smoke exposure in the development of retinopathy of prematurity (ROP) has not been well established, the aim of the current study was to determine whether ROP was related to maternal smoking in the animal model of Oxygen-Induced Retinopathy (OIR).

## Patients and Methods

Sprague-Dawley rats were placed into a closed-chamber smoking system for whole-body smoke exposure 2x40 minutes daily from mating until delivery. For the treatment 4 research cigarettes per occasion were used. Controls did not smoke.

Newborn rat pups and dams were placed into an OIR model that cycled oxygen concentration between 50% and 10% every 24 h for 14 days, and then were placed in room air (RA) for an additional 7 days (rat OIR model). Functional ERG was performed on the 19. postnatal day. After 21 days their eyes were processed to flat mount lectin staining.

## Results

Quantification of avascular to whole retinal areas showed that prenatal smoking increases the vasoobliterated territory and there was also a significant growth in the number of neovascular tufts. These findings were further supported by functional examinations.

## Conclusions

Our results suggest that prenatal smoke exposure can worsen retinal vascular changes and raise the degree of ROP.

Other / Quality improvement and Safety and Error Preventio

## IATROGENIC SKIN DISORDERS AND RELATED FACTORS IN NEWBORN INFANTS (435)

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### Introduction /Case Report

During the past few decades, the rapid improvement of neonatal intensive care has resulted in dramatic decreases in neonatal mortality and impressive improvement in the survival of very premature infants, but the incidence of iatrogenic events has increased simultaneously. A significant proportion of the iatrogenic injuries that occur in NICUs result from skin injuries. The aim of our present study was to assess factors of possible relevance as concerns the development of skin disorders resulting from the immaturity of the skin and various iatrogenic complications in neonates requiring intensive care.

### Patients and Methods

A prospective cohort study was conducted in the NICU at the Department of Pediatrics at the University of Szeged between January 2012 and January 2014. All consecutive full- and preterm infants hospitalized in the NICU were included in the study and underwent whole-body skin examinations. Dermatologic disorders with the gestational age, sex, birth weight, area of involvement, etiology of the disorder, causative factors, diagnosis at admission and comorbidities were recorded, together with the nature of the management (dressings, ointments, medication and surgical interventions).

### Results

During the 2-year study period, a total of 460 neonates of Caucasian origin were admitted to the NICU, 87 of them exhibited some kind of iatrogenic skin disorder. The mean gestational age of the newborn infants with any of the iatrogenic skin injuries was significantly lower than that of the infants without any skin trauma. The length of NICU stay was significantly longer in newborns with iatrogenic skin injuries. The following factors, interventions and conditions proved to be associated significantly with the development of iatrogenic skin injuries: use of the INSURE technique, mechanical ventilation, insertion of an umbilical arterial catheter, circulatory/cardiac support, pulmonary hemorrhage, intracranial hemorrhage, patent ductus arteriosus, bronchopulmonary dysplasia and positive microbiology culture results.

### Conclusions

Iatrogenic dermatologic disorders are frequent in neonates requiring intensive care, may result in important physiological consequences and may lead to prolonged hospitalization. Prevention, early detection, and optimal treatment of these disorders with modern, standardized skin care management strategies can result in significant improvements in barrier function of the skin, increasing the overall efficacy of neonatal intensive care.

Other / Involvement of parents in care

## CLOSE COLLABORATION WITH PARENTS TRAINING PROGRAM IMPROVES FAMILY-CENTERED PRACTICES AND DECREASES MATERNAL DEPRESSIVE SYMPTOMS (236)

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### Introduction /Case Report

The Close Collaboration with Parents Training Program was developed in the NICU at Turku University Hospital (2009-2012) to implement family-centered care philosophy into the care culture of a unit. To make a sustainable change in the care culture, the training was targeted to the whole multiprofessional staff of the unit. The goal was to make the care culture more responsive to the individual needs of infants and parents, and to support collaboration between staff and parents related to decision-making involving the care of the infant. Today the intervention has been carried out in six Finnish hospitals.

### Patients and Methods

We have carried out pre- and post-intervention assessments of the immediate changes in the participating units. In Turku University Hospital, we have carried out long-term follow-up of family well-being. The immediate effects of the intervention on family centered care culture were assessed using the BLISS-audit tool. In two units, unit management, nurses, and parents (n=15) were interviewed pre- and post-intervention. They were asked to evaluate the family centered practices of the unit based on 140 criteria. The long-term effects of the intervention on the maternal depressive symptoms were measured using Edinburgh Postnatal Depression Scale (EPDS) at six months of the child's age (CA). The EPDS scores of 188 mothers (2011-14) were compared with the EPDS scores of 156 mothers (2001-06).

### Results

According to the BLISS-audit interviews, the care culture had changed to be more family centered (Table 1). During post-intervention periods, the family-centered practices were often evaluated as optimal by all groups (parents, staff, and management). The evaluations of the parents and staff became more consistent with each other regarding the different criteria, which were not met in the current practices of the unit even if the parents still saw more room for improvement. The EPDS results showed that the mothers had significantly less depressive symptoms in the post intervention cohort than the mothers in the pre intervention cohort. The mean EPDS score was 6.31 (SD 4.72) during the pre-intervention period and 4.34 (SD 4.52) during the post-intervention period, ( $p = 0.05$ ).

### Conclusions

The Close Collaboration with Parents Training had both immediate and long-term effects. The training intervention was successful in improving family-centered care. Importantly, it decreased maternal depressive symptoms long-term. The Close Collaboration with Parents Training Program offers a new model to implement family-centered care in the neonatal care culture that is beneficial to parental well-being.

Table

**Table 1** Percentages of parents', nurses', and managements' evaluation of the units' family-centered practices assessed with the Bliss-audit tool pre- and post intervention.

Evaluation of family-centered criteria	Unit 1		Unit 2	
	Pre-intervention	Post-intervention	Pre - intervention	Post intervention
<b>Parents</b>				
Fulfilled	24%	31%	25%	49%
Some fulfilled	59%	68%	63%	44%
Not fulfilled	17%	1%	12%	7%
<b>Nurses</b>				
Fulfilled	70%	77%	37%	75%
Some fulfilled	20%	25%	56%	20%
Not fulfilled	5%	3%	7%	5%
<b>Management</b>				
Fulfilled	66%	74%	50%	77%
Some fulfilled	29%	23%	41%	18%
Not fulfilled	5%	3%	9%	5%

## Other

### SAFETY EVALUATION OF RECOMBINANT HUMAN IGF-1/IGFBP-3 FOR THE PREVENTION OF RETINOPATHY OF PREMATURITY (109)

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## Introduction /Case Report

Low insulin-like growth factor (IGF)-1 is associated with retinopathy of prematurity (ROP) in preterm infants. IGF-1 replacement with recombinant human (rh)IGF-1/rhIGF binding protein (BP)-3 is being investigated for the prevention of ROP. We report safety data from a Phase 2 study (Sections A-C) conducted to evaluate the dose of rhIGF-1/rhIGFBP-3, administered by continuous intravenous infusion (from birth), needed to establish serum IGF-1 within physiological levels in preterm infants.

## Patients and Methods

In Section A, infants (gestational age [GA; wks+days] 26+0 to 27+6) received open-label rhIGF-1/rhIGFBP-3 by continuous infusion for up to 7 days. In Sections B/C, infants (GA 23+0 to 27+6) were randomised to receive rhIGF-1/rhIGFBP-3 by continuous infusion or standard care (control) up to a maximum postmenstrual age (PMA) of 28+6 (B)/29+6 (C). Dosing was variable and intended to establish serum IGF-1 within a target range based on intrauterine IGF-1 levels. Adverse events (AEs) were reported up to final examination (PMA 40 wks). In Section A, 5 infants were enrolled and average daily dose ranged from 60-109 µg/kg/d. Nineteen infants were enrolled in Sections B/C (9 treated, 10 control); in treated infants, mean (SD) dose was 95 (11) µg/kg/d and mean (SD) duration of infusion 14 (6) days.

## Results

Section A: All infants had AEs (32 AEs; most mild/moderate). Only 1 AE (polyuria) was considered possibly treatment-related, leading to discontinuation of study drug after 47h. All infants had ≥1 serious AE (SAE; total 9 SAEs); none were considered treatment-related. One infant had 2 episodes of hypoglycemia (p-glc<2.5 mmol/L) but neither was during study drug infusion. Sections B/C: All infants had AEs (75 [treated] and 98 [control] AEs; most mild/moderate); none were considered treatment-related. 5/9 treated infants had SAEs (15 SAEs) and 8/10 control infants (28 SAEs). One infant discontinued study drug due to cardiac tamponade (SAE) with fatal outcome at 18 days of age. No SAEs were considered treatment-related. There were 4 AEs of hypoglycemia in both the treated (during infusion) and control groups, occurring in 4 and 3 infants, respectively; none were considered treatment-related.

## Conclusions

Treatment was generally well-tolerated; there were no safety signals. Frequency of hypoglycemia did not differ between treated and control groups. Investigation at a higher rhIGF-1/rhIGFBP-3 dose is ongoing in Section D.

Other / Quality improvement and Safety and Error Preventio

## MORTALITY AND MORBIDITIES AFTER PRETERM BIRTH: COMPARISON OF THREE BIRTH COHORT IN 15 YEARS IN TAIWAN (468)

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### Introduction /Case Report

Preterm birth is associated with increased rates of neonatal mortality and morbidities. This is an important public health issue as rates of preterm birth are rising worldwide. There are several interventions to reduce neonatal morbidity, including usage of antenatal corticosteroids, increased use of surfactant replacement and centralized delivery and intensive care for the most immature infants in tertiary hospitals etc.. This study was aimed to evaluate the trends of survival, neonatal morbidity, parental socio-economic status, maternal and perinatal conditions for very low birth weight (VLBW) babies born in Taiwan during 2007-2011 compared to those born between 1997-2001 and 2002-2006.

### Patients and Methods

To address this issue, we conducted a retrospective cohort study in VLBW infants registered in the Premature Baby Foundation of Taiwan since 1997. A total of 22 neonatal intensive care units in Taiwan participated in the data collection. A series of studies was conducted and dividing into 3 studying periods (birth cohort 1997-2001; n=4647, birth cohort 2002-2006; n=4005, and birth cohort 2007-2011; n=4507) in a population-based sample. Main outcome measures included survival to discharge from hospital, pregnancy and delivery outcomes, and infant morbidity until discharge.

### Results

Comparing three cohorts (1997-2001, 2002-2006, 2007-2011), we found higher survival rate of extreme prematurity (GA  $\leq$  24 weeks) (18%, 28.7%, 35.5%) and advanced pregnancy age ( $>35y/o$ ) (13.4%, 17.4%, 23.2%). For perinatal condition, there were more high-risk pregnancies (74.3%, 86.4%, 89.5%), increased artificial reproductive assistance (11.4%, 10.8%, 21%), more women receiving complete course of antenatal steroid (27.7%, 35.5%, 43.9%), higher C-section rates (54.7%, 60.6%, 69.4%) and higher rates of maternal transfer (22.6%, 29.9%, 40.8%). There were less surfactant usage (46.4%, 51.8%, 40.6%) and ventilator support (78%, 77.3%, 42.4%). The incidence of PDA ligation increased (2.8%, 6.0%, 9.8%,  $p<0.001$ ). The sepsis rate, NEC, CLD and PVL were all significantly decreased. The ROP rate was similar throughout time, but proportion of severe ROP required treatment increased from 1.5% to 6.4%.

### Conclusions

Survival of VLBW in Taiwan has significantly improved in the past 15 years. Although there were more VLBW infants born from high risk pregnancies, the incidence of neonatal mortality and morbidities including sepsis, NEC, severe IVH, PVL and CLD were all decreased. However, either the overall incidence

for ROP or severe ROP required treatment remained high. Future investigation should be focused on reduction of retinopathy.

Circulation, O2 Transport and Haematology / Systemic circulation and cardiac output

PCT AS A BIOMARKER OF INFECTION IN NEWBORNS AFTER CARDIAC SURGERY BYPASS (767)

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## Introduction /Case Report

Cardiothoracic surgery and cardiopulmonary bypass are potent inducers of the systemic inflammatory response syndrome (SIRS) a systemic inflammatory response syndrome with courses with fever, high white blood cell (WBC) count and an increase C-reactive protein (CRP). It is challenging to differentiate this nonspecific response from sepsis in newborn population, leading to use broad-spectrum antibiotics that may not always be needed. Procalcitonin (PCT) has been proposed as a good biomarker of early-onset sepsis with high specificity and sensibility in adults and children but its utility as infectious biomarker following newborn cardiothoracic surgery is not well defined.

## Patients and Methods

- Asses the kinetics of PCT and CRP after cardiopulmonary bypass.
- Asses if PCT can discriminate better between SIRS and infection in the first 72 hours.
- Asses if PCT has a predictive value of morbidity/mortality during the first 72 hours, including the need of extracorporeal membrane oxygenation (ECMO).

Prospective study of newborn after cardiopulmonary bypass, since January 2013 to May 2015. A group of non-cardiopulmonary bypass surgical newborns were recruited to compare them with the group of cardiopulmonary bypass surgical newborns. Collected variables were: gestational age, sex, weight, diagnoses, cardiopulmonary bypass and ischemia time, CRP and PCT during the first 72 hours after surgery and sepsis diagnose.

## Results

55 patients were recruited, with a median of 39 gestational age and 11.5 days of life, at the time of the surgery. There were 6 infected patients. There were no differences between infected and non-infected patients according to age, bypass time, ischemia time or hypothermia. Regarding with infection diagnosis, statistically significant differences were detected in PCT values without any differences for CRP or WBC.

PCT had better area under the curve (AUC) in all the moments being the cutt-off as a infection >2.9 ng/ml at 24 hours, > 6.1 ng/ml at 48 hours and at 72 hours > 4.2 ng/ml

Higher PCT was independently associated with morbimortality and ECMO need at 48 hours ( $p=0.001$ ).

CRP and WBC did not correlate with infection or post-operative support.

## Conclusions

PCT is a useful marker in sepsis diagnose after cardiopulmonary bypass in newborn patients. High PCT values must alert this complication and other severe complications.

## Table

Table 1. Post-operative values WBC: White blood cell. CRP in mg/dL; PCT in ng/ml; WBC /mm<sup>3</sup>.

	Infected patients Median (p25-75)	Non-infected patients Median (p25-75)	p-value
PCT 24 hours	24.2 (11.8-45.4)	2.5 (1.32-3.67)	0.000
PCT 48 hours	25.5 (19.7-46.3)	3.7 (1.25-4.36)	0.000
PCT 72 hours	26.1 (20.1-48.2)	2.3 (1.28-3.55)	0.000
CRP 24 hours	90.0 (69.9-114.1)	78.75 (53.2-139.2)	0.581
CRP 48 hours	165.2 (118.8-209.7)	135.20 (93.7-199.8)	0.345
CRP 72 hours	170.3 (121.1-211.3)	142.3 (96.2-201.3)	0.267
WBC 24 hours	10.400 (9.300-12.300)	9.200 (7.850-10.950)	0.201
WBC 48 hours	11.500 (8.900-13.700)	9.800 (8.450-11.200)	0.052
WBC 72 hours	11.700 (9.400-13.500)	9.900 (8.520-11.300)	0.063

## Epidemiology / Host responses and early diagnosis of infection

### INCIDENCE AND OUTCOMES OF GROUP B STREPTOCOCCAL SEPSIS IN SWITZERLAND – RESULTS FROM THE SWISS PEDIATRIC SEPSIS STUDY (155)

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#### Introduction /Case Report

Despite the implementation of intrapartum antibiotic prophylaxis, the incidence of neonatal Group B streptococcal (GBS) disease remains high and considerable geographical variability has been reported. We aimed to assess the incidence of GBS sepsis in Switzerland.

#### Patients and Methods

The Swiss Pediatric Sepsis Study prospectively investigates the epidemiology of blood culture-proven sepsis in children in all tertiary care pediatric hospitals of Switzerland. We analyzed cases of GBS sepsis confirmed by positive blood culture over a 3.5 year period (September 2011 to February 2015). Early-onset sepsis (EOS) was defined as infection occurring <7 days of life, and late-onset sepsis (LOS) was defined as infection presenting  $\geq 7$  days of life.

#### Results

In infants (age <1 year) with blood culture-proven sepsis, GBS was the 3rd most common pathogen with 14% (n=74) of episodes. In comparison, *Escherichia coli* and coagulase-negative staphylococci were identified in 23% (n=122) and 19% (n=103) of sepsis episodes. Among cases of GBS sepsis, 30% (n=22) presented as EOS and 70% (n=52) as LOS. The incidence of GBS-EOS and GBS-LOS was 0.12 (95%-CI 0.05-0.23) and 0.36/1000 livebirths (95%-CI 0.23-0.53) for infants born at the study centers. The majority of infants (72%) presented as bacteremia without a focus, and 18% had meningitis. The proportion of patients requiring invasive ventilation was 36% in EOS and 17% in LOS (p=0.04); 27% of patients with EOS and 6% of patients with LOS (p=0.009) developed septic shock. Two patients with EOS and no patients with LOS died, leading to an overall case fatality rate of 3%.

## Conclusions

Despite widespread implementation of intrapartum antibiotic prophylaxis, GBS remains a major cause of neonatal and infant morbidity and contributes to neonatal mortality. In Switzerland, we describe a low incidence of GBS-EOS, and a predominance of GBS-LOS, a pattern which has not been reported in other

## Epidemiology

### URINE ACUTE KIDNEY INJURY BIOMARKERS IN POST NEONATAL ASPHYXIA (723)

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## Introduction /Case Report

Acute kidney injury (AKI) has focused on identifying biomarkers, characterized as early, noninvasive, and sensitive indicators of AKI. The early detection of AKI could optimize and improve patient outcomes. We aimed to evaluate the levels of NGAL (neutrophil gelatinase-associated lipocalin), IL-18 (interleukin-18), NTN-1 (Netrin-1) and NHE3 (Na<sup>+</sup>/H<sup>+</sup> exchanger isoform 3) as new markers in the early diagnosis of AKI in asphyxiated neonates.

## Patients and Methods

AKI biomarkers were measured in 41 asphyxiated neonates (15 with AKI and 26 without AKI) and 20 healthy controls. Urine specimens were collected from neonates with perinatal asphyxia (PA) on postnatal 1st and 4th days. In the control group urine collection was made on 1st day. AKI was defined as persistently increased serum Cr ( $\geq 1.5$  mg/dl) for at least 24 h or rising values  $>0.3$  mg/dl from day of life 1.

## Results

Demographic characteristics of the study patients were as follows: mean gestational age  $38.7 \pm 1.6$  weeks; birthweight  $3264 \pm 509$  g; median of cord blood pH 6.9 (6.8-7.0); and mean base excess  $-20.5 \pm 4.6$  mEq/L. Mean levels of urinary NGAL, NTN-1, NHE3 and IL-18 on 1st day of life with PA were significantly higher than control group ( $p < 0.001$ ,  $< 0.001$ , 0.02,  $< 0.001$  respectively). Urinary NGAL and IL-18 levels collected on the first day of life were significantly higher in PA neonates with AKI. ( $p = 0.002$  and  $< 0.001$ ). But NTN-1 and NHE3 levels were similar. There was also significant difference in urinary NGAL levels in specimen collected on the 4th day ( $p = 0.004$ ). ROC analysis revealed that NGAL and IL-18 have a cut-off value of 81.9 ng/mL and 918 pg/mL respectively. Sensitivity and specificity values were 100% and 76% for NGAL and 93% and 90% for IL-18 for predicting AKI in neonates with PA.

## Conclusions

This is the largest clinical trial that evaluates asphyxiated neonates with AKI in terms of urinary biomarkers. NGAL and IL-18 have an important diagnostic value for predicting AKI in neonates with PA.