Abstracts presented at

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WÜRZBURG, OCTOBER 1 - 3, 2021

"POSTER" SESSIONS

FRIDAY, OCTOBER 1, 2021

I RESPIRATORY CARE, PULMONARY DISEASES AND BPD

Chair: G. Dimitriou, Patras, Greece; J.M. Solano, Bogota, Colombia

II NUTRITION / GROWTH / NEURODEVELOPMENTAL OUTCOME

Chair: H. van Goudoever, Amsterdam, The Netherlands; W.W. Hay Jr., Denver, USA

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III INFECTIONS AND INFLAMMATION

Chair: R. Carr, London, UK; D. Singer, Hamburg, Germany

IV MISCELLANEOUS TOPICS

Chair: T. Curstedt, Stockholm, Sweden; T.W.R. Hansen, Oslo, Norway

POSTER SESSIONS - Friday, October 1, 2021, 13^{00} h

I - RESPIRATORY CARE, PULMONARY DISEASES AND BPD
Chair: G. Dimitriou, Patras, Greece; J.M. Solano, Bogota, Colombia

1

THE COMPARISON OF TWO DIFFERENT WEANING METHODS FOR CONTINUOUS POSITIVE AIRWAY PRESSURE

I. Šliaužienė, R. Brinkis, I. Aldakauskienė, A. Pužas, D. Stonienė, R. Tamelienė

Department of Neonatology, Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Kaunas, Lithuania;

Background. There are still many different strategies of weaning preterm infants from nasal continuous positive airway pressure (nCPAP).
Objective. The aim of our study was to compare two weaning methods for nCPAP: sudden and gradual.
Methods. We included 41 preterm infants < 30 weeks' gestational age who required nCPAP for at least 24 h. Neonates were randomized to a sudden (G1) or a gradual (G2) weaning group.
G1: the nCPAP was finished at once after achieving predefined stability criteria for ≥ 12 hours.
G2: nCPAP was gradually weaned with prolonging nCPAP time off in predefined scheme for two days after achieving stability criteria for ≥ 12 hours. After nCPAP was finished, we assessed predefined criteria for three more days and then stated that nCPAP was finished successfully.
Results. The duration of nCPAP therapy was 18 days in G1 (min. 5, max. 48) and 21 days in G2 (min. 5, max. 77; p=0.69). The duration of weaning from nCPAP was 2 days in G1 (min. 0, max. 20) and 7 days in G2 (min. 2, max. 34; p=0.06). The length of stay in the NICU was 17 days in G1 (min. 6., max. 49) versus 23 days in G2 (min. 6, max. 64; p=0.43). The duration of hospital care was 62 days in G1 (min. 41, max. 95) and 66 days in G2 (min. 40, max. 103; p=0.76).
The neonates were successfully weaned at 30+4 weeks of gestational age (min. 28+4, max. 36+6) and 31+1 weeks (min. 28+6, max. 35+6) in G1 and G2 (p=0.40); the weight was 1295 g (min. 894 g, max. 2210 g) and 1348 g (min. 975 g, max. 2244 g) (p=0.360) in G1 and G2, respectively.
Conclusion. As expected, the sudden weaning strategy of nCPAP was associated with a shorter weaning time. However, there were no statistically significant differences in length of NICU and total hospital stay, age of corrected gestational age and weight at the time point of weaning.

2

RESPIRATORY FAILURE IN A PRETERM NEONATE WITH A COMBINATION OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR GENE MUTATIONS: A CASE REPORT

M. Tsirigotaki, E. Saitakis, A. Kleisarchaki, V. Kotsira, P. Skoula, E. Hatzidaki

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Background. Cystic Fibrosis (CF) is an autosomal recessive disease caused by transmembrane conductance regulator (CFTR) gene mutations. The diagnosis may be suspected following prenatal screening, while respiratory manifestations are rare during the neonatal period.
Objectives. We aim to report the clinical and imaging findings in an unusual case of fatal neonatal CF and to discuss diagnostic and therapeutic challenges.
Methods/Results. A male neonate born at 30 weeks gestation presented with severe ventilator-dependent respiratory distress. Initial radiographic appearances were consistent with RDS. Subsequent radiographs disclosed extensive areas of consolidations and atelectasis despite surfactant therapy together with unilateral pulmonary interstitial empysema (PIE). Thick tracheal secretions were routinely aspirated. Positive cultures of the endotracheal tube were treated with repeated antibiotic courses. There was no pancreatic insufficiency and bowel movements were normal. CT at a later stage disclosed extensive areas of consolidation and atelectasis alternating with areas of ground glass, subpleural luscencies and unilateral PIE. Fatal respiratory failure occurred despite oscillator therapy. Mutation analysis with next generation sequencing revealed three heterozygote CFTR vaiants: c.1265C>Tin exon 10, c.1312A>Gn exon 10 and c.1408G>A in exon 11, each one previously described as neutral when present in isolation.
Conclusions. The diagnosis of CF needs to be considered in neonates with respiratory failure. Imaging appearances are non-specific with an overlap between RDS, bronchopulmonary dysplasia complicated by PIE and infection. Rare CFTR mutations are increasingly recognized as next generation sequencing becomes widely available. Description of cases of new genotype-phenotype associations contributes to better understanding of CF pathogenesis and future prenatal screening.

3

ACCURACY OF TRANSCUTANEOUS BLOOD GAS MEASUREMENT IN CRITICALLY ILL NEONATES

P. Baumann[1,2], V. Gotta[3], S. Adzikah[1], V. Bernet[1,2,4]

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Background. Monitoring blood gases is mandatory in all neonates with respiratory support to prevent deleterious effects of deranged blood partial carbon dioxide (PCO_2) and oxygen pressures (PO_2). Gold standard for controlling blood gases is direct measurement in whole blood with automated blood gas analyzers. Despite the advantage of being exact, blood gas analyses carry several disadvantages such as being non-continuous, causing pain from capillary sampling, and potentially iatrogenic anemia in repeated measurements. Transcutaneous PCO_2 and PO_2 measurement systems offer continuous non-invasive blood gas trend monitoring at bedside.

Objective. Aim of this prospective single-center non-randomized clinical trial was to assess bias and precision of a transcutaneous PCO_2 and PO_2 measurement system in critically ill neonates admitted to the tertiary care intensive care unit or to the intermediate care neonatology unit of the University Children`s Hospital of Zurich. This system incorporates a novel optic PO_2 measurement technique (O_2-Fluorescence-Quenching-Method; Sentec OxiVenT™).

Methods. This study compared transcutaneous PCO_2 and PO_2 measurements to arterial and capillary blood gas values in late premature or term birth neonates (≥34 0/7 weeks gestational age (GA)), age between first day of life and the end of the neonatal period (i.e. 28 days of life or 43 6/7 weeks GA). Bias and precision were calculated by fitting linear mixed models to account for repeated measurements. Influence of the following variables was assessed as secondary endpoint: sensor temperature and application time, soft tissue edema, vasoactive drugs, jaundice of the newborn, capillary refill, intra- or extra cardiac shunt, age, and weight.

Results. We obtained 611 paired transcutaneous and blood gas measurements in 110 patients. Transcutaneous PCO_2 was significantly higher than arterial PCO_2 with an estimated bias of +0.61 (95%CI 0.46; 0.76) kPa, but not significantly different from capillary PCO_2 (-0.23; -0.46-0.002) kPa. Transcutaneous PO_2 was significantly lower than arterial PO_2 (-2.50; -2.94; -2.06) kPa, while no significant difference compared to capillary PO_2 was observed (+0.17; -0.30; 0.64). Precision intervals were ±1.8/2.0 kPa for the comparison arterial vs. capillary PCO_2 and ±4.9/3.3 kPa for arterial vs. capillary PO_2, respectively. Further, sensor operating temperature (43°C vs 42°C), soft tissue edema, vasoactive drugs, weight, and gestational age significantly altered bias ($P<0.05$).

Conclusions. The tested transcutaneous blood gas measurement system showed excellent agreement with capillary PCO_2 and PO_2 and good agreement with arterial PCO_2. Wide precision intervals might be due to altered peripheral tissue and skin perfusion.

4

DD-SURF: SURFACTANT ADMINISTRATION IN BETWEEN INSURE AND LISA

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Background. Whereas surfactant was traditionally administered via an endotracheal tube during mechanical ventilation, it is known that volutrauma damages the lung and ventilation should be prevented. Therefore the concept of INSURE (intubation with ventilation, surfactant administration and extubation) tried to minimize ventilation. The less or minimal invasive surfactant administration (LISA or MIST) avoids mechanical ventilation by giving surfactant intratracheally via a small catheter. Whereas recent studies have shown a benefit of LISA, that intervention has several disadvantages: lack of practice in neonatal intubation, need for secondary intubation due to respiratory deterioration, discontinuation of positive airway pressure, blocking the small tracheal diameter by the surfactant catheter.
Objective. To test an alternative approach of surfactant administration (DD-SURF) that combines the advantages of LISA and INSURE: surfactant administration in spontaneously breathing infants via the side-port of an endotracheal tube under continuous CPAP administration.
Methods. All newborns below 1500g birth weight, admitted to our neonatal intensive care unit (NICU) between 01/16 and 12/18 were included in this retrospective analysis. Success of DD-SURF was defined as surfactant administration in the delivery room (DR) with no subsequent ventilation during the first 72 hours of life.
Results. During the three years period 211 out of 292 included VLBW-infants received at least one dose of surfactant within the first 72 hours. A total of 194 received surfactant in the DR, either as DD-SURF (N=156) or during conventional mechanical ventilation (n=38). All infants with DD-SURF were transferred on CPAP to the NICU after an uneventful DR-management. 19% (30/156) required a re-intubation within the first 72 hours. Newborns requiring intubation after DD-SURF were more immature, smaller and had lower APGAR scores at 1 and 5 minutes. Since DD-SURF was restricted to the DR, a total of 126 VLBW-infants were successfully treated with DD-SURF, representing 60% of all infants receiving surfactant during the first 72 hours of life.
Conclusions. DD-SURF is a promising alternative to INSURE and LISA, combining advantages of both procedures. The success rate is comparable to LISA studies. Since neonatal endotracheal intubation is becoming rarer, DD-SURF offers an opportunity to remain proficient in this skill. DD-SURF still has to be evaluated in a randomized, controlled trial before widespread use can be recommended.

5

PREDICTION OF BRONCHOPULMONARY DYSPLASIA AT BIRTH BY MACHINE LEARNING ANALYSIS OF CLINICAL AND DIGITAL SPECTRAL DATA

H. Verder[1], C. Heiring[2], R. Ramanathan[3], N. Scoutaris[1], P. Schousboe[1], P. Verder[1], T.E. Jessen[4], L. Bender[5], M. Dahl[6], C. Eschen[1], J. Fenger-Grøn[7], J. Reinholdt[8], H. Smedegaard[9], A. Höskuldsson[1]

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Background. Bronchopulmonary dysplasia (BPD) is a long lasting and serious complication in premature infants with high mortality and morbidity. The major causes include chorioamnionitis and preterm birth. The condition may be aggravated by various influences including volutrauma and oxidative stress in combination with invasive mechanical ventilation. No curative treatments are currently available.
Objective. The aim was to develop a predictive machine learning algorithm for BPD with the purpose to optimize the existing symptomatic treatments and to develop more effective treatments.
Methods. Recently we have developed an algorithm to measure lung maturity on gastric aspirates by mid-infrared spectroscopy as lecithin-sphingomyelin ratio (L/S) (doi:10.1111/apa.14896 and 14831). Infants in the clinical part of the studies were followed for 5 days to diagnose RDS. Sixty-one infants with gestational age 24-31 weeks from the clinical L/S-study were included in the actual multicenter non-interventional study. The study time was now expanded to discharge from hospital to diagnose BPD. The main BPD-diagnosis was need of oxygen day 28 with follow up assessment at 36 weeks postmenstrual age. To build the algorithm, chemometrics, a machine learning method to extract information from chemical, spectroscopical and clinical parameters by data-driven means was used. Mid-infrared spectra from gastric aspirates at birth combined with birth weight, gestational age and treatment with surfactant +/- were used to develop the algorithm. Support vector machine (SVM) classifier procedure and partial least square-regression (PLS) analysis were supplemented with cross-validation and other chemometric methods.
Results. Twenty-six infants (43%) had BPD and 35 (57%) no BPD. The algorithm predicted BPD early after birth with a sensitivity of 88% and a specificity of 91%.
Conclusion. We have developed a clinical predictive machine learning algorithm for BPD early after birth. A blind test of the algorithm is planned.

II - NUTRITION / GROWTH / NEURODEVELOPMENTAL OUTCOME
Chair: H. van Goudoever, Amsterdam, Netherlands; W.W. Hay Jr., Denver, USA

6

CHANGES IN HUMAN MILK MACRONUTRIENT, LYSOZYME AND LACTOFERRIN COMPOSITION DURING MILK PROCESSING IN VILNIUS DONOR HUMAN MILK BANK

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Background. Donor human milk is considered a preferred alternative to mother's milk for feeding premature infants. Donor milk undergoes a number of procedures from donation to feeding sick babies, which include freeze-thaw cycles, transferral to different containers and pasteurisation. Holder pasteurisation currently is the most commonly used method in donor human milk banks for the microbiological safety of donated milk. Undergoing procedures can alter nutritional and biological properties of milk, however, available data remains controversial.
Objective. The aim of our study was to evaluate the changes of macronutrient in human milk, energy and bioactive proteins (lactoferrin and lysozyme) during milk processing in the Vilnius donor human milk bank.
Methods. The study was conducted at the Neonatal Centre of Vilnius University Hospital Santaros Klinikos between October 2017 and July 2018. Human milk samples were collected in a volume of 70 mL from forty-two hospitalized women within 14–16 days after delivery. The macronutrients (protein, fat, carbohydrate) and energy concentration in the each sample were first evaluated in fresh milk and again after the milk samples were frozen at −40 ºC, then thawed and pasteurised. Mid-infrared spectrophotometry (MIRIS Human Milk Analyser) was used to evaluate the content of macronutrients and energy in human milk samples. An ultrasonic homogenization of the milk samples was performed with a Miris Sonicator before analysis of macronutrient. Lactoferrin and lysozyme concentrations in each milk sample were also evaluated in thawed unpasteurised milk and after Holder pasteurization by ELISA assays.
Results. Forty-two paired human milk samples were analysed. The macronutrient and energy content in human milk did not differ in fresh and pasteurized human milk samples ($p > 0.05$). The average loss of lysozyme after pasteurisation was 35% and lactoferrin was reduced by > 99%.
Conclusions. While the processing of human milk did not affect the macronutrient content, it did result in a significant loss of lysozyme and lactoferrin concentrations. Milk processing in donor human milk banks should be revised and new methods introduced in order to minimise the loss of the bioactive components in human milk.

7

LACTOBACILLUS ACIDOPHILUS/BIFIDOBACTERIUM INFANTIS PROBIOTICS ARE BENEFICIAL TO EXTREMELY LOW GESTATIONAL AGE INFANTS IN THE CONTEXT OF HUMAN MILK EXPOSURE

I. Fortmann[1], K. Hanke[1], J. Spiegler[1], K. Faust[1], D. Viemann[2], A. Stein[3], E. Herting[1], W. Göpel[1], C. Härtel[1]

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Background. Numerous studies on the therapeutic effects of probiotics in preterm infants have been performed, however, the results remain inconclusive due to a high variability in study protocols, target populations and endpoints, probiotic formulations and the context of nutrition.
Objective. To evaluate the distinct effect of prophylactic Lactobacillus acidophilus/ Bifidobacterium infantis probiotics on outcomes of preterm infants < 29 weeks of gestation in the context of human milk exposure.
Methods. We performed an observational study of the German Neonatal Network (GNN) between January 1st 2013 until December 31st 2018. Prophylactic probiotic use of Lactobacillus acidophilus/Bifidobacterium infantis was evaluated in preterm infants < 29 weeks of gestation (n= 7516) in subgroups stratified to human milk exposure: (I) Exclusively expressed breastmilk (EBM) of own mother and/or donors (EBM group, n=1568), (II) EBM of own mother and/or donor and formula (mix group, n=5221) and (III) exclusive exposure to formula (formula group, n=727). The effect of probiotics on primary outcomes and growth was tested in univariate models and adjusted in linear/logistic regression models.
Results. 5954 (76.5%) infants received Lactobacillus acidophilus/Bifidobacterium infantis. Probiotic use was associated with improved growth measures in the EBM group (e.g. weight gain velocity in g/d: effect size B = 0.224; 95% CI: 2.82 - 4.35; p <0.001) but not the formula group (effect size B = -0.06; 95% CI: -3.05 - 0.28; p= 0.103). The EBM group had the lowest clinical sepsis risk (34.0%) as compared to the mix group (35.5%) and formula group (40.0%). Only in the mix group probiotic supplementation proved to be protective against clinical sepsis (OR 0.69; 95% CI: 0.59-0.79; p<0.001).
Conclusions. Our observational data indicate that the exposure to Lactobacillus acidophilus/ Bifidobacterium infantis probiotics may compensate for the growth disadvantage of exclusively EBM fed infants as compared to formula fed infants. To exert a sepsis-preventive effect, probiotics seem to require the nutritional context of human milk.

8

PREVALENCE OF BREASTFEEDING IN INFANTS DISCHARGED FROM A NICU AND UP TO 2 YEARS OF LIFE

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Background. The admission of neonates in the Neonatal Intensive Care Unit (NICU) has often been blamed as the main obstacle for the establishment of breastfeeding.
Objective. The present study aimed: 1) to assess the prevalence of breastfeeding up to 2 years of age in infants previously hospitalized in our NICU, and 2) to investigate factors which may have affected breastfeeding progression in this population.
Methods. A questionnaire-based survey was conducted, via telephone calls, in mothers, whose newborns or infants were admitted in the NICU of a tertiary Hospital after birth, over a 2 years period (2017-2019). Data on infants’ diet from birth to the day of the interview and on mother's previous breastfeeding experience were collected. Information about the prenatal period, the length of pregnancy, the type of childbirth, the duration of in-hospital stay, and the mode of newborn feeding during hospitalization, were recorded retrospectively from the patients history. Mothers from immigrant support facilities (Hot-Spots) were excluded from the study, due to communication difficulties.
Results. The response rate was 57%. During the first days of life, 75% of all infants received breast milk. The percentage of infants, who exclusively breastfed was 45.7% in the first month, and showed a gradual decrease to 30.3% and 20.7% at the end of the third and sixth month, respectively. The percentage of any breastfeeding at the ages of 12, 18, and 24 months was 10.7%, 5.3%, and 4.2%, respectively. Prematurity, low birth weight and duration of in-patient stay appeared to negatively affect breastfeeding initiation and progression, while the effect of previous breastfeeding experience was positive.
Conclusions. Breastfeeding support is a high priority in our Unit, and this was reflected in the results of the present study. NICUs should support breastfeeding initiation, by providing psychological support to mothers and families, and comprehensive instructions on breastfeeding practices.

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ASSESSMENT OF DEHYDRATION IN EXCLUSIVELY BREASTFED NEONATES

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Background. Exclusively breastfed newborns sometimes experience excess weight loss during the first days of life. It seems there is a disagreement over what constitutes an expected neonatal weight loss, and about when interventions such as supplemental feedings should be considered. The interventions depend on the assessment of neonate’s clinical condition and the rate of weight loss compared to birth weight (BW). Lately, the use of Newborn Weight Loss Tool (NEWT) for the calculation of the percentile of weight loss per hour seems useful in the early identification of infants at risk of dehydration with consequent increased morbidity.

Aim. To evaluate the weight loss rate measurement and the validity of Newt in the early detection of dehydration in exclusively breastfed newborns.

Method. Exclusively breastfed neonates (n= 286) in the maternity department of our hospital over a period of two years were recorded. Laboratory tests and the Newt were performed in 39 (13.6%) neonates with dehydration or weight loss>9% of BW. Correlation of Newt values and weight loss rate with clinical and laboratory findings was performed.

Results. A strong correlation was found between weight loss rate and Newt values (rho +0.68, $p = 0.000$). Furthermore, sodium (Na) levels were positively correlated with weight loss rate (rho +0.35, $p = 0.041$) and Urea levels (rho +0.42, $p = 0.013$), but not with Newt values (rho + 0.18, $p = 0.308$). Two of the study neonates developed hypertonic dehydration and were admitted to the Neonatal Intensive Care Unit.

Conclusion. Early recognition and proper evaluation, by healthcare providers, of issues derived from insufficient breast milk intake in exclusively breastfed newborns, especially in the first weeks of life, are of great importance for the establishment and continuation of breastfeeding along with the avoidance of adverse events for the neonates. Our study showed that the assessment of weight loss rate and the Newt nomogram are reliable methods for the early diagnosis of dehydration in exclusively breastfed infants, with the first prevailing.

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SURGICAL NECROTIZING ENTEROCOLITIS BUT NOT SPONTANEOUS INTESTINAL PERFORATION IS ASSOCIATED WITH ADVERSE NEUROLOGICAL OUTCOME AT SCHOOL AGE

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Background. Gastrointestinal complications during the neonatal period, i.e. necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP), are associated with adverse short-term outcome in very-low-birthweight infants (VLBWI, < 1500g birth weight). However, little is known about the neurological outcome of survivors at school age.
Objective. To analyse the effect of NEC and SIP on neurological outcome at the age of six years.
Methods. Data of 2241 infants followed-up at the age of 6 years were included. To determine the effect of NEC and SIP on cognitive outcome in consideration of other important confounding factors, we used multivariable logistic regression models. In addition, infants with surgical diagnosis of NEC (n=43) or SIP (n=41) were compared to NEC (n=43) or SIP (n=41) negative controls using Mahalanobis distance matching.
Results. Infants with a history for NEC had a three times increased risk (RR 3.0 [1.8-4.2], $p < 0.001$) to develop IQ scores < 85 while history of surgical SIP did not increase the relative risk for lower IQs at school age (RR 1.0 [0.4-2.1], $p = 1.000$). In a matched-cohort analysis, we confirmed that infants with surgical NEC had lower mean IQ results than unaffected controls [SD] (85[17] vs. 94[14], $p = 0.023$) while no differences were found for history of SIP.
Conclusions. Our results reflect that the different aetiology and inflammatory extent of NEC and SIP may lead to disparate neurodevelopment trajectories. Hence, our data suggest a potential role of early gut-brain axis distortion in infants with NEC which needs to be further explored.

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THROMBOELASTOMETRY VARIABLES IN NEONATES WITH PERINATAL HYPOXIA

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Background. Perinatal hypoxia/asphyxia results in varying degrees of hypoxemia, ischemia, and finally metabolic acidosis. It is associated with an increased risk of coagulation disorders by enhancing the consumption of platelets and several clotting factors, due to compromised oxygen and blood supply to the liver and bone marrow among others and thus leading to further derangement of the already immature neonatal hemostatic system. Thromboelastometry (ROTEM), as a viscoelastic method, estimates the dynamics of the whole coagulation process and may represent an attractive tool for studying the coagulation status of hypoxic neonates.
Objective. We aimed to assess the hemostatic profile of neonates with perinatal hypoxia using the standard extrinsically activated ROTEM (EXTEM) assay and to evaluate this method as a prognostic and a therapeutic biomarker for hypoxic neonates.
Methods. A total of 164 neonates with perinatal asphyxia and/or fetal distress hospitalized in the Neonatal Intensive Care Unit of Nikaia General Hospital comprised the study subjects, while 273 healthy neonates served as controls. Hypoxic neonates were divided in two subgroups: 1) 16 neonates with perinatal asphyxia (according to the AAP and ACOG definition), and 2) 148 neonates with fetal distress. Demographics, clinical characteristics, and laboratory results were recorded for all study neonates. SNAPPE score (Score for Neonatal Acute Physiology Perinatal Extension) was calculated within the first 12 hours of admission and EXTEM test was performed during the first 3 days.
Results. Hypoxic neonates presented a hypocoagulable profile, as it is expressed by significantly prolonged CT, CFT and reduced A10, A20, A30, α-angle and MCF, when compared to healthy neonates. Furthermore, asphyxiated neonates had a significantly prolonged CT and CFT and reduced A10 and α-angle relative to neonates with fetal distress. Moreover, in hypoxic neonates, significant correlation was noted between EXTEM parameters and hepatic and renal function biomarkers (SGOT, LDH, ALBUMIN and Cr), platelets, nucleated red blood cells, SNAPPE score and mortality.
Conclusions. In neonates with hypoxia, hypocoagulability, deriving from EXTEM parameters’ results, appears to be a promising biomarker for the early detection of coagulation disorders, while the degree of coagulopathy may correlate with the severity of hypoxia.

POSTER SESSIONS - Saturday, October 2, 2021, 13^{00} h

III - INFECTIONS AND INFLAMMATION
Chair: R. Carr, London, UK; D. Singer, Hamburg, Germany

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EARLY-ONSET SEPSIS IN PRETERM INFANTS: DIAGNOSTICS AND TREATMENT DIFFERENCES IN 2011 AND 2016

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Background. Early - onset sepsis (EOS) is a blood infection that occurs in neonates within 72 hours after birth. Preterm delivery is an important risk factor with higher incidence of sepsis at smaller gestational ages.
Objective. The aim of this study was to identify confirmed and suspected EOS in preterm infants and to compare the presence of risk factors, clinical and laboratory signs, empiric antibiotic therapy as well as initiation and duration of antibiotic therapy in Hospital of Lithuanian University of Health Sciences Kauno Klinikos Department of Neonatology (HLUHS KK DN) in 2011 and 2016.
Methods. Suspected episodes of EOS in HLUHS KK DN of 2011 and 2016 were retrospectively reviewed. Collected data included demographics, results of clinical and laboratory tests, antibiotic therapy and diagnosis. We compared the amount of confirmed diagnoses of EOS in preterm infants, risk factors, clinical and laboratory signs, also information about treatment between the years (2011, 2016).
Results. There were 141 out of 557 patients (25,3%) in 2011 and 77 out of 486 patients (15,8%) in 2016 to whom antibiotic therapy was initiated during the first 72 hours. Birth weight was higher in 2016 with an average of 1771 g (SD 840 g) compared with 1506 g in 2011 (SD 634 g) (p=0,017). Presence of risk factors was higher in 2011 – 12,1% compared with 2016 – 3,9% (p=0,044). Presence of clinical signs did not differ between the years (p=0,61). There was no statistically significant difference in the time points of initiated antibiotic therapy (p=0,46). The length of antibiotic therapy did not differ between the cohorts. Duration of treatment was as follows: <72 hours 79 (56%) and 46 (59,7%); 73-119 hours 9 (6,4%) and 2 (2,6%); >120 hours 53 (37,6%) and 29 (37,7%) in 2011and in 2016 respectively. There was no difference between the years comparing the incidence of confirmed EOS diagnoses (22% in 2011 and 24,7% in 2016).
Conclusions. There was no statistically significant difference in presence of risk factors, clinical and laboratory signs and the use of antibiotics. No differences were found comparing confirmed cases of EOS.

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ROAD TO THE NEW WORLD OF EARLY ONSET SEPSIS PRACTICE

A. Ahmed, P. Gopalakrishnan

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Background. Early onset neonatal sepsis (EONS) is defined as blood or cerebrospinal fluid (CSF) culture-proven infection within 72 hours after birth. U.K Hospital use either NICE or RCOG Guidelines or a hybrid version of these two guidelines which fails to consider the “wellness” at birth and how that modifies the risk of EONS. Kaiser Permanente Sepsis group from Northern California used Bayesian approach to create a multivariate model for predicting the risk for EOS. The algorithm uses: Population risk, intrapartum risk, infants’ clinical condition at birth, wellness after birth and derives a computational risk score. KPSC does not consider “C” reactive protein

Methods. We used Kaiser Permanente Neonatal Sceptic Calculator on retrospective data on the use of empirical antibiotics in our postnatal ward care. We projected KPSC on 76 late preterm and term infants ≥ 34/ 40 weeks at birth over period of five months who received empirical antibiotics to prevent E.O.S

Results. If we have used KPSC as it is in this cohort of babies, we would have given antibiotics to only 24 babies out of 76 babies (31.6%). This would have prevented 52 babies (68.4%) from getting antibiotics. If we take an extremely cautious approach as we should - any baby with any symptom or sign on first clinical examination to be included in “Equivocal” group -, we would have still given antibiotics to 54 babies in this cohort (71%) and have prevented 22 babies from getting antibiotics (29%). In addition, it would have reduced antibiotic exposure by 66 days, presence of Junior medical staff by 44 hrs, working time of NICU nursing staff by 396 hrs and maternal separation by 528 hrs.

Conclusions. Judicious adoption of KPSC could potentially reduce interventions and antibiotic use and promote bondage without missing additional cases of early onset neonatal sepsis

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SEPSIS MORTALITY OF EXTREMELY PRETERM INFANTS IN GERMANY AFTER THE INTRODUCTION OF COLONIZATION SCREENING

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Background. According to German infection surveillance guidelines updated in 2013, a weekly screening followed by extended hygiene precautions for infants colonized with drug-resistant or highly epidemic organisms is mandatory for neonatal intensive care units (NICU). The scientific evidence of this recommendation is limited.
Objective. We aimed to evaluate the sepsis incidence and pathogen specific fatality rates before and after the guideline update in a large population-based cohort of preterm infants.
Methods. The German Neonatal Network (GNN) is a prospective cohort study including data from 62 German level III NICUs. Preterm infants born between 2011 and 2018 with a gestational age between 22+0 and 28+6 weeks were included in this study. We compared infants born before (2011-2013) and after publication of the updated guideline (2014-2018). The primary outcome was sepsis-related mortality.
Results. In-hospital mortality of extremely preterm infants was 12.9% (1654/12823). 277 non-survivors (16.7%) were classified as sepsis related deaths. Infants discharged between 2014 and 2018 (n=8903) had a lower total mortality (12.5% vs. 13.8%, p=0.036) and reduced rates for clinical sepsis (31.4 vs. 42.8%, p<0.001) and culture-proven sepsis (14.4% vs. 16.5%, p=0.003) as compared to infants discharged in 2011-2013 (n=3920). Nine pathogens were significantly associated with sepsis related mortality. Pseudomonas aeruginosa had the highest case-fatality rate [8/16, 50%, OR 47 (17-126), p<0.001)] followed by Candida albicans [13/55, 24%, OR 15 (7.8-28), p<0.001], E. coli [19/181, 10-5%, OR 5.6 (3.5-9.2), p<0.001)], extended spectrum ß-lactamase (ESBL) E. coli [4/37, 11%, OR 5.6 (2.0-16), p=0.01] Klebsiella spp. [9/83, 11%, OR 5.4 (2.6-11.2), p<0.0001], Streptococcus agalactiae [8/88, 9.1%, OR 4.7 (2.2-9.7), p=0.001] Enterococci [9/114, 7.9%, OR 4.0 (2.0-8.0), p=0.001], Enterobacter [6/108, 5.6%, OR 2.7 (1.2-6.2), p<0.0001] and Staphylococcus haemolyticus [12/220, 5.5%, OR 2.7 (1.5-4.8), p=0.003]. Discharge after guideline update had no effect on pathogen-specific case fatality. In addition, total sepsis-related mortality (2.1% vs. 2.3%, p=0.54) and culture-proven sepsis rates with pathogens detected by colonization screening remained unchanged. While the exposure of GNN infants to cefotaxime declined over time (31.1 vs. 40.1%, p<0.001), the treatment rate with meropenem increased (31.6 vs. 26.3%, p<0.001).
Conclusions. Sepsis remains an important cause of death in extremely preterm infants. Weekly colonization screening is associated with reduced sepsis rates, but has no effect on sepsis-related mortality and sepsis with screening-relevant pathogens. The increasing exposure to meropenem should be a target of antibiotic stewardship programs.

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ANTIMICROBIAL SKIN PEPTIDES IN PREMATURE INFANTS: CHARACTERIZATION AND IMPACT OF PERINATAL FACTORS

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Objectives. Antimicrobial peptides (AMPs) are important molecules of the innate immune system and have immunomodulatory functions. Preterm infants are surrounded by an artificial environment, have rare mother-child contact, and are often exposed to antibiotics. It could be argued that these factors lead to shifts of the composition of AMPs. However, as no data exist about the characteristics of AMPs of preterm and term infants, we aimed to characterize the expression of skin AMPs and to describe factors possibly influencing its expression in both age groups.
Methods. In a prospective study with preterm and term infants we analyzed skin wash probes for AMPs via ELISA. In detail, the expression of human ß-Defensin (hBD)-2, RNase 7, and Psoriasin was studied. Preterm infants were born < 34 weeks gestational age and followed-up for 28 days. Term infants were born > 37 weeks and were washed on day 0 and on day 28. Univariate analyses were carried out and tested via Kruskal-Wallis and Mann-Whitney-U test.
Results. On the skin of preterm infants (n=37) with mean gestational age of 28.8 (2.4) weeks and term infants (n=21) at 39.5 (1.2) weeks, hBD-2 was not expressed. Psoriasin and RNase 7 are both expressed and accelerate significantly over time. Gestational age did not affect the expression of AMPs. Mode of birth impacts expression of psoriasin and RNase 7 with increased rates of psoriasin and decreased rates of RNase 7 in vaginal delivered preterm infants. Inflammatory hits as histologically proofed chorioamnionitis, early-onset sepsis or late-onset sepsis increase concentrations of psoriasin in preterm infants significantly.
Conclusions. Psoriasin and RNase 7 concentrations increase over time on the skin and seem to be independent on gestational age. We could describe an effect of chorioamnionitis and sepsis on the expression of skin AMPs. This is of particularly interest as the role of AMPs on a maturing skin microbiome is unclear. This needs to be determined in further studies.

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EPIDEMIOLOGY OF STAPHYLOCOCCUS AUREUS INFECTION IN THE NEONATAL PERIOD: A 12-YEAR SINGLE CENTER EXPERIENCE

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Introduction/Objectives. Staphylococcus aureus (S. aureus) is a common cause of neonatal infections worldwide. Aim of this study was to evaluate the incidence, clinical manifestations and resistance patterns of culture proven S. aureus infections in neonates admitted to a tertiary-care neonatal intensive care unit over a 12-year period.
Methods. We performed a retrospective cohort study in neonates with culture-proven, invasive and non-invasive, methicillin resistant (MRSA) or susceptible (MSSA) S. aureus infections admitted to a tertiary neonatal intensive care unit from January 2008 to December 2019. CDC criteria were used to define Community-acquired (CA), community-onset healthcare associated (COHA) and hospital-acquired (HA) infection. One isolate per patient was included.
Results. Overall 71 clinical isolates were identified (57 CA, 13 HA, 1 COHA). Mean birth weight was 3259 gr [range 1000-5050], mean gestational age was 38 weeks and median age at diagnosis was 11 days. Skin and soft tissue infections were the most common (22/71, 30.9%), while invasive infections were rare (5/71, 7%). Twenty-two isolates were MRSA (30.9%). Erythromycin and clindamycin resistance occurred in 20.9% (13/62) and 14.4% (10/69) of isolates respectively. Resistance to rifampicin and trimethoprim/sulfamethoxazole was found in 1.5% (1/67) and 2.9% (2/68) of the strains. No resistance to vancomycin, teicoplanin and linezolid was noted. No mortality occurred. The incidence of S. aureus infections increased during the study period from 3.58 per 1000 admissions in 2008-2013 to 27.53 per 1000 in 2014-2019. The number of CA infections increased and a significant rise of MSSA was noted from 1.9 to 14.8/1000 in the years 2014-2019.
Conclusions. The burden of S.aureus infections is considerable in the neonatal period. Over a 12-year period, we observed rising trends of CA infections along with an increase in methicillin sensitive strains.

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EPIDEMIOLOGICAL STUDY OF HOSPITAL-ACQUIRED CONJUCTIVITIS IN A LEVEL III NEONATAL UNIT

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Background. Hospital-acquired conjunctivitis (HAC) is one of the most common infections encountered in neonatal intensive care units (NICUs) and a significant cause of ocular morbidity if not adequately treated.
Objectives. To determine the etiology and antimicrobial susceptibility of pathogens causing HAC in a tertiary care reference NICU over a 3-year period.
Methods. Hospital databases were retrospectively searched for neonates with culture-proven HAC. Antimicrobial susceptibility testing data according to EUCAST guidelines were identified for all isolated microorganisms from January 2017 to December 2019. HAC cases were defined using the ECDC criteria as described in the HAI-Net ICU protocol, version 2.2 after reviewing the patient's chart. Cultures were not routinely tested for Chlamydia.
Results. HAC occurred in 151 hospitalized neonates (151/1278, 11.8%). The most common pathogens were gram-positive bacteria (67.3%), followed by gram-negative bacteria (29.8%) and fungi (2.9%). Among gram-positive pathogens, CoNs were the predominant organisms (66.3%), while Enterococcus spp, viridans streptococci, and S. aureus were less frequent (15.0%, 10.7%, and 5.9%, respectively). The most common gram-negative pathogens were Pseudomonas aeruginosa (28.9%) followed by Klebsiella (22.9%) and Enterobacter species (15.7%). Resistance rate to tobramycin, empirically prescribed as 1st line treatment, was significant (58.8%), while none of the isolates were resistant to chloramphenicol.
Conclusions. HAC is common in NICU. Continuous surveillance and physician awareness are required to prevent treatment failure with potentially serious sequelae for neonatal health, especially in premature neonates. Given the observed resistance patterns, tobramycin resistance should be considered in selecting empiric antibiotic treatment. It is worth emphasizing the importance of the implementation of strict infection control measures to prevent the dissemination of resistant strains.

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VANCOMYCIN-INDUCED OTOTOXICITY IN VERY-LOW-BIRTHWEIGHT INFANTS

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Background. Vancomycin is an extensively used anti-infective drug in neonatal intensive care units. However, exposure-toxicity relationships have not been clearly defined in preterm infants.
Objective. To evaluate the risk profile for hearing deficits in vancomycin-exposed very-low-birthweight infants (VLBWI).
Methods. In a large cohort study of the German Neonatal Network (GNN; n=16 967 VLBWI) we assessed the association of intravenous vancomycin treatment and pathological hearing tests at discharge and at five year follow-up. In a subgroup of 1042 vancomycin-treated VLBWI we performed additional audits on vancomycin exposure, drug levels, dose adjustments and exposure to other ototoxic drugs.
Results. Twenty-eight percent of VLBWI (n=4739) were exposed to intravenous vancomycin therapy in the GNN cohort. In multivariable logistic regression analysis, vancomycin exposure proved to be independently associated with pathological hearing test at discharge (OR 1.18, 95% CI 1.03-1.34, p=0.016). Among vancomycin-treated infants, a cumulative vancomycin dose above the upper quartile (>314 mg/kg bodyweight) was associated with pathological hearing test at discharge (OR 2.1, 95% CI 1.21-3.64, p=0.009), whereas a vancomycin cumulative dose below the upper quartile was associated with a reduced risk of pathological tone audiometry results at five years of age (OR 0.29, 95% CI 0.1-0.8, p=0.02, n=147).
Conclusions. Vancomycin exposure in VLBWI was associated with an increased, dose-dependent risk of pathological hearing test results at discharge and at five years of age. Prospective studies on long-term hearing impairment are needed.

IV - MISCELLANEOUS TOPICS
Chair: T. Curstedt, Stockholm, Sweden; T.W.R. Hansen, Oslo, Norway

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AN OBSERVATIONAL STUDY ON THE USE OF PERIPHERAL LINES VERSUS CENTRAL LINES IN NEONATAL INTENSIVE CARE UNITS

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Background. There is a debate regarding the best choice of the intravenous (IV) access for preterm infants – peripheral or central (umbilical or peripherally inserted central catheter). Each has its own advantages and disadvantages.
Objective: To study practices regarding selection of vascular access devices and outcomes related to them.
Methods. Prospective data collection on all IV lines used in a cohort of all the preterm infants born in Bnai Zion Medical Center's NICU over a seven month's period. Data was also collected on patients' demographics and outcomes related to IV access, including nutritional and infectious outcomes.
Results. The cohort included 120 infants, 94 of whom required IV line. Preterm infants born at ≤ 32 weeks gestation, or with head circumference ≤ 29 cm were more likely to require two or more IV lines or a central line for administration of parenteral nutrition or medications for longer periods. However, central lines were not associated with better nutritional status at discharge based on weight z-scores. Only one episode of infection - central line associated bloodstream infection in a peripherally inserted central catheter - was recorded, and no other line associated complications.
Conclusions. Our data supports the use of central IV access for preterm infants born at ≤ 32 weeks or with head circumference ≤ 29 cm. Our findings should encourage other NICUs to study their data on the use of central vs. peripheral IV lines and outcomes, in order to draw their own practice guidelines with recommendations for best choice for IV access in preterm infants.

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IS PHOTOTHERAPY ASSOCIATED WITH FUTURE CANCER RISK? A SYSTEMATIC REVIEW AND META-ANALYSIS OF 6,637,417 CHILDREN

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Background. Phototherapy is the main treatment option for neonatal jaundice to prevent bilirubin encephalopathy. While generally believed to be safe, some studies have pointed out its possible association with childhood cancer. We aimed to assess the effect of neonatal phototherapy on the future cancer risk.

Methods. In December 2018, a comprehensive search in 13 databases was carried out to identify studies reporting childhood cancer development after exposure to phototherapy. A meta-analysis was done and Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated and pooled. Quality assessment was performed using the NIH tool for included studies.

Results. Ten studies were included and were eligible for qualitative and quantitative analysis. The studies had a considerably good level of quality. We found a statistically significant association between phototherapy exposure and any type of cancer [(OR = 1.23, 95% CI = (1.07–1.42), p = 0.004)], kidney cancer [OR = 2.52, 95% CI = (1.38–4.58), p = 0.003)], any leukemia [(OR = 1.73, 95% CI = (1.31–2.30), p< 0.001)], and myeloid leukemia [OR = 2.89, 95% CI = (1.80–4.63), p< 0.001].

Conclusions. Phototherapy may carry the risk of childhood cancers, especially kidney cancer, any leukemia and myeloid leukemia. Thus, it should be used only when indicated and searching for more conservative guidelines may be appropriate.

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"NEOBRIS" A RISK SCORE FOR PREDICTING THE INCIDENCE OF HEMORRHAGE IN CRITICALLY ILL NEONATES

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Background. Critically ill neonates constitute a very fragile population, at high risk of bleeding and in need of transfusions. Despite the lack of firm basis, transfusion of platelets and fresh frozen plasma is a common practice in Neonatal Intensive Care Units with a high level of inappropriate use. Considering the potential hazards of blood product transfusions, the significance of evidence based guidelines for plasma and platelet transfusions is undisputed.
Thus, the establishment of bleeding assessment tools and predictive scores, which could help estimate the risk/benefit ratio of transfusions, is of great importance for supporting clinical decisions and bleeding management in this vulnerable population.
Objective. Our aim was to develop and validate a prediction model for hemorrhage in critically ill neonates which combines rotational thromboelastometry (ROTEM) parameters and clinical variables.
Methods. The cohort study included 332 consecutive full-term and preterm critically ill neonates. We performed ROTEM and used the neonatal bleeding assessment tool (NeoBAT) to record bleeding events. We fitted double selection least absolute shrinkage and selection operator logit regression to build our prediction model. Bleeding within 24 hours of the ROTEM testing was the outcome variable, while patient characteristics, biochemical, hematological, and thromboelastometry parameters were the candidate predictors of bleeding. We used both cross-validation and bootstrap as internal validation techniques. Then, we built a prognostic index of bleeding by converting the coefficients from the final multivariable model of relevant prognostic variables into a risk score. A receiver operating characteristic analysis was used to calculate the area under curve (AUC) of our prediction index.
Results. EXTEM A10 and LI60, platelet counts, and creatinine levels were identified as the most robust predictors of bleeding and included them into a Neonatal Bleeding Risk (NeoBRis) index. The NeoBRis index demonstrated excellent model performance with an AUC of 0.908 (95% confidence interval [CI]: 0.870–0.946). Calibration plot displayed optimal calibration and discrimination of the index, while bootstrap resampling ensured internal validity by showing an AUC of 0.907 (95% CI: 0.868–0.947).
Conclusions. Our prediction model, by including platelet counts, creatinine plasma levels and EXTEM variables (A10, LI60), probably provide the most comprehensive insight into the haemostatic profile of the critically ill neonates. We developed and internally validated an easy-to-apply prediction model of the 24-hour bleeding risk in critically ill neonates. External validation by other NICUs is needed before its implementation as a potential tool for supporting decisions in daily clinical practice.

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EVALUATION OF THE FAMILY-INTEGRATING CARE CONCEPT NEOPASS FOCUSING ON PARENTAL STRESS, SELF-EFFICACY, SENSE OF COMPETENCE AND THE PARENT-CHILD BONDING

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Background. The psychosocial burden and resilience of families with premature newborns can affect the quality of the parent-child bonding, the family quality of life and additionally the preterm infant's motoric, cognitive and social development (Reichert and Rüdiger, 2012).
With the concept NeoPAss, a family-integrating care approach for preterm infants and their families at the Children´s Hospital Passau, there could be gained several achievements in the infant's development. This study aims to figure out whether the NeoPAss concept also shows effects on parental resilience and psychosocial stress.
Methods. For this purpose, five different questionnaires were processed by parents with a preterm infant supplied with the family-integrating NeoPAss concept in the period from 2015 to 2020, asking about different aspects of their psychosocial burden and resilience.
The questionnaires used were the SWE (Jerusalem and Schwarzer, 1986) to measure parental self-efficacy expectation, the PSOC (Johnston and Mash, 1989) asking about the sense of competence, the PBQ-16 (Brockington et al. ,2001) for evaluating the parent-child bonding, the PSS-NICU (Urlesberger et al., 2017) measuring parental stress experience and the EPDS (Cox and Sagovsky, 1987) to figure out the risk for postpartum depression (n=48 – n=103). Afterwards the results were compared in a benchmark analysis with results from previously published studies with the level of significance set at $p < 0,05$.
Results. The comparison of this study´s results with results from previous studies showed a statistically significant better result for every parameter. The SWE questionnaire measured a score of 3.26 with a comparison score of 2.95 and the PSOC a score of 78.61 compared to 67.6. The PBQ-16 had a score of 3.32 with a comparison score of 4.46, the PSS:NICU a score of 2.75 compared to 2.99 and the EPDS a score of 8.49 compared to 11.33.
Conclusion. The various parameters measured in this study can be used to evaluate parental resilience. Therefore, the statement can be made that the family-integrating care concept NeoPAss influences the resilience of parents with a premature newborn in a positive way and can cause an improvement of the family quality of life and the preterm infant's development.

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COMPARATIVE SPECTROSCOPY OF THE 25 PAIRS OF THE FETAL (HB-F, CORD BLOOD) & MATERNAL (HB-A) HEMOGLOBIN

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Background. Human Hemoglobin is a tetrameric metalloporphyrin. Porphyrin part is formed by pyrrole rings. The globin part is of two pairs of amino-acid chains. Healthy adults have Hemoglobin-A made of two alpha and two beta chains (α2 β2) while a newborn baby has Hemoglobin-A (α2 β2) and Hemoglobin-F (α2 γ2). There are scant reports of absorption spectrum of hemoglobin in cord blood.
Objective. To compare the absorption spectrum of hemoglobin in cord blood and maternal blood by spectrometry.
Methods. This observational study was approved by the Ethics Committee. Cord blood (neonatal blood) samples were collected from placental end in EDTA tube after the delivery. Maternal blood was collected in EDTA tube by peripheral venipuncture after delivery of baby and placenta. A diluted red cell suspension was prepared suitable for the spectroscopy. All measurements were carried out at 25°C. Transmittance of the diluted solution (0.1%) was measured for using slandered solution as a reference with the help of two-beam VIS-NIR spectrometer (Lambda 900, Perkin Elmer, Germany). The sample thickness varied from 1 to 10mm within the wavelength region, depending on the absorption. The samples were scanned between 400 nm to 700 nm and peak positions were detected.
Results. All blood samples showed Soret Band of similar peak and wavelength. We expected different spikes corresponding to four globin chains namely alpha, beta, gamma, and delta. But interestingly, both neonatal and maternal blood samples had 2 identical peaks (440-450 nm and 540-550 nm).
Conclusions. Both cord blood and maternal blood was in venous (deoxygenated) state and similar peaks of absorption were observed for Hb-F and Hb-A. Therefore, a spectroscopy based method for estimation of adult hemoglobin could be reliably used for hemoglobin measurements in the newborns. Efforts are currently underway to develop a technology for non-invasive hemoglobin monitoring in newborns (proprietary of Shani Biotechnologies LLC, Austin, Texas).

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40 YEARS OF EXPERIENCE IN A PRIVATE NICU IN GREECE

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Background. The MITERA NICU, a tertiary Center and the first private NICU in Greece began its operation in April 1979, as part of the newly founded MITERA Maternity Hospital.
Objective. To evaluate perinatal/neonatal mortality, survival rate and disease incidence of babies born at MITERA and admitted to the NICU from January 1980 up to December 2018.
Methods. Our data were retrospectively collected and analyzed from clinical archives and annual reports by the MITERA NICU. We report summary statistics of total births, NICU admissions, prematurity rate, perinatal/neonatal mortality, disease specifics and overall survival.
Results. Years 1980-2018: Total births in Greece 4193263, births at MITERA 462111 (11.03%). Total NICU admissions 82269, total neonatal deaths 1844, neonates survived at MITERA 460567, survival rate at MITERA 99.60% and at MITERA NICU 97.76%. Perinatal/Neonatal Mortality: Significant decrease of PNM from 13.3‰ in 1980 to 4.23‰ in 2018 and impressive decrease of NM from 8.1‰ in 1980 to 0.38‰ in 2018.
The prematurity rate gradually increased from 6.0% in 1980 to 14% in 2018. Survival rate of babies with RDS significantly increased from 68% in the pre-surfactant era 1980-1992 to 100% in 2018. The survival rate according to birth weight increased impressively, especially in the VLBW and ELBW, up to 98.71%. Survival according to gestational age increased up to 95-100%. The incidence of BPD in the last 7 years was very low (4.99%). The incidence of early onset sepsis was very low 1,48 cases/ per 1000 live births, in the last 8 years and that of late onset sepsis 4.51%, mostly due to CoNS. No deaths were attributed to sepsis in our NICU within the last 8 years.
Conclusions. Our results indicate a substantial overall decrease in perinatal and neonatal mortality, significant increase in survival rates and low incidence of BPD and neonatal sepsis of babies born at MITERA and admitted to MITERA NICU during the years 1980-2018.

Additional accepted abstracts:

THORACIC FLUID CONTENT AND RESPIRATORY DISTRESS IN PRETERM INFANTS: A LONGITUDINAL BIOREACTANCE STUDY

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Background. Thoracic fluid content (TFC) is an indicator of total lung fluid and is measured non-invasively using thoracic impedance technology. TFC is calculated as 1000/Z0 (kΩ-1), where Z0 (impedance) is inversely proportional to thoracic fluid. Bioreactance is a modified bioimpedance technology with less signal:noise ratio. Bioreactance has been shown to predict respiratory distress in term infants but no data is available in preterm infants.
Objective. To determine (1) changes of TFC over first 72 hours of life and (2) the effect of CPAP and surfactant on TFC in preterm (≤ 32 weeks) infants.
Methods. This was a retrospective descriptive study at Tygerberg Hospital, Cape Town, South Africa in preterm infants (≤ 32 weeks), admitted within 3 hours of life. Infants with congenital cardiac and pulmonary disease (except PDA), requiring invasive ventilation, inotropic support and those not expected to survive 72hours were excluded. NICOM® Reliant (Cheetah Medical, Massachusetts) monitor was used to measure TFC continuously for 72hours after birth. Various clinical parameters were correlated with TFC and TFCd (TFC change over time) at predetermined time points (0, 6 & 72hrs). Changes of TFC and TFCd were evaluated 6-hourly. Standard institutional neonatal RDS management guidelines were followed.
Results. 36 infants were included in the study: average 29.8 (±1.7) weeks and 1367 (±307)g. 57% infants had mild-moderate RDS on a CXR. 80% required CPAP initially and 22% required surfactant replacement therapy (SRT). Average TFC was 46.6±10.5 kΩ-1. TFC decreased over time and differed significantly at all time points. Respiratory support method and SRT requirement significantly affected TFC values. TFCd changes only differed over the first 18hours of life. Only time (p=0.000) and CPAP (p=0.002) significantly affected TFC after multivariate regression. TFC centiles were constructed for the first 72hrs of life. ROC analysis showed that a TFC>55kΩ-1 at time 0 predicted SRT requirement (sensitivity 38%, specificity 92%).
Conclusion. This is the first study of TFC in preterm neonates utilizing bioreactance technology. TFC is dependant on time and the degree of pulmonary disease. TFC monitoring may be able to predict SRT requirement, prolonged (>48hrs) CPAP requirement. More research is required to confirm these findings.

EVALUATION OF RIGID AND FLEXIBLE CATHETERS FOR LESS INVASIVE SURFACTANT ADMINISTRATION IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME

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Background. Less invasive surfactant administration via thin catheters is the current standard for treating respiratory distress syndrome due to surfactant deficiency in preterm infants. The most commonly used catheter system is a flexible nasogastric tube inserted intratracheally with Magill forceps. Recently, a Less invasive surfactant administration specific, more rigid tool has been launched, the LISAcath®. This study compared a conventional nasogastric tube with the LISAcath® in terms of procedure duration and subjective preference in handling.
Methods. 40 medical students, 40 nurses and 12 neonatologists from the University Hospital in Salzburg took part in this study. The time to successfully place either catheter in the trachea of a preterm simulator has been recorded and monitored via video-laryngoscopy. Measurements were separated by groups and method used, resulting in three groups – students, nurses and doctors – with two subgroups for the methods.
Results. For the groups “medical students” and “nursing staff”, the median procedure time was significantly shorter when using the LISAcath®. They took 79.2 and 69.5 seconds with the nasogastric tube compared to 25.0 and 28.2 seconds with the LISAcath® ($p < 0.0001$). In the doctors’ group, the median time difference between both catheters was also visible but not significant. They required 34.6 seconds with the nasogastric tube and 18.3 seconds with the LISAcath® ($p = 0.1320$). The majority of each group ranked the LISAcath® to be easier in handling compared with the nasogastric tube.
Conclusions. The LISAcath®, specifically developed for less invasive surfactant administration, required shorter procedure times compared to a nasogastric tube used with Magill forceps and is subjectively easier to use.

SEVERE EXTRA-UTERINE GROOWTH RETARDATION IN VERY LOW BIRTHWEIGHT INFANTS

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Background. Extrauterine growth failure (EUGF) is common for many very low birth weight(VLBW)s. Besides nutritional intake, postnatal management, treatment of Patent Ductus Arteriosus, short term neonatal complications and also morbidities may all contribute. We aim to study prenatal, perinatal and also neonatal morbidities in a cohort of VLBWs infants admitted to a tertiary care unit to determine the associations leading to severe (sEUGF).

Methods. A retrospective study of all VLBW admitted from 2007–2016 was conducted. sEUGF infants had their z score changed negatively by more than 2.5 SD from birth till discharge.

Results. 156 infants were audited. Half of the infants had sEUGF (mean change of weight z score -3.45±0.86 vs those without(-1.67±0.56). Those with sEUGF were significantly younger at birth (26.1±1.2) weeks and lighter (866.7±187)g vs those without (27.1 ±1.0)weeks and (993.7±199)g, P <0.001). sEUGF were sicker at birth (CRIB-11) score (11.3 ±2.4 vs 9.3±2.2, p<0.001). More of them required surgical treatment of the PDA(20/78 vs 3/78 Chi square=26.9, p <0.001). Those with sEUGR were more likely to have sepsis (26/78 vs 9/78 , p <0.009), severe grades of Intraventricular hemorrhage(IVH) (19/78 vs 3/78, P <0.001), and stage 3 Retinopathy of prematurity(ROP) (21/78 vs 4/77, P<0.001). Chronic lung disease (CLD) at 36 weeks was significantly more common in those with sEUGF (40/78 vs 11/77, P <0.001). Rates for necrotising enterocolitis and periventricular leukomalacia were similar. Those with sEUGR had a longer stay (108±37 vs 74±27 days, p <0.001), their weight, length and OFC at discharge were similar. The sEUGR were more mature by 4 weeks at discharge (41.4 vs 37.4 weeks, p<0.001). Gender, birthweight z score, mode of delivery and antenatal risk factors and growth restriction at birth were not different between the 2 groups.

Conclusion. Despite availability of total parenteral nutrition, human milk fortification and standardised feeding protocols, conditions at birth, immaturity, PDA management, sepsis and severe stage of IVH contribute to sEUGR and are associated with ROP and CLD. More can be done to reduce sEUGR.

IMPLEMENTATION OF TELEMEDICINE SCREENING FOR RETINOPATHY OF PREMATURITY IN RURAL AREAS IN GUATEMALA

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Background. ROP is one of the most common preventable cause of childhood blindness in the world, it is responsible for up to 60% of blindness in children in some countries. Because of inadequate neonatal hospital care, the burden of ROP blindness has shifted to the moderately developed countries of Latin America.

Methods. There are 39 national hospitals with neonatal care in Guatemala, only 7 of those have an ophthalmology department and/or a ROP screening program. Most of the other centers refer the patients to ophthalmology clinics after detecting that children have obvious signs of poor vision, which usually means that the disease is in the most advanced stages and the treatment options are limited.

Preterm newborns were screened according to the guidelines established by the Guatemalan National Health Department. These guides suggest to screen for ROP in all newborns with a birthweight of less than 2000 grams and/or younger than 36 weeks of gestational age. Patients were screened for the first time at 4 weeks of age or at 32 weeks of post gestational age, while hospitalized or in the outpatient clinic. The technicians selected for the project were enrolled in a 3 month training program, which included: basic eye anatomy, fundamentals of ROP, manipulation of preterm infants and the use of the portable camera (Pictor Plus). Images and patient information (risk factors and medical history) was uploaded to a data base. A pediatric ophthalmologist with experience in ROP management analyzed the data base and gave indications regarding follow up and/or treatment needed.

Results. 487 premature neonates from 6 hospitals were included. All of them were followed using telemedicine from April to November 2019, with the screening criteria mentioned above. Mean gestational age of the neonates was 34.48 weeks (+SD) , mean birth weight was 1747.93 gr (+SD) and 3.58% required treatment.

Conclusions. Although the gold standard for ROP diagnosis is indirect ophthalmoscopy done by an ophthalmologist with experience in ROP, the reality in most low/middle income countries like Guatemala does not allow this to happen. This is why there is a need to develop strategies to give coverage to this at-risk population and one of those strategies can be telemedicine based screening programs.

LONG TERM EFFECT OF PREMATURITY ON CARDIOPULMONARY EXERCISE TESTING IN CHILDHOOD

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Background. Preterm birth is a major determinant of neonatal morbidity. There is a growing data regarding short- and long-term effects of both early and late prematurity. The purpose of our study was to evaluate the long-term effect of prematurity on exercise capacity in childhood.
Methods. We studied children aged 7-10 years in four groups: two groups of "Early preterms born before 30 weeks with and without BPD, "Late preterms" - born between 34+0/7 and 36+6/7 weeks , and a control group of healthy children born >37+0 weeks ("term"). All participants completed a comprehensive functional evaluation using cardiopulmonary exercise test (CPET). The primary outcome was exercise capacity as measured by maximal oxygen uptake (VO2max); secondary outcomes included lung functions and other parameters from the CPET.
Results. Eighty-four children were recruited, fifteen "early preterms" with, and 23 without BPD (age 9.7±1.0), 21 "late preterm" children (age 9.9±0.8), and 25 "term" children (age 8.8±0.9). FEV1 was significantly lower (=78.4 ± 15.0% pred) in early preterms with BPD compared to the three other groups. A statistically significant lower VO2 was found between the term and all preterms groups (45.2 ± 7.4 ml/min/kg compared to 33.9±10.8($p<0.01$), 40.2±11.5($p=0.04$) and 37.6±6.8($p=0.031$) in early preterm without and with BPD and late preterms, respectively). The term group had a higher oxygen pulse (118.8 ± 19.1%pred, $p<0.005$) compared to all preterms groups (90.7±21.4, 102.8±24.1 and 94.1±15.4) in early preterm without and with BPD and late preterms, respectively). Oxygen saturations were normal and without differences between the groups.
Conclusions. This study demonstrated lower exercise capacity in children aged 7-10 years with a history of late prematurity compared to healthy term children and with no difference from children with a history of late and early prematurity, with and without and without BPD. Data regarding morbidity and possible functional limitations may help in adapting a personalized approach to patients and their families, active lifestyle, regular exercise, improving exercise capacity, and monitoring for possible exercise limitations. Further large studies are needed to better understand the specific characteristics of different preterm populations.

GENETIC PREDISPOSITION TO EARLY-ONSET NEONATAL SEPSIS DEPENDING ON GESTATIONAL AGE

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Background. Early-onset neonatal sepsis remains one of the major causes of neonatal mortality. Genetic association studies may help to detect molecular mechanisms that are causally related to the disease occurrence. A number of potential functional candidate gene variants have been described but the data remain variable and in some points controversial most likely due to heterogeneity and small number of patients.
Objective. To investigate genetic polymorphisms in neonates according to GA, in order to find genes potentially involved in response to infection.
Methods. The study included 379 neonates (24-41 weeks of gestation) < 72 hours of life. All neonates had signs of respiratory distress and required respiratory support. Peripheral blood samples for genotyping DNA were taken in all patients at the same time of sepsis-workup. We examined SNP in several groups of genes. Genotyping was performed by the specific PCR product melting curve analysis elaborating "kissing" (adjacent) probes (DNA-technology, Moscow, Russia).
In a retrospective analysis all patients were divided into 2 main groups depending on the reason of respiratory distress (infectious or non-infectious): Group 1: 161 neonates with RDS or transient tachypnea of neonate (TTN), Group 2: 218 neonates with early-onset neonatal sepsis (EOS). Based on the gestational age, the neonates of the 2 main groups were divided into 4 subgroups according to gestational age (GA): 24-28 wks, 29-32 wks, 33-36 wks, ≥37wks.
Results. We identified statistically significant differences in the distribution of alleles and genotypes in neonates having infectious and non-infectious cause of respiratory distress for various genes depending on GA. The distribution of the following genotypes and alleles was statistically different: in subgroup of preterm infants 29-32 wks - NOS3-786, NOS3-894, IL1b; in neonates 33-36 wks - AGTR2, IL4R1902, IL8, GNB825, HTR2A; in neonates ≥37 wks - IL8, ADD1, ADRB3.
Conclusion. The development of early-onset infection is not only associated with the genes of innate immunity, but also with genes regulating vascular tone and energy metabolism, indicating a complex mechanism of the process. Detected genetic associations vary among neonates in association with GA and may be related with maturation patterns of different systems.

NEONATAL OUTCOMES IN PATIENTS WITH HEMOLYTIC DISEASE OF THE NEWBORN AFTER INTRAUTERINE TRANSFUSIONS: A 7- YEAR SINGLE-CENTER EXPERIENCE

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Background. Due to major advances in the management of hemolytic disease of fetus and newborn (HDFN) immune hydrops - a severe and potentially lethal condition – has nearly disappeared in developing countries. Nevertheless, the problem of HDFN – associated morbidity and mortality is still highly relevant in populations with limited access to high quality medical care.
Objective. To investigate the course of HDN in neonates after IUTs and to identify strategies for further improvement.
Materials and Methods. This single-center retrospective study included 52 neonates with Rh-antiD-alloimmunization who underwent IUTs and were born in our Center in 2012-2019. The mothers were referred to the Center from distant regions of Russia mainly after telemedicine consultations.
Results. 1-st trimester antibody screening was performed in 94% of admitted women; anti-D-Ig prophylaxis was absent in 96% of women. Median GA at the time of maternal admission was 29 weeks (min-max 20-35). 25 fetuses (48%) presented with hydrops at the time of first IUT. Median number of IUTs was 2 (min-max 1-5). Intrauterine reversal of hydrops was achieved in 32% of fetuses (8/25) and most of these patients (7/8) did not have severe HD postnatally; only 1 patient required exchange transfusion (ET). All neonates were born prematurely and admitted to our NICU. Median GA at birth was 32,5 weeks (min-max 29-36,5), body weight - 2170g (min-max 1430 - 3350g). ET was required in 61,5% (32/52) of cases. Neurologic complications were registered in 3,8% (1 antenatally diagnosed PVL, 1 postnatal IVH ≥III). Overall survival was 91% (47/52), survival among neonates with hydrops – 71% (12/17).
Conclusions. Our data show, that in a specific population of patients, managed with IUTs, all neonates were born prematurely and required intensive care. The high percentage (48%) of hydrops before 1st IUT indicates late referral to a tertiary center. Despite a fairly goodscreening rate for HDFN and introduction of IUTs, the incidence of fetal hydrops was relatively high; moreover, reversal of fetal hydrops was achieved in only 1/3 of patients. Extension of proper immunoglobulin prophylaxis and timely referral to tertiary centers appear to be the key factors for further improvement.