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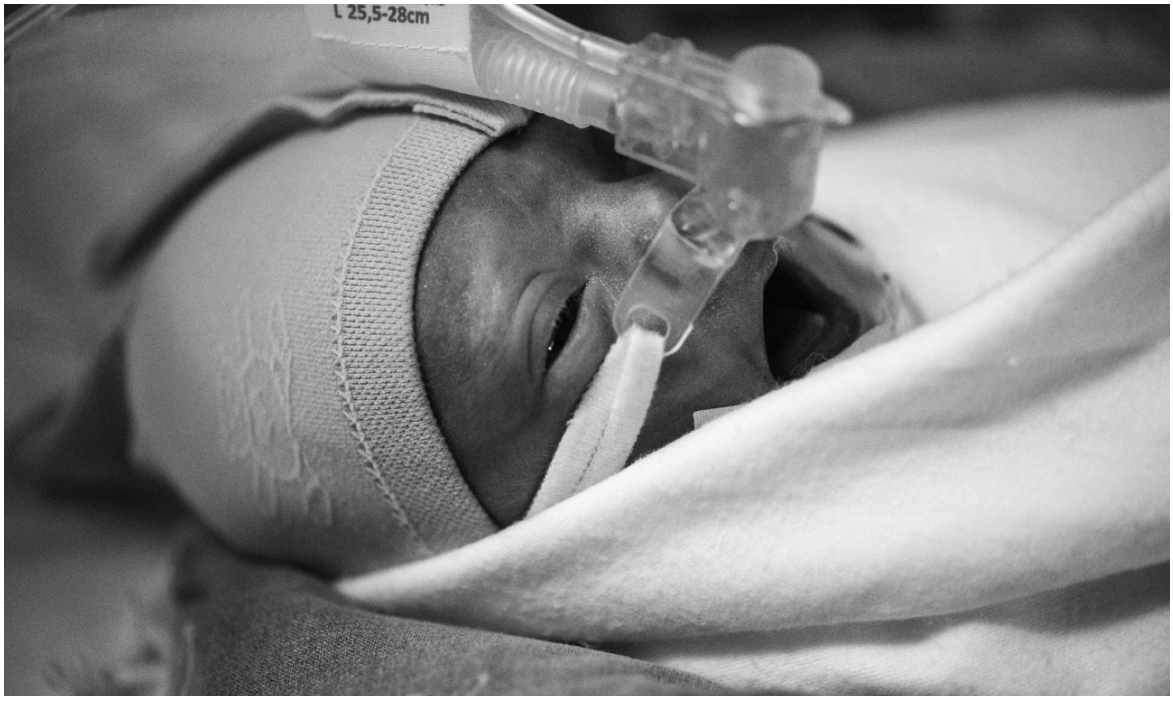

C. Chammartin

TUESDAY, JANUARY 16, 2018

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Abstract book

Meningococci in preterm babies!? Case report of a rare pathogen for late onset sepsis and meningitis in a late preterm neonate

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Introduction In neonates, Neisseria meningitidis is a rare cause for sepsis. Due to better prevention of other pathogens, it has gained in importance.

Case report 12 hours of poor feeding motivated the emergency consultation of a preterm boy (gestational age 35 3/7 weeks, birth weight 2410 g) on day of life 12. He appeared ill and major findings were fever, floppiness and decreased response to stimuli. Suspecting sepsis, empiric antibiotic therapy (amoxicillin/gentamicin) was started immediately after blood sampling for culture. Given the clinical deterioration, septic work-up was completed with a delay of 6 hours. Cerebral spinal fluid (CSF) was consistent with bacterial meningitis (WBC 6926/mm3, 91 % polymorphonuclear). While CSF-cultures remained sterile, blood culture grew gram-negative diplococci within less than 24 hours finally identified as serogroup Y meningococci. Antibiotic therapy was changed for cefepime with excellent clinical response. The boy was discharged home after a total of 14 days of antibiotic treatment without clinical or ultrasonographic signs of cerebral impairment.

An asymptomatic nasopharyngeal carriage of the same serogroup Y meningococci was detected in the father and the grandmother of the boy, who were in close and regular contact since birth. Only the postexposure prophylaxis was given to them.

Discussion Invasive meningococcal disease (IMD) is a rare entity in neonates with high mortality/morbidity manifesting usually as late onset sepsis with findings of meningitis. According to our literature research, only term born neonates have been described so far in case series of neonatal IMD and neonatal meningococcal meningitis. In contrast to common pathogens for neonatal sepsis, that colonize either the maternal rectovaginal area (early onset sepsis) or the neonatal intestinal tract (late onset sepsis), N. meningitidis is a known bacterial commensal of the human nasopharynx. In our case, transmission by close family members seems highly plausible, as the same serogroup Y meningococci had been detected in two family members. As this serogroup is not included in the standard vaccine recommended in Switzerland, current vaccination strategies against meningococci would not have been preventive in this case.

Conclusion This report describes an exceptional case of late onset sepsis and meningitis due to N. meningitidis serogroup Y in a late preterm boy illustrating the potential importance of an asymptomatic carrier status in parents. To our knowledge, this is the first case description of an IMD in a preterm child and the first with documented carriage of the same pathogen in family members.

Personalised prediction of weight changes in the first days of life

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Aims and objectives Physiological newborns lose weight during the first days of life before they begin to gain weight. An excessive loss should be avoided as it increases morbidity whereas too early intervention complicates breastfeeding. The aims of this work were to (i) characterise physiological weight changes and effects of supplemental feeding in neonates during the first week of life; (ii) identify and quantify multiple neonatal and maternal factors influencing weight change; (iii) provide an educational online tool allowing caregivers to forecast individual weight changes and supplemental feeding effects up to 1 week of life.

Materials and methods Retrospective study on prospectively recorded clinical data from all healthy infants born with more than 34 weeks gestational age (GA) at the University Hospital Basel in 2009 and 2010 (n = 4196). Exclusion criteria: only one recorded weight (n = 141), transfer to a neonatal ward (n = 269), multiples (n = 148). Two thirds (n = 2425) were randomized to develop a semi-mechanistic model characterising weight changes as a function of the balance between time-dependent rates of weight gain and weight loss and to characterise linear dose-effects of formula and breast milk. Population analysis was implemented using NONMEM7.3. Model selection and evaluation were based on statistical criteria, goodness-of-fit plots and simulations. For evaluation the remaining third (n = 1213) was used.

Results Key patient characteristics (median, range) were as follows: GA 39.9 weeks (34.4-42.4), birth weight 3394 g (1980–5230), mother's age 32 years [15-51], delivery by caesarean section 26 %, girls 51 %. Model evaluation demonstrated a good predictive performance (bias = 0.01 %, precision = 0.56 %). The model was able to accurately forecast individual weight changes and dose dependent effects of supplemental feeding up to 1 week after birth (bias = 0.15 %, precision = 1.43 %). The following characteristics were identified as key predictors of postnatal weight changes up to 1 week of life in our population: Birth weight, GA, gender, delivery mode, type of feeding, mother´s age and parity.

Conclusions We present the first model that describes physiological weight changes and effects of breast and formula milk feeding during the first week of life in term and late preterm neonates. We developed an user-friendly online tool to support caregivers to forecast individual weight changes and assist decision making regarding formula milk supplementation, discharge home timing, and to further personalise the care of neonates.

Neurofilament serum levels as biomarker of neuronal injury in very preterm born infants

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Aims and objectives Neurofilament light chains (NfL) are part of the unique cytoskeletal proteins of neurons, are shed to the cerebrospinal fluid, are detectable at low concentrations in peripheral blood of healthy adults and represent a highly promising serum biomarker of neuronal injury in adults. Prematurity is worldwide the leading cause of infant death and an important risk factor for neurodevelopmental deficits. Therefore early identification is needed to detect premature infants with an elevated risk for later neurodevelopmental disorders. The present pilot study investigates for the first time NfL serum levels in very preterm infants, aiming to understand the impact of prematurity on brain development.

Materials and methods We performed a prospective observational study enrolling 99 very preterm infants with 28.6 ± 2.4 weeks of gestational age (GA) born at the University Hospital of Basel. Blood samples were taken at 7 days of life and NfL concentrations were measured using a newly developed ultrasensitive single-molecule array (Simoa). Clinical data and cranial ultrasound were recorded serially until discharge home. Statistical analyses included descriptive statistics, Spearman correlation analyses and multiple linear regression using NfL as dependent variable and GA, birth weight (BW), oxygen supply duration and intraventricular hemorrhage (IVH) as explanatory variables.

Results The median serum concentration of NfL was 129 pg/ml (IQR 79 – 225.5). The NfL levels significantly ($p<.001$) correlated with GA ($r=-.48$), BW ($r=-.54$), Apgar score at 5 minutes ($r=-.26$), duration of oxygen supply ($r=.38$), IVH ($r=.27$) and bronchopulmonary dysplasia (BPD) at 36 weeks GA ($r=.34$). A significant linear regression was found ($F(4,93)=9.36$, $p<.001$) with an R2 of .29. In particular GA ($ß=.68$), BW ($ß=-.46$) and oxygen duration ($ß=.57$) explained the most of the NfL serum levels.

Conclusions Serum levels of the neuronal injury marker NfL are in very preterm born infants on average 5-fold higher than in healthy adults and comparable to levels of stroke patients. NfL levels are negatively correlated with GA and BW. Brain immaturity with high turnover of neurons, leakage of the blood brain barrier or the existence of neuronal injury associated with prematurity are possible explanations for the high serum NfL levels in preterm infants.

Analysis of blood transfusion practices in newborns in Switzerland

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Aims and objectives Switzerland does not have a nationwide guidelines about blood transfusion practices in newborns. Therefore, the aims of this study were to gather the transfusion practices and the internal recommendations of all Swiss neonatology clinics and laboratories, to compare them with international recommendations and to find out whether there is a need to develop a valid nationwide recommendations.

Material and methods All Swiss neonatology clinics level III und II according to the CANU classification and their laboratories were consulted from April to November 2016 by means of two different online surveys concerning their blood transfusion management. Neonatology clinics were kindly asked to submit their internal guidelines of transfusion thresholds. The blood products are provided in Switzerland in close collaboration with the regional blood donor services, so they were also asked to participate.

Results Out of the 34 total neonatology clinics in Switzerland, 29 carry out blood transfusions in newborns. A total of 26 of these 29 clinics participated in the survey. A total of 26 of these 29 clinics participated in the survey (participation rate 90 %). All 12 clinics having internal guidelines submitted these to the comparison. Out of a total of 25 laboratories, 18 took part in the survey (participation rate of 72 %) The result of the survey revealed a considerable diversity of different transfusion practices, ranging from the preparation to the administration of blood products (quantity, time, conservation, control policy etc.). The clinic internal blood transfusion thresholds were also completely different. Despite existing recommendations of blood donation SRK Switzerland, most laboratories and blood donor services demonstrated a different management of the blood transfusions provision in newborns.

Conclusion Regarding blood transfusion strategies, the present study thus clearly shows high diversity in transfusion practice. To our opinion, it would make sense to develop a common recommendation for the handling of blood transfusions in newborns in Switzerland. A nationwide guideline would be a valuable aid for all health professionals in the daily management of blood transfusions and an opportunity to positively influence neonatal care. Furthermore, Switzerland could keep pace with other countries and position itself in an international context.

Postnatal MR-Imaging and ADC measures in congenital cerebral Cytomegalovirus infection provide an added diagnostic value in characterizing white matter disease

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Introduction Congenital Cytomegalovirus (cCMV) infection carries heavy long term clinical neurological burden, but not much has been reported so far regarding the most appropriate diagnostic cerebral imaging tools and which lesions would qualify for treatment. One of the cerebral affections seen postnatal in cCMV is white matter disease (WMD), often temporal, developing in the late trimester, which could potentially benefit from early postnatal treatment.

Hypothesis The objective of this retrospective cohort case control study was to compare in cCMV infants the respective diagnostic values of postnatal cerebral ultrasound (cUS) and MRI in relation to the lesions seen in cCMV and particularly WMD, and to determine the added value of ADC values measured in 6 different regions of interest (ROIs) of the WM in WMD positive and negative patients.

Methods All patients born between 2004 and 2017 with confirmed cCMV by postnatal PCR (urinary) evaluated with both postnatal cUS (GE, Vivid) and MRI (3T, conventional T1 and T2 sequences and Diffusion Weighted Imaging) were included. Clinical, epidemiological and imaging data were collected and analyzed. Measures of ADC were performed according to a standardized protocol in 6 different ROIs of the frontal, parietal and temporal WM bilateral.

Results 38 newborns (24F/14M) were included; 24 were neurologically symptomatic (≥ 2 symptoms: microcephaly <P3 (n = 15), abnormal: cUS (n = 23), MRI (n = 29), evoked auditory potentials (n = 12)). Cerebral findings were germinolytic pseudocysts in 55 % (n = 21), WMD in 45 % (n = 17) and ventricular dilatation in 29 % (n = 11). When considering all cerebral findings, 24cUS (58 %) against 29 MRIs (88 %) were pathological. Mean ADC values were significantly increased in WMD positive patients with 190 (±31), 189(±16) and 196 (±35) mm2/sec, in contrast to non WMD patients, with 160 (±23.66), 172 (±12) and 155(±14) in parietal, frontal and temporal WM respectively.

Conclusions In a cohort of patients with cCMV infection, WMD represented 50 % of all imaging cerebral anomalies found. While MR imaging was concordant to cUS for usual findings, it was definitively superior and provided an added value to cUS for the diagnosis of WMD, not only temporal but also parietal and frontal, suggesting to be a valuable tool for WMD identification and quantification and possible tailoring to the postnatal treatment. The definitive clinical long term value of WMD has yet to be determined.

Early onset intrauterine growth restriction: an independent risk factor for poor perinatal outcome in very preterm infants?

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Objective Intrauterine growth restriction (IUGR) represents a complex pathological condition that is characterized by the fetus' failure to achieve its optimal growth potential. Existing definitions are inconsistent and blur the boundaries between IUGR and the

constitutional state small for gestational age (SGA). The aim of this retrospective cohort study was to assess the independent contribution of early onset IUGR to neonatal mortality and morbidity in very preterm infants.

Materials and methods Live-born infants with 24-to-32 weeks of gestational age (GA) from our center between 2000 and 2013 were included. Exclusion criteria were major malformations or a priori palliative care. IUGR was defined as an estimated fetal weight (EFW) < 5th centile and umbilical artery Doppler (UAD) resistance index > 97th centile and SGA as EFW < 10th and normal UAD parameters. Neonatal death and five morbidities (necrotizing enterocolitis, sepsis, bronchopulmonary dysplasia, retinopathy of prematurity > grade 2, major brain injury) that are known to have predictive value of neurodevelopmental outcome at 2 years of age were compared between IUGR and SGA infants and to the control infants with birth weight ≥ 10th centile. Controls were 1 :1 matched to the IUGR group for sex, GA, multiple births, prenatal steroids and birth year. Logistic regression was applied.

Results Among 1652 live-born infants, data from 119 (7 %) IUGR, 25 (1.5 %) SGA and 119 (7 %) control infants were analyzed. Perinatal and demographic characteristics of all groups were similar except in birth weight and the caesarean section rate that was significantly lower and higher, respectively, in IUGR infants compared to the controls. Univariate comparison showed higher mortality (OR = 3.6, 95 % CI [1.7, 7.3]) and higher composite neonatal morbidity (OR = 2.3, 95 % CI [1.3, 4.2]), i.e. the presence of one or more morbidities, in IUGR infants compared to controls. There was no between group differences in morbidity rate at single level. After adjusting for birth weight no difference in the neonatal outcome was observed.

Conclusion In this cohort of very preterm infants, the factor IUGR did not appear to be an independent predictor of neonatal mortality and morbidity when compared to the control group. The lack of any differences between IUGR and SGA groups might be due to the small SGA sample size or owing to the fact that birth weight exerts the highest impact on neonatal outcome in this GA range. The IUGR effect might be more prominent in a later stage of life.

Neonatal withdrawal syndrome: a 2011-2016 retrospective audit in the Hôpital neuchâtelois

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Aim and objectives The incidence of neonatal withdrawal syndrome (NWS) is reported to increase. Opiate or polydrug NWS are generally treated with oral morphine solutions. There is a lack of consensus in the literature about morphine dosage or other drugs use. The aim of our study is to analyze our practice, compare it with literature report and try to improve it.

Methods We are the only neonatal unit caring for sick neonates of a 160 000 population (about 1700 births/year) up to grade IIb level. We use a clinical guideline based on Finnegan scores to treat neonates with NWS. In addition to non pharmacological care, we use as first line therapy oral morphine when needed and adapt it stepwise without any pre defined maximal single dose or daily dosage. We analyzed all charts of neonates with a diagnosis of NWS (ICD-10 P96.2) who were cared for in our neonatal unit between 01.01.2011 to 31.12.2016.

Results Twelve cases were found (out of 10 653 births, ie 1.1/1000 births), with a M/F sex ratio of 3, a median birth weight of 2780 g (range 1345-3920) and a median postmenstrual age of 38 weeks 5/7 (range 31 4/7- 39 5/7). 6/12 mothers used > one drug. 8/12 mothers were on substitution methadone (median daily dosage 100 mg, range 15-160 mg), 9/12 neonates were treated pharmacologically with oral morphine and 4/9 with additional phenobarbital . The maximum daily morphine dosage was 7.3 mg/kg/day (median 1, range 0.48 - 7.3), with few side effects (only one case of constipation). The 4/9 cases with additional phenobarbital had the highest maximal daily morphine dosage (1.5-4-4.8-7.3 mg/kg/day). Wide single patient day-to-day morphine dosage variations were noted, associated with wide Finnegan scores fluctuations. 3/12 mothers breastfed. Median hospital stay was 45 days (range 4 - 96). 3/12 and 9/12 newborns were discharged home, respectively foster home.

Conclusions In comparison with the international literature, we found: 1) a very low incidence of NWS in the Canton of Neuchâtel, 2) a maximum daily oral morphine dosage that exceeded by far 2014 AAP guidelines, 3) long hospital stays. We also noted wide single patient day-to-day morphine dosage variations and difficulties in discharging patients to foster homes on oral morphine. We would like to learn from other Swiss neonatal units experience, particularly with the use of opiates after discharge or methadone instead of morphine bearing in mind the longer half-life of the former and its eventual more stable effects.

Two-year outcome of extremely preterm infants < 26 weeks of gestation born in Switzerland: is intensity of perinatal care associated with increased neurodevelopmental impairment?

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Objectives In Switzerland, a substantial difference in neonatal mortality of infants with gestational age <26 weeks is observed among the 9 perinatal centres and few is known about the neurodevelopmental outcome in survivors. This study aimed to investigate the impact of centre-specific levels of perinatal interventional activity on neonatal mortality and neurodevelopmental outcome at the corrected age 2 years.

Methods Prospective geographically defined cohort study including all live-born infants in Switzerland between 2006 and 2013 from <26 weeks gestation without major congenital abnormalities. Perinatal interventional activity was derived from 3 obstetric and 4 neonatal indicators. Outcomes at 2 years were mortality, survival with any major neonatal morbidity and survival with severe-to-moderate neurodevelopmental impairment (NDI, defined as one of following: cerebral palsy with GMFCS >1 ; a developmental test score <-2SD from the respective norm; hearing loss; uni- or bilateral blindness). Crude and adjusted odds ratios between levels of perinatal interventional activity were calculated using multivariable regression models.

Results Among 927 included infants, 567 (61 % of cohort) died before discharge and 325 (90 % of survivors) were assessed at 2 years corrected age [46 % females, mean (SD) gestational age 25.1 (0.5) weeks]. Among all live-born infants, 466 and 461 were born in centres with high and low perinatal interventional activity, respectively. Moderate-to-severe NDI was observed in 18 % of survivors. After risk adjustment, mortality was significantly lower (0.22, 0.15-0.31) in centres with high compared to centres with low perinatal interventional activity, while no significant association was observed between level of perinatal interventional activity and the rates of any major neonatal morbidity or moderate-to-severe NDI.

Conclusions Centers with high perinatal activity have a significantly lower risk for mortality and death or NDI while having comparable outcome among survivors. Further research is required to better estimate the accompanying burden added on the surviving child.

Neo (neonatal esophageal observation) tube – a feeding tube with monitoring function

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Aims and objectives Preterm infants show signs of autonomic dysregulation such as apnea, bradycardia and difficulty in swallow-breath coordination. Therefor monitoring of heart rate (HR) and respiration rate (RR) as well as feeding via gastric tube is required. Today surface electrodes are commonly used to monitor HR and RR. However, their use results in movement artefacts and frequent skin irritation. Neonatal esophageal observation (NEO) would combine enteral feeding with monitoring of autonomic dysregulations. Our aim was to assess whether monitoring of HR and RR is feasible via gastric feeding tube and to compare NEO monitoring with standard monitoring on the NICU.

Methods We performed a prospective single center study in the NICU at the University of Basel Children's Hospital. We included preterm infants with postconceptional age > 32 weeks. Standard feeding tubes were replaced by an Edi-tube. This tube is equipped with 8 electrodes and is normally used to measure diaphragm activity enabling neurally adjusted ventilatory assist (NAVA). On 5 consecutive days multichannel signals from the Edi-tube and standard monitoring data (extracted from Philips IntelliVue using ixTrend) were captured and synchronized with customized software. Signals were visually analyzed and for each measured hour a period of 10 minutes, in which NEO and NICU signals are of high quality, was selected. A wavelet transformation was used to detect R-peaks and the breathing cycle, both of which were subsequently used to calculate the NEO HR and RR.

Results Between July 2015 and March 2016 we performed 60 measurements in 13 preterm infants (6 male). Study participants had a mean gestational age of 33.0 weeks and mean birth weight of 1621 g. No adverse events were noted. Standard monitoring and NEO data showed a median (iqr) difference of 0.55 (25.3) ms for HR and -118 (361) ms for RR, respectively. The difference is not significant for HR (p = 0.053, Wilcoxon signed rank test), but significant for RR (p<0.001).

Conclusion Extracting R peaks and respiration from an Edi-tube in preterm infants is feasible. HR derived from NEO showed no significant difference to standard monitoring. Differences in RR were significant between the two signal sources. This is probably due to skeletal muscle activity causing noise in surface electrodes. We see great potential in further developing the NEO approach to improve monitoring in preterm infants.

An unusual event at the maternity ward

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A.P. was boy born from a 2G 0P 34 year-old women, at term. A caesarean section was performed after 2 attempted vacuum extractions. Apgar score was 9/10/10. At 30 hours, the infant was uncomfortable, pale, had mild respiratory distress and a 4 cm increase of the cranial perimeter. He was admitted to NICU with major haemodynamic instability. On clinical examination, the skull showed a massive, hard, pitting oedema without fluctuations but protruding ears. Pulse oxymetry was 100 % in room air, heart rate 135 bpm and BP 66/32(43) mmHg. Blood gases revealed severe metabolic acidosis and anaemia (pH 6.84; lactatemia 23 mmol/l; Hb 46 g/l). Coagulation test were abnormal (PT 35 %; aPTT>160 sec; fibrinogen 1.2 g/l).

The baby was intubated, transfused with O negative blood and placed in hypothermia for 72 hours. The cerebral US showed a soft tissues collection and the CT suggested subgaleal hemorrhage (SGH). During hypothermia, the status was marked by severe generalised hypotonia, but after rewarming, the neurological status considerably improved. MRI at 4 days was normal. Coagulation remained abnormal. Factor VIII activity was <1 % and led to the diagnosis of severe Hemophilia A. A heterozygotic mutation of the F8 gene was later identified in the mother. The atypical presentation of this closed skull haemorrhage led to a delayed diagnosis. Haemophilia certainly contributed to this unusual presentation.

The suspected SGH is a severe, life-threatening, closed bleeding, due to the rupture of emissary veins that requires prompt diagnosis and treatment in case of hypovolaemia. Localized beneath the epicranial aponeurosis, borders are ill-defined and the collection usually fluctuating. The diagnosis is clinical and imaging not pathognomonic. Atypical presentations make the differential diagnosis with caput succedaneum difficult. The slow progress and firmness of the collection suggested infiltration of soft tissues, whereas the massive volume loss more typically fitted SGH. The coagulation deficit lead to a life-threatening event.

Coagulation in the newborn is challenging because factor levels are considerably lower, and pre-analytic factors more critical than in adults and methodologically variable. Although acquired clotting disorders are more common in neonates, inherited disease need consideration: haemophilia remains the most common. Atypical or severe presentations of neonatal bleeding need investigation of congenital clotting disorders.

Piperacillin-Tazobactam dosing regimen harmonization across neonatal intensive care units in Switzerland

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Aims and objectives An important variability in piperacillin-tazobactam (Pip-Tazo) dosing regimens in neonates has been observed across international guidelines and neonatal intensive care units (NICUs) in Switzerland. Among 12 different dosing approaches, 7 use age- and body weight-related covariates to establish the appropriate dose administration. Our objective was to harmonize Pip-Tazo dosing in neonates admitted in NICUs in Switzerland by comparing Pip exposures under the existing recommended dosing regimens.

Materials and methods Piperacillin concentration-time profiles in 1000 neonates were simulated for the 12 identified dosing approaches by applying a published population pharmacokinetic model developed in a neonatal population [1]. The demographic characteristics of our study population were similar to those of the Antibiotic Resistance and Prescribing in European Children (ARPEC) project dataset. The exposure target was defined as free drug concentration (fu) higher than the minimal inhibiting concentration

(MIC) over the whole dosing interval (100 % fuT>MIC). MICs of the most frequent pathogens in NICUs were retrieved from the European Committee on antimicrobial susceptibility testing (EUCAST). A dosing regimen was considered adequate if the exposure target was attained in >90 % of simulated neonatal patients.

Results Three regimens, i.e. two international guidelines and one from a Swiss hospital, were associated with target attainment for MIC up to 16 mg/L in more than 90 % of patients. The Swiss hospital recommends a dose of 75 mg/Kg/6h for all neonates, whereas the two international guidelines recommend a dose stratification based on post-menstrual age and actual body weight. More than 80 % of neonates would achieve the target when administered with 100 mg/kg/8h, as proposed by two Swiss hospitals and one international guideline.

Conclusions These results suggest that many proposed Pip-Tazo dosing regimens do not allow the target attainment of 100 % fuT>MIC in infections with MIC > 4 mg/L. A standard dose of 75 mg/kg/6h would achieve appropriate exposure coverage for MICs up to 16 mg/L in more than 90 % of patients. A more convenient dosing of 100 mg/kg/8h would also be associated with target attainment in similar percentage of neonates. More complex dosing regimens are unlikely to result in better effective drug exposure than simpler strategies.

Cohen-Wolkowiez M, et al. Antimicrob Agents Chemother. 2014;58(5):2856–65.

Enterovirus associated hemophagocytic lymphohistiocytosis in a newborn infant born to a mother with a heterozygote mutation of factor 2 hla b27

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Introduction Secondary hemophagocytic lymphohistiocytosis (HLH) is triggered by various factors including infections and autoimmune diseases.

Case report We report of a newborn infant, born @ 37 6/7 WG from a healthy 35 year-old mother carrier of a heterozygote mutation of factor 2 HLA B27. The healthy boy was born by vaginal delivery after an uncomplicated pregnancy. The mother developped fever and inflammatory syndrome 48h after delivery. On day of life (DOL) 4, the infant presented fever and signs of poor perfusion, motivating his hospitalisation in a regional hospital and starting empirical antibiotics. Laboratory findings showed rapidly progressive Tc-penia (15G/L) leading to his transfer to the NICU on DOL 5. His course was marked by bleeding, severe coagulation test abnormalities with hepatic insufficiency, anemia, extreme hyperferritinemia (113650µg/L), elevated serum LDH, ALAT and triglycerides (TG), abdominal distension with hepatosplenomegaly and ascites. PCR of respiratory secretions and blood were positive for enterovirus (EV). Treatment with multiple transfusions of fresh frozen plasma, thrombocytes, erythocytes, immunoglobulins and iv-steroids normalized the patient's coagulation parameters by DOL 14 and Tc-counts by DOL 17. Testing for Tc-alloimmunization was negative, as well as screening for inborn errors of metabolism. Based on these findings, secondary HLH triggered by EV was suspected.

Discussion Neonatal EV infection and HLH share overlapping features. Increased TG and anemia are nonspecific markers of inflammation, whereas an elevated ferritin level, especially >10,000 mg/L, is suggestive of HLH. Viral infections seem to interfere with cytotoxic T-cell function, representing a possible mechanism of infection-associated HLH. Differentiation between isolated EV infection and HLH in neonates is thus difficult, but important for prognosis. In HLH, therapy with steroids, chemotherapy and immusuppressive drugs needs to be considered.

In this patient, an inherited HLA B27 mutation might have contributed to immune dysregulation of CD8 T-cell activation, leading to increased cytokines production inducing HLH. However, a panel targeting genes involved in familial HLH and a subgroup of HLA B27 associated HLH was negative.

Conclusion Neonatal HLH is a life-threatening condition with high mortality. It should be considered in patients with persisting coagulopathy associated to viral infection, in particular EV with a severe inflammatory reaction.

Meropenem dosing regimens in neonates across seven swiss neonatal intensive care units and in seven international guidelines. Is it effective?

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Objectives To assess achievement of adequate drug exposure across recommended neonatal meropenem dosing in Swiss NICUs and international guidelines.

Materials and methods Dosing regimens for meropenem were collected from the 7 Swiss level III NICUs (Zurich, Basel, Bern, Aarau, Luzern, Geneva and Lausanne) and 7 international guidelines (BNF for children®, Neonatal Formulary®, Frank Shann's Drug Doses®, Nelson's Pediatrics Antimicrobial Therapy®, Lexicomp®, Neofax®, FDA). Simulations were performed, based on pharmacokinetic (PK) model developed from a large PK study of meropenem in neonates, to compare dosing regimens with respect to their ability to maintain drug levels above predefined minimum inhibitory concentrations (MICs) during the entire dosing interval. Simulations used demographic data from > 1000 neonates (ARPEC point-prevalence survey in Europe).

Results Meropenem dosing regimens used in the 7 Swiss level III NICUs and recommended in 7 international guidelines showed considerable variability with 11 of the 15 dosing regimens being different with respect to dose, dosing interval, and demographic factors (weight, gestational age (GA), postnatal age (PNA)) used to adjust the dose and interval. Recommended dosing ranged from 10 mg/kg to 30 mg/kg every 8 hours. None of the current recommendation was associated with appropriate target attainment for MICs ≥ 2 mg/L, with best performance for Shann, Nelson and FDA recommendations. Simulations showed that doses of 10 mg/kg were not sufficient to achieve effective drug exposure. A dosing of 20 mg/kg q8h for neonates with a GA < 32 weeks, and 30 mg/kg q8h for neonates with a GA ≥ 32 weeks would maintain concentrations above a MIC of 2 mg/l during the entire dosing interval in 80 % of patients. For target MICs ≥ 4 mg/L, more frequent administration would be required (every 6 to 4 hours).

Conclusions There is considerable inconsistency in current neonatal meropenem dosing resulting in variable and likely subtherapeutic drug exposures. There is a clear need for harmonizing neonatal meropenem dosing in Switzerland. Based on current simulations we suggest a simplified dosing regimen based on GA to maintain target exposures in this vulnerable population.

Inter professional hands on neonatal simulation workshops

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Introduction MPS is a group of pediatric professionals accredited internationally in health care simulation. Although MPS conducted 3 successful neonatal simulation workshops, this study is designed after the 4th workshop.

We aim to enhance the decision making in neonatal emergencies, the skills for procedures and vascular accesses and to demonstrate and disseminate the effective Inter professional team dynamics.

Methods The MPS conducted 4 inter professional multiphasic hands on workshops in 2 days in collaboration with Ain Shams Society for Neonatal Care and Continuous Medical Education. Those were Neonatal Emergencies Simulation workshop, Neonatal Ventilation Simulation Workshop, Neonatal Procedures Simulation workshop and Neonatal Vascular Accesses Simulation Workshop. Each workshop lasted for 3 hours. There were 93 attendees of different educational and professional background. The learners were divided into 2 groups. An on line survey was sent to the attendees.

Results Out of the total 93 attendees, we received 43 questionnaire's responses. The attendees are a mix of inter-professionals as shown in our results. There are 25 Senior Neonatologists, 5 Junior Neonatologists and trainees, 7 general pediatricians, 4 pediatric subspecialty physicians and 3 allied health professionals. Most of the attendees were very impressed with few comments for further improvement.

Conclusion The authors concluded that Neonatal Inter Professional Simulation Workshops were very effective learning tools to improve the quality of care and to enhance the patient safety. However, there are some potential opportunities which require improvement.

Key words Bayoumi, Elbaba, Elzubier, Mahgoub, Mobile Pediatric Simulation (MPS), Inter Professional Education (IPE), Neonatal Simulation Workshops.

Necessity is the mother of invention: the mobile pediatric simulation (mps) hand made task trainers

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Introduction A collaborative work amongst three simulation specialists built a team named Mobile Pediatric Simulation (MPS) in 2016. We have our own equipment including many manikins of medium fidelity. We also have our SPs and few task trainers. The team used to move from our base in Qatar to other countries overseas to conduct our simulation events. We faced many challenges because of the mobile nature of simulation to be delivered. One of the major challenges is the task trainers; we need to ship or travel with many strange pieces of equipment in the flights.

Methods To overcome the difficulty of transporting many task trainers required for psychomotor skills for intervention in simulation practice, MPS has invented four commonly required task trainers in pediatric practice from very basic materials but with high fidelity. These hand-made part task trainers are: Lumbar puncture, chest tube insertion, peripheral IV cannulation and umbilical catheterization for the newborn.

Results The learners attending our workshops used the newly created task trainers and engaged better during those simulation experiences. The sense of realism which reflects the high fidelity nature of the models was achieved as learners mentioned this in their feedback. MPS successfully demonstrated the integration of high fidelity with low technology resources.

Conclusion The author will demonstrate and share the newly innovated task-trainers with the audience. MPS believes that creativity is an essential requirement for any simulation specialist or educator.

Key words Bayoumi, Elbaba, Mahgoub, creativity, Mobile Pediatric Simulation (MPS), task trainers, high fidelity, neonatal simulation.

Fetomaternal transfusion syndrome as a cause of severe neonatal anemia

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Aims and objectives The fetomaternal transfusion syndrome is defined by the loss of fetal blood into the maternal circulation. A relevant transfer of more than 80ml of fetal blood,occurs in 1 of 1000 pregnancies.

Materials and methods Two newborn boys were born with severe anemia and hematocrit values <20 % at the Clinic of Neonatology of the University hospital in Zurich. The clinical history was evaluated, summarized, and put into context with prior publications about this syndrome.

Results The first newborn became apparent in the 27 week of gestation because of intrauterine growth retardation, pericardial and abdominal effusions, ahydramnion and fetal anemia requiring one blood transfusion through the umbilical cord vein. Cesarian section was performed at 28 4/7 weeks of gestation because of suspected amnion infection. Apgar scores were 1/5/8, the arterial umbilical cord pH value was 7.24 and birthweight 650 g. The first blood analysis revealed a hematocrit of 17 %. 15 ml/kg erythrocyte transfusion was performed directly delivery room. Following two further blood transfusions over 48 hours to prevent cardial strains. With a positive Kleihauer-Betke test of 1.1 % of HbF in the maternal blood circulation, the fetal blood loss was estimated to be 55ml. The following clinical presentation was uneventful with spontaneous ventilation and CPAP support.

The second newborn became apparent in the 33 5/7 week of gestation because of reduced fetal movements and pathological CTG. After delivery with cesarian section, the Apgar was 1/5/6, NapH was 7.09, birthweight 2230g and hematocrit 7 % (hemoglobin 19g/dl). Despite good clinical presentation, correction of the blood hematocrit with a total of 60 ml/kg erythrocyte transfusion was performed upon a short time interval of six hours. Consequently, the newborn was intubated and ventilated as well as hemodynamic compromised. From the 3rd day of life clinical presentation was uneventful. With 9.4 % of HbF in the maternal blood circulation, the fetal blood loss prenatally was probably higher or equal as the fetal blood volume of 120ml/kg.

In neither of the two newborns, a definite cause for the fetomaternal transfusion could be detected.

Conclusions Fetomaternal transfusion syndrome is a potentially fatal condition which may present prenatally with decreased fetal movements and CTG abnormalities and low hematocrit values. Diagnosis is suspected in the case of a chronical and highly regenerative anemia and confirmed by a positive Kleihauer-Betke test or Flow cytometry with HbF specific antibodies allowing to detect fetal erythrocytes in maternal blood. While very low hematocrit levels of <20 % need immediate transfusion, the complete correction of hematocrit should be achieved slowly in order avoid cardiopulmonary compromise, either by erythrocyte transfusions or by exchange transfusion.