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Challenges in perinatal and neonatal infectious diseases

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Abstract book
To date little data has been published on treatment of neonatal diabetes mellitus (NDM) in premature infants, whether transient neonatal diabetes mellitus (TNDM) or monogenic permanent neonatal diabetes mellitus (PNDM). Initial treatment usually consists of continuous insulin infusion. If a genetic mutation is detected it is a genes responsible for potassium channels (e.g. KCNJ11 and ABCC8) treatment may be switched to oral sulfonylurea, overlapping with continuous insulin application. Particularly the technical difficulties in administering an accurate dose of NovoRapid® preventing hypoglycemia. Firstly, Insulin U100 had to be diluted and stability of the insulin was critical. When switching from i.v. insulin to CSII we encountered various technical difficulties in administering an accurate dose of NovoRapid® preventing hypoglycemia. Interestingly, no mutation was found. Genetic testing for mutations in KCNJ11, ABCC8 and INS genes was carried out at Exeter Molecular Genetics Laboratory, no mutation was found. Insulin requirement was continuously reduced and CSII was discontinued on day of life 33.

When switching from i.v. to CSII we encountered various technical difficulties in administering an accurate dose of NovoRapid® preventing hypoglycemia. Initially insulin U100 had to be diluted to U10 in order to maintain appropriate flow rate in the catheter. Secondly, all subcutaneous devices readily available are designed for deliveries over 1500g and thus we oversupplied insulin when we fed the preterm infants below 2000g. Thirdly, localization of sufficient subcutaneous fatty tissue in a severely UGIR infant posed an additional problem, inducing repeated hypoglycemia episodes. Insulin U100 had to be diluted to U10 in order to maintain appropriate flow rate in the catheter. Secondly, all subcutaneous devices readily available are designed for deliveries over 1500g and thus we oversupplied insulin when we fed the preterm infants below 2000g. Thirdly, localization of sufficient subcutaneous fatty tissue in a severely UGIR infant posed an additional problem, inducing repeated hypoglycemia episodes. Asymmetric translucency in chest radiographs of neonates is often assigned to atelectasis, pulmonary inflammation, or pneumothorax; congenital pulmonary malformations are rarely in the forefront of the differential diagnosis. We present a ten-day-old female premature infant was born at 24 2/7 weeks of gestation with a suspected congenital lobar overinflation (formerly known as congenital lobar emphysema). She was admitted with respiratory support by CPAP and an oxygen requirement below 25%, and needed mechanical ventilation in the second week of life for severe apnea. Areas of varying opacification in consecutive chest x-rays (pictures) were originally interpreted as atelectasis. However, at the age of 4 weeks, the radiologic findings were consistent with pulmonary hypoplasia in the area of the upper lobe pulmonary lobe that, retrospectively, had evolved unnoticed over the past few weeks. The picture was best matching congenital lung malformation, assumed to represent a true congenital lobar emphysema that leads to progressive lobar expansion postnatally. Despite the impressive radiologic findings [picture] with herniation of the upper lobe into the mediastinal space, the girl continued in moderate levels of supplemental oxygen and with stable circulation. In agreement with the thoracic surgeons, we decided for a conservative management. Here, we show the course of this girl’s pulmonary finding until discharge [pictures]; and we discuss this particular condition to raise the awareness of the neonatologist for the class of congenital pulmonary malformations, which might or might not need urgent surgery in the neonatal period.

The impact of maternal grave’s disease for the newborn – a case presentation

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Objectives Neonatal Graves’ disease (GD) develops in about 1% of neonates born with GD. It is caused by the passage of maternal TSH receptor antibodies (TSHR-Ab) and can lead to prematurity or symptoms of hyperthyroidism in the newborn. The objective of this presentation is to present the case of a premature infant born to a mother with GD.

Background Neonatal GD is caused by the transplacental passage of maternal stimulatory TSHR-Ab binding to the fetal receptor. On the other hand, blocking TSHR-Ab may cause hypothyroidism in the newborn, thus resulting in retardation of growth and development. No significant neonatal complications are seen, though TSHR-Ab are present. The measurement should be repeated on day 4 and within 7-10 days. If the thyroid function is normal and the child is on levothyroxine treatment, no further investigation is necessary. Otherwise, an individual treatment needs to be discussed. Generally, prognosis of neonatal GD is good as it often resolves spontaneously within 3-12 weeks when maternal antibodies have decreased.

Case Description A premature boy (33 4/7 weeks GA, 2,588g) was born to a mother with GD. Previously, the mother was treated with radioactive iodine at 28 1/7 weeks GA after medical intervention for maternal hyperthyroidism. The maternal serum thyroid stimulating hormone (TSH) and free T4 were normal. No maternal hyperthyroidism was documented. The newborn was born at 24 2/7 weeks of gestation and was initially hypothyroid (TSH 41 mU/l) and hyperemotional. The thyroid function was normal by day 2. The mother was treated with radioactive iodine and suppressed TSH. Over the next few days the T4 level decreased gradually below the normal range. Therefore, he was started on Euthyrox on day 41.

Conclusion Maternal GD can lead to hyper- or hypothyroidism in the newborn. If TSHR-Ab are elevated in the 3rd trimester, it is important to check the newborn’s thyroid function and the clinical state of mother and infant. The neonatologist needs to discuss the possibility of maternal hyperthyroidism during the first days of life, which resolved spontaneously. He consequently developed hyperthyroidism which resolved spontaneously. We expect that he can be weaned off such therapy at the age of 6-12 months.

The enlightened chest in an extremely preterm girl

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Asymmetric translucency in chest radiographs of neonates is often assigned to atelectasis, pulmonary inflammation, or pneumothorax; congenital pulmonary malformations are rarely in the forefront of the differential diagnosis. We present a ten-day-old female premature infant was born at 24 2/7 weeks of gestation with a suspected congenital lobar overinflation (formerly known as congenital lobar emphysema). She was admitted with respiratory support by CPAP and an oxygen requirement below 25%, and needed mechanical ventilation in the second week of life for severe apnea. Areas of varying opacification in consecutive chest x-rays (pictures) were originally interpreted as atelectasis. However, at the age of 4 weeks, the radiologic findings were consistent with pulmonary hypoplasia in the area of the upper lobe pulmonary lobe that, retrospectively, had evolved unnoticed over the past few weeks. The picture was best matching congenital lung malformation, assumed to represent a true congenital lobar emphysema that leads to progressive lobar expansion postnatally. Despite the impressive radiologic findings [picture] with herniation of the upper lobe into the mediastinal space, the girl continued in moderate levels of supplemental oxygen and with stable circulation. In agreement with the thoracic surgeons, we decided for a conservative management. Here, we show the course of this girl’s pulmonary finding until discharge [pictures]; and we discuss this particular condition to raise the awareness of the neonatologist for the class of congenital pulmonary malformations, which might or might not need urgent surgery in the neonatal period.

Genetic susceptibility to neonatal group B streptococcal disease

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Aims and objectives Group B streptococcus (GBS) or Streptococcus agalactiae, a Gram positive β-hemolytic bacterium, is one of the most common pathogens causing neonatal sepsis. The incidence of GBS disease is higher in the neonatal period...
Amoxicillin dosing regimens in neonates across nine Swiss neonatal intensive care units and in four international guidelines

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Introduction
Paediatricians often want to avoid underdosing or overdosing antibiotics in the neonatal period. It is an important and complex task. The aim of this study was to describe the different amoxicillin neonatal dosing regimens used in Switzerland and in four international guidelines.

Multiple infantile hemangiomas in a very preterm infant

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Introduction
Hemangiomas represent the most common tumors of infancy with a higher incidence in preterm infants. The incidence is increasing with decreasing gestational age, ranging from 1 in 10 newborns in infants with a birth weight >1000 g, with a female and Caucasian predominance. They occur in the first few days to weeks after birth and proliferate in the following weeks to months. The typical duration of hemangiomas is several months to years. The aetiology of hemangiomas is not yet fully understood. One hypothesis is that hemangiomas are associated with the expression of vascular endothelial growth factor (VEGF), which also plays a predominant role in the aetiology of hemangiomas.

Multiple hemangiomas; they are usually small in size. Occasionally, they can be associated with visceral hemangiomas, particularly in the liver.

Case report
We present a male preterm infant born to a healthy 31-year-old G3P1 at 28+4 weeks due to preclampsia. The baby had a birthweight of 1100 g and his postnatal age was unremarkable. At about 3 weeks of age, he presented with multiple NCUs and in the body with a size of a pinhead (pictures). Over the next few weeks and days the number and size of hemangiomas increased. Abdominal ultrasound revealed multiple liver hemangiomas. As the cutaneous hemangiomas were small in size and not located close to orifices, no therapeutic measure was mandatory.

Discussion
Multiple hemangiomas mainly appear on the skin, but also occur in the integumentary system. For this reason, these infants require clinical and sonographic follow-up, and appropriate treatment until a natural stabilization of the hemangiomas is achieved. Usually, therapy depends on the skin location and size of the lesions, as well as on the risk factors for complications. Hemangiomas which are big in size and those located either on the face (eyes, nose) or in the intestinal tract usually require treatment. Therapeutic options include systemic and local treatment with beta blockers, laser coagulation, or corticosteroids. However, overall treatment is rarely required and the long-term outcome is good.

Conclusion
We report the clinical presentation of an infant with multiple hemangiomas. Our findings add to the published literature on infantile hemangiomas and demonstrate the importance of a multidisciplinary approach. The follow-up of this infant showed that, despite the large number of hemangiomas, no complications occurred and the lesions resolved spontaneously over time.

Psychomotor development in children prenatally exposed to methadone

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Background
Methadone treatment during pregnancy (MTP) has been accepted as therapy for opioid-addicted pregnant women since several decades. Previous studies indicate increased risk of psychomotor difficulties in children prenatally exposed to opioids.

Objectives
To determine the effect of MTP in women on infant’s neonatal outcome, growth parameters and neurodevelopment.

Method
We performed a retrospective study. Data were collected from 53 children exposed to MTP during pregnancy and born from 2004 to 2014. Mental and motor function of the children were assessed at 6 months and 18-24 months with the Bayley Scales of Infant Development (BSID II). MDI and PDI scores respectively represent motor and psychomotor development and were standardized and compared to normative data for all ages. All the children presented psychomicroscopy. After birth, the children were examined for Neonatal Abstinence Syndrome requiring pharmacological treatment. Mean duration of infant’s treatment before discharge was 55.3 days and the average length of hospital stay was 76 days. At 6 months, 37children were assessed with the BSID II; MDI mean score was 102.2 (SD=17.7) and PDI mean score was moderately delayed (M=76.3; SD=15); moreover, the proportion of children having scores below standard deviation (SD) of the norm for MDI and 1.77 for the PDI. This trend tends to persist at 18-24 months of age, with PDI mean score raising slightly. With higher maternal methadone dose there was an increase in rate of BSID II MDI <85th percentile and PDI <70th percentile. The rate of Neonatal Abstinence Syndrome longer and spending longer periods in hospital. At 18-24 months, children in the high dose group were treated for Neonatal Abstinence Syndrome requiring pharmacological treatment, and PDI mean score was lower in the high dose group as well, but the difference between groups did not reach significance.

Results
Birth, mean gestational age was 37.8 (+/- 2.1) weeks, the proportion of infants with a birth weight <2500 g was 10.7%, >2500 g but <10th percentile and 26% of them presented microcephaly. All the children developed a Neonatal Abstinence Syndrome requiring pharmacological treatment. Mean duration of infant’s treatment before discharge was 55.3 days and the average length of hospital stay was 76 days. At 6 months, 37children were assessed with the BSID II; MDI mean score was 102.2 (SD=17.7) and PDI mean score was moderately delayed (M=76.3; SD=15); moreover, the proportion of children having scores below standard deviation (SD) of the norm for MDI and 1.77 for the PDI. This trend tends to persist at 18-24 months of age, with PDI mean score raising slightly. With higher maternal methadone dose there was an increase in rate of BSID II MDI <85th percentile and PDI <70th percentile. The rate of Neonatal Abstinence Syndrome longer and spending longer periods in hospital. At 18-24 months, children in the high dose group were treated for Neonatal Abstinence Syndrome requiring pharmacological treatment, and PDI mean score was lower in the high dose group as well, but the difference between groups did not reach significance.

Parechovirus infection: a rare cause of neonatal encephalitis

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Introduction
Parechovirus infections show a variety of clinical manifestations. Infections in early childhood are often severe. We present a case of parechovirus infection in a neonate.

Case report
This female term infant was born in a regional hosp- ital by elective caesarean section after a pregnancy marked by gastrointestinal problems. Good postnatal adaptation with Apgar 8 at 1, 5, and 10 minutes. Respiratory distress due to well lung and lung immaturity was treated with CPAP for 24h, and then changed to nasal CPAP. MRI showed no signs of intracranial lesions except for 39.1°C. Two days later, she showed clinical decline with irritability, central apnea and desaturations and again respiratory sup- port by CPAP and a mix PCO2 of 0.3. Emergency transfer to the NICU was necessary. Regarding the cardiovascular system she remained stable. Cerebral function monitoring and EEG showed normal functions. Blood smear showed normal lumen blood without pleocytosis. However, PCR for parechovirus in the LCR was strongly positive while PCR for enterovirus was negative. Ce- rebral parenchymal and subcortical white matter areas with necrotization and edema in the periventricular white matter. At day 10, neurological examination normalized. High flow nasal cannula, introduced at day 3, was stopped.

Discussion
Parechovirus is, like enterovirus, part of the pi -
Evaluation of ROP screening criteria in Switzerland and results on possible new screening criteria

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Aim and Objective Retinopathy of prematurity (ROP) is a severe complication of preterm birth. Criteria for ROP-Screening differ between countries as well as between units in Switzerland and usually include patients of less than 31-32 weeks of gestational age (GA) and/or a birthweight (BW) of less than 1250-1500g. Our aim was to evaluate the incidence of ROP in Switzerland and to assess if it is possible to change screening criteria so that fewer patients are screened without missing patients at risk.

Material and Methods Cohort study of prospectively collected data of very preterm infants born alive in Switzerland from 2006 to 2015 (SwissNeoNet, SNN). Missing data on ROP intervention was collected retrospectively.

Incidence of ROP and ROP treatment as well as patient characteristics were analyzed in order to assess if changing screening criteria was a feasible option in Switzerland.

Results Of the 7871 eligible SNN patients, data on ROP-treatment was missing in 1116 patients of which we were able to retrospectively complete and exclude 942 cases. ROP-treatment was necessary for patients with a GA of 24, 25, 26, 27, 28, 29, 30, 31 and 32 weeks in 14.5%, 7.3%, 2.7%, 1.1%, 0.5%, 0.1%, 0.2% and 0.1%, respectively. Record completeness of all infants according to the newborn statistical system was 96%.

Logistic regression for the outcome ROP intervention was performed with predictors GA, days of supplemental O2, days of mechanical ventilation, birth weight (Z-score), surfactant, multiple birth, aneuploidy, brain insult, and growth per week. The final model contained the first 7 predictors up to multiple birth and reached a predictive c-statistics value of 0.912.

The model's application on data collected during 2013-2015 predicted a reduction in the number of screened patients to 281/2809 (13.5%) compared to current screening with a sensitivity of 87.3% and a false negative rate of 12.7%. Reducing the screening accordingly would roughly save 100,000 CHF / year. However, all patients would have required screening to reach a sensitivity of 100%.

Conclusions The rate of ROP-treatment in Switzerland during the observation period was very low (5.2% for children born below 32 weeks in infants born between 2006 and 2015). It may be possible to optimize existing screening criteria based on risk factor analysis and subgroup analysis. We recommend a prospective setup to test the possibility of ROP screening reduction and subgroup definition.

Early neonatal death caused by severe ketoacidosis in a pregnant woman with poorly-regulated type-1 diabetes

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A 27-year-old G2P1 with type-1 diabetes was admitted at 32+3 weeks with premature labour. She had a history of vomiting for two days. Tocolysis with hemapirine had been initiated in the transferring hospital. On admission, she was in reduced condition with vomiting, tachycardia and headache. Blood pressure was normal. Urin dipstick revealed protein- and ketonuria. Blood glucose (BG) was 7.5 mmol/l. There was no evidence of preeclampsia other than headache. Transillumination ultrasound was unremarkable except cardiomediately. Due to increasing maternal tachycardia and contractions the tocolytics drug was changed to atosiban. Delivery was induced as it was not possible to perform an (fHR) tracing showed variable decelerations and was recurrently not feasible. Confirmation of fHR with ultrasound was necessary. Urgent caesarean section was performed 6 hour after admission because of fetal tachycardia. Apgar scores were 0, 0 and 0 at 1, 5, and 10 minutes, respectively. Multiple fluid resuscitations, intubation and placement of umbilical venous line, adrenaline was administered repeatedly. Fluid bolus were given twice. Transfer of packed red cells was performed. Diaphanoscopy was not suggestive for pneumoniae, nevertheless, bilateral chest drains were placed. Repeated echocardiography showed asystoly and resuscitation was discontinued in minute 50. Repeated blood gas analyses (BGA) revealed hyperpyergenic metabolic acidosis with a pH=6.9 and hyperkalemia. Just before the decision to withdraw life support, a meconium aspirate was removed. Meconium was also present in the stomach. Blood culture from umbilical venous line grew Clostridium perfringens. BGA was performed until after birth, no insuline was given as the maternal blood glucose level was initially normal. However, intravitam blood glucose was 28 mmol/l. Amoxicillin 10 mg/kg was given three times 8 hours after delivery due to Clostridium perfringens. No supportive care was performed anymore.

Conclusion The case report displays that ketoacidosis is a severe complication of diabetes. In summary, this case report illustrates the significant impact of ketotic acidosis in pregnancy on perinatal outcome. We recommend a prospective setup to test the possibility of ROP screening reduction and subgroup definition.

Distal humeral epiphyseal separation

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A preterm infant with clostridium perfringens intestinal gangrene

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Airway malfunction due to caesarean section in a woman who de

Discussion NEC typically affects premature infants and has a multifactorial aetiology. Among the risk factors, imbalance of gut microbiota and review of the current literature was performed. A single case study was conducted and review of the current literature was performed. Results The premature baby, born at 25 0/7 weeks of gestation with a birth weight of 750 g and a 324-g term placenta due to chorioamnionitis. Antibiotics were given for the first two days of life (DOL), blood cultures and septic workup were negative. Passage was established at the first DOL and enteral feedings with formula milk were increased daily up to DOL 8.

On the 12th DOL, the baby presented with progressing apnoeas and distended abdomen. Antibiotics were started and oral feeding was stopped. Abdomen X-rays (picture) showed advanced signs of NEC with portal gas and pneumoperitoneum. Within two hours, peritoneal drainage was inserted. However, this baby deteriorated to respiratory failure and heart failure two hours later, showed complete gangrenous necrosis of the small intestines as well as the major part of the colon, which were partly liquified. Resection of the whole intestinal tract was no longer an option so palliative care was instated after discussion with the parents. The baby died less than 24 hours after the first onset of symptoms. Cultures of peritoneal lavage grew for Clostridium perfringens whereas the blood culture remained negative.

2 cases of failed delivery room resuscitation -> unexpected and why?

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A preterm infant with clostridium perfringens intestinal gangrene

Conclusions

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In the first case we knew about some malformations seen in the fetal ultrasound (US) as club feet, retrognathia, possible malposition of the fingers. Additional polyhydramnion, and sparse fetal movements. A genetic workup showed a normal chromosome set and a normal micro array.

In the second case we didn’t have much information. The progress of the pregnancy seemed normal. The mother was transferred to our unit because of decreasing fetal movements confirmed in the US.

In both cases the main problem was the respiratory system. They both failed to start breathing. No chest excursions could be observed. In the first case we were unable to ventilate the lungs by bag-mask. Several attempts of oro-tracheal intubation also with smaller tubuses were unsuccessful. The newborn died 44 minutes after birth.

In the second case we also intubated because of lack of breathing. Ventilation with a bag-mask failed. The intubation was successful but we were not able to ventilate the lungs as well with a tubus regardless of which pressure we used. The right position of the tubus was controlled by inspection with the laryngoscope. This newborn also died 60 minutes after birth.

After both cases a lot of questions were remaining. To find answers is not only important for the parents but also for us clinicians. A diagnostic workup following an unexpected perinatal death including an autopsy is essential to find these answers. When parents don’t agree to an autopsy we have the possibility to conduct a postmortem computer tomography and a biopsy (stanzza) of the skin to cultivate a fibroblast culture for a genetic workup.

Fortunately both parental couples agreed to conduct an autopsy. In both cases a severe lung hypoplasia was responsible for the failed ventilation or/and oro-tracheal intubation. Additional malformations were also found in both patients.

The next question would be the underlying genetic problem.

In the first case we found 2 mutations in the NEB gene responsible for Nemalin-Myopathy. A severe form of this myopathy (10-20%) causes absent fetal movements and severe lung hypoplasia.

In the second case we found a variation of CHD7 Gene which hypothetically could be responsible for a neuromuscular impairment and resulting lung hypoplasia. The parents refused further investigations.

Material and Methods  In this prospective cohort study very preterm infants born before 32 weeks PMA were measured by an ultrasonic flowmeter and a mainstream CO2 sensor in spontaneous sleep at 36 weeks PMA and slopes of phase II (SII) and phase III (SIII) were calculated.

Results  Volumetric capnographies were calculated from 99 infants (16 infants with BPD36, 83 without BPD36) (mean gestational age 28.3 ± 2.4 weeks, mean birth weight 1040 ± 370 g). SII was less steep in infants with BPD36 (227 ± 203/L) compared to infants without BPD36 (420 ± 208/L; P = 0.006). SII was steeper in infants with BPD36 (173 ± 58/L) compared to infants without BPD36 (106 ± 56/L; P < 0.001). SII and SIII were significantly associated with the duration of supplemental oxygen requirement (coefficient $\beta$ = -0.003, P = 0.019 and coefficient $\beta$ = 0.008, P = 0.04 respectively).

Conclusions  Indices derived from volumetric capnography at 36 weeks PMA seem to be associated with sequelae of neonatal lung disease. Volumetric capnography appears to be a promising tool in the assessment of respiratory outcome after preterm birth.

Volumetric capnography is associated with duration of supplemental oxygen requirement in very preterm infants

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Aims and Objectives  Volumetric capnography may reflect sequelae of neonatal lung disease and might discriminate between infants with and without bronchopulmonary dysplasia (BPD). Our aim was to determine indices derived from volumetric capnography in spontaneously breathing preterm infants at 36 weeks post-menstrual age (PMA) and investigate its association with BPD defined as supplemental oxygen requirement at 36 weeks PMA (BPD36) and with the duration of oxygen supplementation.