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P001

The child with no chest: a case of spondylo-costal dysostosis (Jarcho-Levine syndrome)

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We report the case of a baby boy born from non inbred parents originating from Portugal. The mother was a healthy 35 year-old women, gravida 2 and nulliparous (1 previous spontaneous abortion in 2007). It was a spontaneous and harmonious pregnancy (negative serologic exams except for an old mumps infection, normal alpha fetoprotein level, normal amniocentesis with XY karyotype) until 27 weeks of gestation at which time the fetal ultrasound revealed thoracic spine deformation, confirmed by prenatal CT scan and MRI. The radiologic exams confirmed the deformation of the chest, anomalies of the vertebral spine at the level of the 10–12th thoracic vertebrae with narrowing of the vertebrae and intrauterine growth retardation compatible with the fetal diagnosis of spondylo-costal dysostosis. The baby was born at 39 1/7 gestational weeks by caesarean section for absent maternal contractions and maternal desire with harmonious intrauterine growth retardation [birth weight 2.620 kg (P <10), height 46.5 cm (P <10), head circumference 33 cm (P <10)]. Neonatal adaptation was remarkable for severe respiratory distress syndrome with the Apgar score at 2/7/8, motivating immediate neonatal resuscitation in the delivery room including cardiac compressions and 100% oxygen mask ventilation followed by rapid endotracheal intubation. Echocardiography just after birth revealed severe suprasystemic pulmonary hypertension with normal size branch pulmonary arteries, right to left shunting through the patent ductus arteriosus and bidirectional shunting through the patent foramen ovale, with no improvement after initiation of inhaled nitric oxide. In the setting of hypercapnic acidosis and respiratory distress syndrome, surfactant was administered and the baby was ventilated with high frequency oscillation. The postnatal CT scan showed no diaphragmatic abnormalities but lung hypoplasia with bilateral bronchiectasia and right pleural effusion. The osteo-articular status was remarkable for impressive thoracic spine deformation with the thoracic costal margins not joining the sternum and the aspect of a "floating" sternum. In the setting of no long-term curative therapeutic alternative, nursing was moved towards comfort care at ten days of life and the baby died soon after stopping the ventilation. A post-mortem lung biopsy revealed pulmonary capillary hemangiomatosis. Genetic analyses are currently underway.
Discussion: Spondylo-costal dysostosis refers to a heterogeneous group of diseases characterized by a defect of vertebral segmentation with costal anomalies related to abnormal formation of the somites. Three genetic mutations involving the "Notch" signaling pathway (SCDO = Delta-Like3 mutation (DLL3), SCDO2 = MESP2 mutation, SCDO3 = LFNG mutation) have been described in patients presenting osteo-articular involvement. However, an association with capillary hemangiomatosis responsible for pulmonary hypertension has never been previously described.

P002

When unbalanced sharing becomes insalubrious: A case of twin-to-twin transfusion syndrome

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Introduction: Unbalanced placental vascular anastomoses in monochorionic twins may lead to acute or chronic inter-twin transfusion resulting in a twin anemia-polycythemia sequence (TAPS), with severe anemia in the donor and polycythemia in the acceptor twin. This condition is characteristically associated with the twin oligo-polyhydramnios sequence (TOPS). Twin-to-twin transfusion syndrome (TTTS) often leads to dual fetal demise. Selective endoscopic laser ablation of connecting placental vessels has to be done before 26 weeks of gestation and is the only effective treatment modality to halt the syndrome and to improve perinatal and neonatal outcome.
Methods: Case report and review of literature.
Findings: We report a case of TTTS, which was diagnosed at 26 weeks of gestation. The donor presented with an anhydramnios, the acceptor with a polyhydramnios and a distended bladder. Given the advanced gestational age no laser ablatio could be accomplished but amnioreduction was done. At 27 1/7 weeks of gestation cesarean section was effected because of pathological Doppler sonography of the donor twin. At delivery, the acceptor twin was plethoric with a hematocrit of 0.58 and presented with a gangrene of his right leg. He developed bilateral grade 3 intracerebral hemorrhage, therefore palliative care was offered and the acceptor twin died on day5. The donor twin presented with severe anemia and hematocrit of 0.25. His birthweigth of 450g matched with severe intrauterine growth retardation. After repetitive red blood cell transfusion the donor twin developed well and showed only mild signs of bronchopulmonary dysplasia. The placenta showed neither macroscopic nor microscopic visible anastomoses.
Discussion: Almost all monochorionic twins share a single placenta with inter-twin anastomoses leading to TTTS. In up to 5% an isolated twin anemia-polycythemia sequence (TAPS) occurs, 15% of monochorionic twin pregnancies present a classical TTTS with TOPS. The postnatal management of both the donor and the acceptor twin is challenging. Morbidity in surviving twins after TTTS includes prematurity, neurological, cardiovascular and renal complications as well as hypoxic ischemic lesions in limbs, intestines and liver.
Conclusion: This case illustrates the physiopathology of TTTS in utero as well as postnatally: TOPS was very distinct, followed by severe anemia and growth retardation in the donor and polycythemia leading to in utero acquired limb ischemia in the acceptor.

P003

Keep cool: long term benefit from whole body hypothermia in neonatal asphyxia

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Aim: Previous studies have shown a significant benefit from hypothermia as a therapy option for infants suffering from perinatal asphyxia. Yet, data regarding the long term outcome of this therapy are scarce. We therefore investigated the long term neurodevelopmental outcome of asphyctic infants treated with or without whole body hypothermia (WBH) in a single center study.
Methods: In a retrospective chart review we evaluated all infants born in our perinatal center at Basel between January 2008 and February 2009 who met the criteria for asphyxia (cardiopulmonary resuscitation and/or 10' Apgar <6, and/or umbilical artery <7.10 and/or BE >14 mmol/l and/or severe peripartal event). Nine infants received WBH, and were included in the cooled group (CG) and nine infants did not meet the criteria for WBH for different reasons, and were included in the non-cooled group (NCG). Outcome measures at 6–8 months and 12 months were: 1. presence or absence of neurodevelopmental delay (Test: Griffiths' mental developmental scale), 2. disabling cerebral palsy (Test: gross motor function classification system), and 3. the presence of multiple disabilities in clinical assessment, including hearing loss, no vision, and seizures.
Results: Neonatal characteristics of both groups were comparable. Regarding neurodevelopmental outcome and degree of disability no differences could be found between the CG and the NCG: No persisting seizures, disabling hearing or visual problems were detected in either groups. The median Griffith score was 100 (76-101) with 2/7 infants below average in the CG vs 96 (56-122) with 1/7 infants below average in the NCG. Disabling CP was found in 1/7 infants in the CG vs none in the NCG.
Conclusion: Our results could not show an obvious difference in the outcome measures between the CG and NCG in this rather small study cohort. But it is not clear, how much worse the neurodevelopmental outcome would have been, if the CG had not been cooled. However, we observe far less severe asphyxial encephalopathy (proved by clinical symptoms and neuroimaging) since WBH is performed in our center as a regular therapy option. Thus more standardized data (European Hypothermia Network) are required to asses the benefit and to define the best clinical implementation of therapeutical hypothermia in asphyctic neonates.

P004

Hairy polyp – a rare differential diagnosis for acute respiratory distress in neonates

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Introduction: Hairy polyp (HP), a rare congenital malformation (incidence 1 in 40000 live births) typically is localised in the nasopharynx (60%) where they may cause nasal obstruction, vomiting and even life-threatening acute respiratory distress. HP consists of a conglomerate of disorganized proliferating ecto- and mesodermal pluripotential cells. An association with others malformations is possible (such as ancyloglossia, cleft palate).
Case: A baby-girl born after an uneventful pregnancy at term (APGAR: 9/10/10, umbilical artery pH 7.22) presented shortly after birth with recurrent vomiting, repeated oxygen desaturations and obstructed nasal breathing. To rule out a choanal atresia, a naso-gastric tube was inserted into both nostrils. After a scarcely audible "clack" sound, the infant was free of dyspnoea whilst an inhomogeneous mass (4 x 3 cm) could be recovered from the nasopharynx. Henceforward infant clinically had no more dyspnea. Inspection of the oral cavity revealed

no other abnormalities and laryngoscopy simply showed mild laryngomalacia. Chest X-ray was normal and cerebral MRI excluded further tumour masses in the nasopharyngeal space. Histopathological examination of the regurgitated mass confirmed the supposed diagnosis of a hairy polyp: a polypoid mass, possibly from the lateral wall of the nasopharynx or even the superior aspect of the soft palate, essentially consisting of lipid components with a fibrous stalk. Due to non-specific feeding difficulties the infant was kept in hospital until the 15th day of life but then could be discharged home without any respiratory distress.
Conclusion: Hairy polyps are infrequent benign tumours of the nasopharynx that need to be considered as one possible differential diagnosis of acute upper airway obstruction in new-borns. However histology and even further imaging should be performed in order to determine the nature and the true extent of the tumour.

P005

Acute neonatal cardiomyopathy after maternal local anaesthesia by mepivacaine

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Background: Local anaesthetics (LA) are widely used in obstetrics in order to relieve pain during delivery. However it is crucial to know pharmacokinetics of these drugs to prevent potential side-effects for mother and child.
Case: We report a case of severe acute neonatal cardiomyopathy induced by mepivacaine perineal infiltration anaesthesia administered to a parturient presenting for vaginal delivery in presence of female genital mutilation (FGM). A newborn presented as "floppy infant" and at first successfully was treated by naloxone to relieve a query hang-over of maternal opioids. Since marked cyanosis persisted a congenital heart condition or a query intoxication respectively was suspected. The infant was started on prostaglandin E1 and blood samples were collected. Thus echocardiography showed normal anatomy but markedly limited cardiac function (SF <10%). We therefore initiated dobutamine and milrinone. Only on day three mepivacaine turned out to be present in toxic levels in the probes we had collected as a precaution. Heart function completely recovered and the infant could be discharged healthy home after 12 days.
Conclusion: Local anaesthetic toxicity resulting in a such life-threatening cardiomyopathy has not been reported as yet. We wish to alert clinicians that injudicious use of LA's for de-fibulation may jeopardise neonatal outcome.

P006

Severe postnatal dehydration based on a Netherthon Syndrom

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History: We report a male, preterm (36 1/7 wkg) with a severe dehydration, hypernatremia of 186 mmol/l and generalized scaly eryhtroderma. After correction of the hypernatremia, the stabilization of the hydration was only possible with a high humidity (60–80%) in the incubator. At the age of 9 days he developed sepsis/meningitis with enterobacter aerogenes and staphylokokkus aureus. At the age of 4 weeks alopecia and ichthyosis, persist. In addition he showed severe failure to thrive. After exclusion of a severe combined inmmunodeficiency (SCID) type omen syndrome we made the diagnosis of the Netherton Syndrom by biopsy (Deficiency of LEKTI epidermal by immunohistochemistry) and the clinical manifestation.
Introduction: Netherthon Syndrom is a rare autosomal recessive genodermatosis characterised by ichthyosis, hair abnormality (trichorrhexis invaginata) and atopic manifestations. The ichthyiosis is mostly present at birthcombined with severe hypernatremia and dehydration. Because of the limited skin barrier there is a higher incidence of severe bacterial infections in the first year of life. Some of the children are affected with immunodeficiency.
Conclusion: Keep the Netherthon Syndrom in mind whenever a severe dehydration, hypernatremia is accompanyied by congenital ichthyosiform erythroderma.

P007

Newborn girl with neonatal seizures and vesicular rash: Incontinentia pigmenti

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Introduction: Incontinentia pigmenti, or Bloch-Sulzberger syndrome, is a rare X-linked dominant genodermatosis which affects mostly females. This neurocutaneous disorder may present as an acute neonatal encephalopathy suggesting an infectious or thromboembolic etiology. A characteristic vesicular rash may be the clue to early diagnosis.
Case report: We describe a girl born vacuum-assisted at term. Family history was unremarkable. Maternal serology was negative for HBV, HIV and protective for rubella. The mother had a known genital herpes which had not been active for several weeks before birth or at birth. GBS screening was negative. On day 3 the girl developed focal myoclonic neonatal seizures, irritability and muscular hypertonia prompting transfer to the neonatology intensive care unit. The girl was in a reduced general state of health, general physical examination was normal except for the encephalopathy and a polymorphous, partly vesicular, partly maculopapulous rash on arms and legs, which initially was interpreted as toxic exanthema of the newborn. Anticonvulsant therapy with phenobarbitone and empirical antimicrobial treatment with ampicillin, gentamycin and acyclovir was started and stopped after blood + CSF-cultures/PCR-testing remained negative. Myoclonic as well as subtle seizure activity detected on EEG-monitoring stopped with high phenobarbitone serum levels. A cranial ultrasound showed multiple echogenic lesions in the right frontal white matter. Cranial MRI detected right hemispheric multifocal gray and white matter lesion as well as cerebellar lesions resembling ischemic injuries. Haematological and coagulation work-up were as well as echocardiography normal. Control electroencephalograms after 4 days and 2 weeks showed persisting multifocal spiking but improved background activity. The polymorphic rush changed and waned during hospitalisation but never completely disappeared, leading us to a dermatological consultation which established the diagnosis of incontinentia pigmenti stage I. Diagnosis was confirmed with a skin biopsy which showed an eosinophilic spongiosis with intraepidermal vesicle filled with eosinophils as well as multiple apoptotic ceratinocytes. Opthtalmological control at the age of 3 weeks was normal.
Conclusion: Incontintentia pigmenti is a rare neurocutaneous disorder which should be included in the differential diagnosis in newborns presenting with neonatal seizures, encephalopathy and vesicular rash.

P008

Short inspiratory times in newborn ventilation: recent ventilators can do it, now it's up to you

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Background: Spontaneously breathing preterm infants have short physiologic inspiratory times (IT). This population is particularly vulnerable to lung injury caused by volu- and/or barotrauma. Ventilating with short IT could reduce both the risk of volutrauma and the risk of air trapping, allowing the lung to empty between cycles and eventually enabling increased respiratory rates.
Objective: Bench test to assess performances of specific neonatal and polyvalent ICU ventilators to ventilate newborns with short IT.
Design/Methods: Four polyvalent ICU ventilators (GE Engstrm Carestation, Draeger Evita XL, Maquet Servo-I and Hamilton G5) and two neonatal ventilators (Draeger Babylog 8000 and BOMImed Leoni Plus, both capable of high frequency ventilation) were connected to a test lung (5601i-Adult/Infant PNEUVIEW Michigan Instruments Inc) simulating the breathing of a newborn lung (compliance 1 ml/cmH_20, airway resistance 5 cmH_2O/ml/s and respiratory rate 50 x bpm). With both an IT of 0.25s and 0.35s, accuracy of delivering the prescribed Positive Inspiratory Pressure (PIP) from 10 to 30 cmH_2O, Positive End Expiratory Pressure PEEP) from 5 to 8 cm H_2O and Volume (V) from 5 to 10 ml in Pressure-Controlled (PC) and Volume-controlled (VC) mode were measured and compared.
Results: In VC-mode and with prescribed volumes of 5 and 10 ml and with a PEEP of 5 and of 8 cmH2O, G5 and Leoni delivered only 84–86% of the desired volumes. In both PC and VC-modes, there wasn't any significant difference between the performances of the six ventilators with an IT of 0.25s and 0.35s. However, Babylog was only able to deliver 90% of the 30 cmH_2O PIP with an IT of 0.25s.
Conclusions: Recent ventilators are able to deliver desired volumes and pressures with short IT of 0.25s. However, clinicians need to be careful about specific neonatal respirators, as they tend to overcompensate leakage around ET tube. Are we neonatologists ready to apply short IT to our patients?

P009

Polyvalent ventilators for newborns: Bench-testing of the performances of the High Frequency Ventilation mode

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Background: Few ventilators are specifically designed for newborns and small children and are able to offer both conventional ventilation (CV) and high frequency ventilation (HFV).
Objective: To assess the performances of the HFV of neonatal polyvalent ventilators, performing both CV and HFV, compared to the gold standard in HFV.
Design/methods: Two neonatal-pediatric ventilators able to perform CV and HFV (Draeger Babylog 8000 and BOMImed Leoni Plus) and a Viasys SensorMedics 3100A were connected to a test lung (5601i-Adult/Infant PNEUVIEW Michigan Instruments Inc) simulating the features of ill newborn lungs (compliance of 1 ml/cmH_2O). Performances were measured with a Fluke Biomedical VT PLUS HF gas-flow analyzer.
Results: SensorMedics showed the highest increase in tidal volumes with increasing amplitudes at a constant oscillation frequency of 12 Hz. The least decrease in tidal volume was also demonstrated by Sensormedics at 3 different oscillation frequencies (5, 10 and 15 Hz) with maximal amplitude. In both tests, Leoni performed about 50% of the Sensormedics capabilities, while Babylog reached only 10 to 15%. Babylog and Leoni were both able to keep a constant mean airway pressure of 15 cmH_2O with increasing amplitudes (at constant respiratory rate of 12 Hz). SensorMedics showed a decrease of 20% of the mean airway pressure with high amplitudes (>80% of the ventilator capability). With an increase of the mean airway pressure from 5 to 25 cmH_2O, both Leonie and SensorMedics were able to keep, given an unchanged amplitude, a constant tidal volume of 2 ml.
Conclusions: In HFV, Leoni Plus performance is about 50% of Sensormedics, while Babylog doesn't seem powerful enough with increasing settings. Being aware of such limitations, Leoni Plus seems well adapted for VHF use in neonatology. The option to rapidly switch from conventional to HFV offers great practical and economic advantages, in particular for smaller neonatal intensive care units.

P010

100% versus 40% oxygen for resuscitation in the delivery room: outcome at 2 years of preterm infants born 25 0/7 – 31 6/7 weeks gestational age

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Background: Animal and human studies have shown that 100% oxygen concentration for resuscitation is harmful in term infants immediately after birth. There is a lack of data for preterm infants regarding lower oxygen concentrations on short- and long-term outcome.
Objective: The aim of this study was to compare the short- and long-term outcome of preterm infants after resuscitation in the delivery room with either 100% or 40% oxygen.
Methods: Retrospective study on preterm born children with a gestational age (GA) between 25 0/7 and 32 0/7 weeks. Only children with a neurodevelopmental examination at the age of two years were included (n = 104). One group consisted of preterms born between 1992 and 1994 and exposed to 100% oxygen during the resuscitation in the delivery room (100%-group, n = 55), the other group were preterms born between 2000 and 2002 and exposed to 40% oxygen (40%-group, n = 49). Due to a change from Bayley I to Bayley II between the two study periods, a correction had to be introduced to allow for comparison for both oxygen-groups.
Results: Both groups were comparable with respect to GA, birth weight, umbilical artery pH, preeclampsia, chorioamnionitis, lung maturation, birth mode, and regarding major neonatal complications (retinopathy, bronchopulmonary dysplasia, intraventricular bleeding (IVH) grade III & IV, pneumothorax, sepsis, and periventricular leucomalacia. With regard to the immediate postnatal adaptation, the 1 minute ($p = 0.048$), the 5 minute ($p = 0.034$), and the 10 minute Apgar ($p = 0.032$) scores were significantly better in the 40%-group. The 100%-group had a higher rate of IVH grade II ($p = 0.001$). After correction for the Bayley scores I there was no difference in cognitive ($p = 0.355$), but for the motor outcome in favour of the 100%-group ($p = 0.001$).
Conclusions: This study showed that reducing the initial FiO_2 to 40% for delivery room resuscitation in preterm infants led to better immediate neonatal adaptation. Importantly, there was no change in cognitive outcome at two years. The improved motor outcome in favour of the 100%-group can possibly be explained by the retrospective design with differences in follow-up rate and possibly by test differences, even after introducing a correction factor.

P011

Fetal echogenic bowel: clinically relevant?

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Case 1: An 8-month old infant hospitalized for vomiting and abdominal distension. Abdominal ultrasound showed ascites, intestinal distension and absence of calcification. Radiological enema excluded volvulus and abdominal tomography showed thickened intestinal walls. Exploratory laparotomy showed meconium peritonitis with small bowel stenosis, imposing a bowel resection and a termino-terminal anastomosis. An echogenic bowel was present in prenatal ultrasounds, but abdominal X-ray and ultrasound at birth were normal and genetic work-up for cystic fibrosis was negative. Interim medical history was unremarkable and weight gain was normal.
Case 2: A newborn with a prenatal ultrasound at third trimester showing oligamnios and echogenic bowel. The baby was born at 41 weeks of gestation by cesarean section, with patent esophagus at nasogastric suction. Meconium stool was emitted in the first 24 hours. Abdominal X-ray and ultrasound were unremarkable and stool elastase was also normal. Genetic work-up for cystic fibrosis was negative. Fetal echogenic bowel is by definition discovered by second trimester's prenatal ultrasounds. Hyperchogenicity can be diffuse or focal. Bowel echogenicity is usually compared to this of the adjacent bone. At the most severe forms, bowel and bone present the same echogenicity. Meconium peritonitis is a chemical aseptic inflammatory peritonitis, secondary to the presence of meconium in the peritoneal cavity due to in utero intestinal microperforation. This condition can lead to cloisonned ascites, abdominal cyst, adhesions, calcifications and meconium ileus. An association between meconium ileus and cystic fibrosis is found in 8–40% of cases. The prevalence of fetal echogenic bowel at second trimester is estimated between 0.5 and 1% and it usually disappears spontaneously within a few weeks.
A french cohort based in 682 cases of fetal echogenic bowel showed: normal newborns (66%), multiple malformations (7%), prematurity (6%), major chromosomal abnormalities (4%), intra-uterine growth retard (4%), cystic fibrosis (3%), cytomegalovirus or parvovirus infection (3%), intra-amniotic bleeding (3%), undefined in utero death (2%) and preeclampsia (1%).
Conclusion: Fetal echogenic bowel is often found in normal foetuses, but occasionally can be associated to pathologic conditions, which should be ruled-out by obstetricians and neonatologists.

P012

Automated infant auditory screening using the ALGO® 3i

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Introduction: Universal neonatal hearing screening started in 2000 in Switzerland with Transient Evoqued Acoustic Oto Emissions (TEAOE). AABR (Automated auditory brainstem responses) is newly used in neonatal period for screening. The TEOAE test is rapid, simple, cheap and does not require electrode attachment but has a high false positive rate (0.7–8.8%). The AABR test is also a reliable hearing screening method, quick, easy to administer, but more expensive and time consuming.
Objective: An ALGO® 3i screener was used to evaluate AABR in neonates hospitalized in our intensive unit. The goal of this study is to compare two different hearing screening methods in newborns from a practical point of view and to try to reduce false positive rates.
Methodology: The ALGO® 3i Newborn Hearing Screener is a portable, non-invasive device for screening infants between 34 weeks of corrected gestational age and six months, using Automated Auditory Brainstem Responses. It delivers faint click sounds at 35 or 40 dBnHL ("normal hearing level" scale) to the baby's ears through disposable earphones. An abnormal result means that the test failed in both ears. If the result is abnormal, the exam was repeated and if it is still abnormal, the child was referred to an ENT for audiologic assessment.
Results: During 6 months (08.2009–02.2010), 48 newborns at risk were tested for AABR. 62 tests were realised. 11 were abnormal (2) or failed (9) at the first test (23%). At the second test only 2 of 10 failed (4%). 1 of the 11 didn't have a second test but had normal TEOEA. 1 of the 2 had a third test normal. 17 newborns (35.4%) underwent both AABR and TEOAE tests. In our small number of tested newborns AABR allowed to diagnose normal hearing in four newborns with abnormal TEOEA (false positive). The mean time of AABR screening is about 17 minutes per test, which is considerably longer than the mean time of TEOAE (about 5 minutes).
Conclusions: The screening of premature babies and neurologically affected newborns with the ALGO® 3i screener was easy to perform and did not require time-consuming teaching of the doctors or nurses

and did not cause disturbances to the neonates. The final AABR pass rate is 96%. False positive rate (4%) is lower than with TEOAE. TEOAE remain a useful test for a rapid systematic screening of all normal newborns, but the AABR should be performed in all high risk newborns in addition to TEOAE to provide a better screening and to exclude a retrocochlear pathology.

P013

Arterial hypertension as a consequence of neonatal hypercalcemia caused by subcutaneous fat necrosis

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Introduction: Subcutaneous fat necrosis is a classic, albeit uncommon, cause of neonatal hypercalcemia. It occurs in newborn infants within the first month of life following a complicated delivery. The diagnosis is usually easy because of the presence of red-purple plaques in fatty areas along with firm subcutaneous nodules. Hypercalcemia may cause arterial hypertension in infants or children.
Case report: A 3-week-old neonate, born macrosomic (diabetic fetopathy) and with a perinatal asphyxia (Apgar 0/2/3), presented with small firm subcutaneous nodules on the cheeks and back. Ultrasound of these lesions showed alteration of the subcutaneous fat without calcification. The association of perinatal stress with subcutaneous nodules led to the diagnosis of subcutaneous fat necrosis. Two days later, hypercalcemia (3.17 mmol/l) together with arterial hypertension (mean arterial pressure 84 mm Hg, 95th centile 80 mm Hg) was observed. Kidney ultrasound with Doppler of the renal arteries showed enlarged kidneys without nephrocalcinosis and normal blood flow. Plasma levels of phosphorus was 1.97 mmol/l (1.56–3.08), PTH <3 pg/ml (10–73), 25-OH vitamin D 50 nmol/l (23–113) and (1,25)-OH2 vitamin D 120 pmol/l (48–160). Calcium excretion in urine was increased. ECG was normal. Prophylactic vitamin D substitution was immediately stopped and low-calcium formula was started. Serum calcium levels remained elevated for weeks, however, as the patient was not symptomatic no treatment was established.
Conclusion: Subcutaneous fat necrosis may induce severe hypercalcemia which can lead to arterial hypertension. Therefore we recommend carefully monitor of calcium levels and blood pressure values in neonates with subcutaneous fat necrosis.

P014

Air within the spinal canal in spontaneous pneumomediastinum: case report and extensive review of the literature

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Background: Spontaneous pneumomediastinum is an uncommon benign condition that is occasionally associated with air within the spinal canal.
Methods: We describe a further case in a 14-year-old girl and suggest a classification system based upon a detailed review of the previous literature.
Results: 48 patients with spontaneous pneumomediastinum and intraspinal air accumulation (36 male and 12 females, age range 4–72, median age 18) were grouped into those with underlying lung disease (n = 13), those with other underlying etiological factors (n = 22), and those arising spontaneously (n = 13). Neurological symptoms or signs were noted in one case. The remaining cases were successfully managed conservatively.
Conclusions: In spontaneous pneumomediastinum accumulation of air within the spinal canal is self-limiting and benign. The same management is advised in spontaneous pneumomediastinum with and without intraspinal air accumulation.

P015

Nervous system dysfunction in Schönlein-Henoch syndrome: systematic review of the literature

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Objective: Central or peripheral nervous system dysfunction sometimes occurs in Schönlein-Henoch patients.
Methods: We reviewed all Schönlein-Henoch cases published after 1969 with cerebral dysfunction without severe hypertension and neuroimaging studies (n = 35), cranial or peripheral neuropathy (n = 15), both cerebral and peripheral nervous system dysfunction without severe hypertension (n = 2) or nervous system dysfunction with severe hypertension (n = 2). Forty-four of the 54 patients were <20 years of age.
Results: In patients with cerebral dysfunction without or with severe hypertension the following presentations were observed in decreasing order of frequency: altered level of consciousness, convulsions, focal neurological deficits, visual abnormalities and verbal disability. Imaging studies disclosed the following lesions: vascular lesions almost always involving two or more vessels, intracerebral hemorrhage, posterior subcortical edema, diffuse brain edema and thrombosis of the superior sagittal sinus. Following lesions were noted in the subjects with cranial or peripheral neuropathy without severe hypertension: peroneal neuropathy, peripheral facial palsy, Guillain-Barre' syndrome, brachial plexopathy, posterior tibial nerve neuropathy, femoral neuropathy, ulnar neuropathy and mononeuritis multiplex. Persisting signs of either cerebral (n = 9) or peripheral (n = 1) nervous system dysfunction were sometimes reported.
Conclusions: In Schönlein-Henoch syndrome, signs of nervous system dysfunction are uncommon but clinically relevant. This review helps clinicians managing Schönlein-Henoch syndrome with nervous system dysfunction.
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P016

PEHO syndrome or variant?

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PEHO (Progressive Encephalopathy-Edema-Hypsarrhythmia-Optic atrophy) syndrome is a rare disorder, first described in the Finnish population, although few cases have now been reported in other countries. Besides supportive criteria such as edema of the face and extremities with tapering fingers, necessary ones as defined by Somer[1] include infantile (often neonatal) hypotonia, seizures (myoclonic jerking and infantile spasms), severe psychomotor retardation, visual impairment with optic atrophy, and progressive brain atrophy (cerebellum and brainstem in particular). However, some patients show neither optic atrophy nor typical neuroimaging findings, and this variant has been called PEHO-like syndrome. Inheritance is considered to be autosomal recessive, but the causative gene is as yet unknown. We describe a 19-month-old girl suspected of having this syndrome or its variant. She was born at term of Swiss non-consanguineous parents. Head circumference at birth was 31 cm. Puffy hands and feet, as well as hypotonia and poor visual fixation were noted in the neonatal period. Eye fundus examination showed bilateral optic atrophy. Brain MRI revealed supratentorial, pancerebellar and brainstem atrophy. Seizures started at 6 month of age in the form of severe focal seizures. This patient fulfills most criteria for PEHO syndrome, but some features, such as multifocal epilepsy without infantile spasms/hypsarrythmia and the prenatal-onset microcephaly, are atypical. As long as the genetic etiology remains elusive, it will remain difficult to know on clinical grounds alone if PEHO syndrome and its variant form constitute a single disorder or not.

[1] Somer M. 1993. Diagnostic criteria and genetics of the PEHO syndrome.

P017

Severe Narcolepsy/Cataplexy in a 9 year old girl: a case report

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Introduction: Narcolepsy with cataplexy (NC) is a rare neurological disorder characterized by excessive daytime sleepiness (EDS), cataplexy (episodes of muscle weakness, sometimes triggered by emotions) and striking transitions from wakefulness into rapid eye movement (REM) sleep. On the basis of possible autoimmune mechanisms, several case studies reported about positive effects of treatment with intravenous immunoglobulin (IVIg) in NC. We report on a girl diagnosed with NC and treated with IVIg therapy.
Case report: An 9 year old girl with unremarkable personal history and previous normal sleep behavior presented in January 2010 with severe daytime sleepiness of sudden onset. Cataplexy was also present as spontaneous, rarely emotional triggered episodes of muscle weakness (up to 100 episodes per day). She also showed visual hallucinations and nightmares. Brain magnetic resonance imaging (MRI) and search for oligoclonal bands in CSF and blood were negative. A multiple sleep latency test (MSLT) indicated a mean sleep latency of 3 minutes and 3 sleep-onset REM periods. She was

positive for HLA DRB1*1501 and DQB1*0602. CSF hypocretin-1 level was 129 g/ml. IVIg treatment showed some subjective and objective improvement of both EDS and cataplexy.
Conclusion: NC is a rare disorder in children. The diagnosis is confirmed by MSLT, HLA Typing and hypocretin-1 levels. IVIg therapy for NC may be effective.

P018

Infant poisoning, when should we think about it? A case report and discussion of its clinical lessons

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An eleven month old girl was brought to the emergency department for rapidly evolving neurological symptoms. She first had difficulty staying on her legs and sitting, and dysmetria when reaching for her bottle. Then she felt sleepy, seeming to gaze in space. She didn't have any systemic symptom and there was no history of tonicoclonical movements. After excluding meningoencephalitis, atypical seizure, cerebral vascular disease and metabolic disease the final diagnosis was cannabis intoxication. This unusual case points out that we should always keep in mind the possibility of an intoxication, whenever the story and the clinical findings are not clear, especially in a toddler. What are the red flags?

P019

Congenital myasthenia: a case report

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Introduction: Congenital myasthenic syndromes (CMS) are rare genetic disorders of the neuromuscular junction. They are traditionally classified by the site of neuromuscular transmission defect (presynaptic, synaptic and postsynaptic). Generic diagnosis of a CMS is often possible on the basis of myasthenic symptoms and findings on electrodiagnostic evaluation. In suspected cases molecular genetic testing can often confirm the diagnosis.
Case report: We report on a CMS patient with a post-synaptic syndrome due to an underlying rapsyn mutation. The boy presented at birth with severe muscular hypotonia and weakness, apneas, absent sucking, macrocephaly and mild dysmorphic features. Because of respiratory insufficiency he required ventilation for 8 days. Initial investigations including cranial magnetic resonance imaging, electroencephalography, creatinkinase and metabolic screening were normal. There were no signs for myotonic dystrophy or myasthenia in the mother. The clinical condition improved spontaneously, but general muscle weakness and feeding problems persisted. At 5 months of age, a viral infection led to transient respiratory insufficiency. A neuromuscular transmission defect was diagnosed on the basis of a positive intravenous edrophonium (Tensilon®) test and a decremental response to 3 Hz repetitive stimulation. A therapy with pyridostigmine bromide (Mestinon®) was started and resulted in significant clinical improvement. A current neurological examination at the age of 2 years revealed age-appropriate motor and mental development and a mild generalized weakness predominantly involving the facial and bulbar muscles. Further respiratory crises following infections were managed with intermittent increase of the pyridostigmine dosage. A molecular testing showed the most common recessive N88K mutation in the RAPSN gene. Rapsyn is a acetylcholine receptor (AChR)-associated protein at the synapse, which is responsible for the clustering of AChR in the post-synaptic membrane.
Conclusion: CMS are to be considered in the differential diagnosis of a hypotonic neonate. A precise diagnosis including genetic testing is highly recommended for rational therapy, prognostic information and genetic counseling of the patient and the family. Some children, e.g. those with rapsyn mutation, become progressively less weak with age.

P020

Neurological Presentation of two children with ADEM

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Introduction: Acute Disseminated encephalomyelitis (ADEM) or post infectious encephalomyelitis is a rare immune-related multifocal inflammatory disease (incidence between 0.4 to 0.07/100'000) of the central nervous system (CNS) seen most often in young children. It is usually monophasic but can occasionally be multiphasic. Although the aetiology is currently unknown, the majority of patients have signs of a recent infection or immunisation, supporting a CNS-autoimmune response to triggering pathogens. The clinical presentation is variable and non-specific and not always suspected by the general paediatrician.
Case report: We report 2 cases, admitted to the emergency department of our hospital, with diverse neurological symptoms and history of previous viral infection. The first child of 20 months of age was admitted with signs of poor equilibrium, associated with unusual quietness. Her neurological status revealed walking instability, lower limb hyper-reflexia and general hypotonia. The second child of 6 years of age was admitted for incapacity to remain standing, fatigue and poor speech. Her neurological status revealed horizontal and vertical bilateral nystagmus, oculo-motor skew deviation, dysarthria, general hypotonia, and cerebella ataxia. Complete workup was conducted in both children including lumbar puncture which was non-conclusive. The diagnosis of ADEM was confirmed on MRI examination. Both children were treated initially with intravenous corticosteroids followed by oral treatment over 4 weeks. At 4 months follow up, both children showed complete recovery. MRI examination is planned at 6 months to confirm regression of initial radiological signs.
Conclusion: These reported cases illustrate the importance of considering the diagnosis of ADEM in children with non-specific and often multi-focal CNS symptoms. The diagnosis is made presumptively after exclusion of other diagnoses and confirmed by brain MRI, as seen by widespread patchy lesions involving predominantly the subcortical white matter. MRI diagnostic criteria can help differentiate ADEM from patients with an initial attack of Multiple Sclerosis.

P021

Meningeal melanocytosis, an ectodermal migration?

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We present the case of a 10½ year old female with no significant past medical history who was diagnosed at our institution with meningeal melanocytosis. Our patient was first admitted to the emergency room for an acute partial seizure with headheache. On the clinical exam residual left hemiplegia and a cutaneous depigmented lesion present from birth was noted on the left trunk. MRI showed aspecific lesions in the cortical-subcortical left gray mater and moderate hydrocephalus. Blood tests excluded an infectious, inflammatory, thrombophilic or metabolic event. 8 days later, our patient clinically recovered and a follow-up MRI demonstrated a regression of the lesions. 4 weeks later, a new clinical episode appeared with headaches and subjective non-specific acute visual impairment. During the out-patient follow-up visit, our patient was confused, displayed signs of aphasia and had a fluctuation state of consciousness (9/15 on the glasgow coma scale). Signs of cranial hyperTA? She was transfered to the intensive care unit for observation and a new MRI was performed. At this time, an important hydrocephalus was present with signs of meningeal hypertrophy and hypersignalisation with Gadolinium contrast. Spinal fluid analysis showed mildly elevated protein with oligoclonal bands. Due to the important hydrocephalus, an external drainage was performed. During the procedure, a meningeal biopsie was performed. The histology revealed an organized cellular invasion with very mild inflammation and without signs of malignancy. The immuno-histochemistry revealed positive markers of the cells for HMB45 et Myelan A. These resluts demonstrated the presence of melanin pigment and confirmed the diagnosis of a meningeal melanocytosis localized to the brain. Interestingly, there were no singificant cutaneous naevi found, and the ophthalmologic exam did not reveal an Ota naevus. For theses reasons, the patient did not fulfill criteria for a neuro-cutaneous syndrome. The patient was discharged from the hospital with a permanent ventriculo-peritoneal derivation with mild headache only. A great question that we could not answer for the moment: Is there a relationship between the cutaneous depigmented lesion and the melanocytes in the brain?

P022

Menkes disease: a rare but important diagnosis

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Introduction: Menkes disease or kinky hair disease is a rare X-linked neurodegenerative disorder caused by a mutation of a copper-transporting ATPase resulting in low copper levels and thus deficient function of various enzymes. This results in progressive hypotonia, seizures, irritability, developmental arrest and death in early childhood. Other typical features of disease are hyperelastic skin, coarse, brittle and fair hair (pili torti) and vasculopathy with tortuosity and fragility of vessels leading to thromboembolic disease and hemorrhage.
Case report: A 5-month old boy presented to our emergency department with new onset seizures. There was an uneventful birth after a normal pregnancy, birthweight of 2810 g. Already during the first months he was realised to be irritable and to have insufficient head control. At three months of age failure to thrive became evident. Four days prior to admission multifocal seizures appeared. On admission he

was a 5-month-old boy with muscular hypotonia, missing head control, fair skin and sparse, fair hair and eyebrows. Electroencephalogram revealed atypical hypsarrhythmia. Cerebral ultrasound was normal, but magnetic resonance imaging showed marked white matter abnormalites, temporally predominant (leucodystrophy) and typical vessel tortuosity. Spectroscopy showed a peak at 0.9 ppm representing the methyl group of the branched chain aminoacids, but screening for urea cycle disorders was negative. The striking neuroimaging pattern led to suspicion of Menkes disease which was confirmed by low levels of copper and coeruloplasmin in serum and by genetic testing showing a frameshift mutation at Xq13.3 in ATP7A-gene. By treatment with Vigabatrin not only seizure freedom but also decrease of irritability could be achieved. Because of limited clincial efficacy (effect only on seizures and irritability) and significant side effects, subcutaneous copper replacement was not considered to be of benefit at the time being.
Conclusion: This case report illustrates a typical presentation of classical Menkes disease. Diagnosis of this severe x-linked neurodegenerative disorder is important to provide adequate supportive treatment and counceling of the family. The possibility of copper histidine treatment has to be considered and discussed with parents, but there should be an individual decision.

P023

Two sisters with non-syndromal congenital hydrocephalus: A case report suggesting the presence of autosomal recessive congenital hydrocephalus in men

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Various hydrocephalus genes have been described in animal studies. The most common mode of inheritance of congenital hydrocephalus (CH) in humans is X-linked. Congenital hydrocephalus due to stenosis of the aqueduct of Sylvius is the only hydrocephalus gene that has been identified in humans. Kindreds indicating an autosomal recessive form of congenital hydrocephalus have been described, but to date the loci and genes are not known. We describe two sisters with congenital hydrocephalus due to stenosis of the aqueduct of Sylvius. Both had prenatal diagnosis of hydrocephalus, presented with important macrocephaly at birth (42 and 41.4 cm) and had a ventriculoperitoneal shunt placed in the neonatal period. Both sisters developed epilepsy and developmental delay later-on (EQ 67 and 76). The family history is unremarkable. There is no known consanguinity although the parents originate from the same region which makes distant consanguinity possible. There was a normal female karyotype in both cases, and array comparative genomic hybridization (CGH) revealed no causative abnormalities. This case report gives further evidence for the presence of autosomal recessive congenital hydrocephalus in men. To detect causative mutations further studies including larger cohorts are needed.

P024

Brown-Séquard-Syndrome after scoliosis surgery-provoking risk factors as homocygous MTHFR mutation and hperlipoproteinemia

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Background: Spinal dysfunction in children as a possible complication after surgical correction of scoliosis are well known, but fortunately infrequent. Aetiologically ischaemic lesions and intraoperative distention are discussed. In the presence of other risk factors for thrombo-embolic events (such as pathological coagulopathies) an ischaemic event after surgery is more likely. An homozygous mutation in the C677T-Variant of the Methylene-Tetrahydrofolate-Reductase (MTHFR) gene as well as elevated lipoprotein A are known to interfere with coagulation and to present risk factors for verebrovascular ischaemic events in children.
Case report: We report on a 15 year old girl suffering from severe idiopathic scoliosis (Cobb angle of >80°), who underwent surgical correction. After the first step of the operation without any correction, only ventral disketomy, the postoperative course was complicated by an incomplete Brown-Séquard Syndrome (acute flaccid monoparesis associated with absent tendon reflexes, decreased tactile sensibility of the ipislateral side and decreased sensibility for pain and temperature on the contralateral side). Although repeated MRI did not reveal any abnormalities in the spinal cord, the clinical picture was very suggestive for an unilateral acute ischemic event in the anterior spinal cord in a branch of the anterior spinal artery. Laboratory screening for the risk factors of thrombo-embolic events showed a homozygous mutation of the C677T-Variant of the MTHFR-Gen and an elevated homocystein in the serum as well as an elevated value of Lp(a). After 6 weeks of intensive inpatient rehabilitation, including daily physical therapy, her motor functions had improved and she could be discharged being able to walk on crutches.
Conclusion: Although rare in the pediatric population – spinal stroke may be a complication of spinal surgery independent of the correction. Neuroimaging in spinal ischaemia is known to be not significant in many cases. The association of spinal surgery, risk factors as homozygous C677T-Variant of the MTHFR-Gen and elevated Lp(a) support the idea of thromboembolic respectively ischaemic event. The laboratory screening for risk factors in patients suffering from spinal strokes are mandatory – as treatment and/o

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P025

Acute otitis media related ataxia

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Background: Acute otitis media (AOM) is a common infection in children. Although AOM occurs in all ages, the disease, defined by the presence of fluid in the middle ear with acute symptoms of middle ear inflammation is most prevalent in infancy. Complications of AOM include conductive hearing loss, mastoiditis, cerebral sinus venous thrombosis or labyrinthitis. The latter may present with ataxia.
Case reports: We report two cases, a two and a four year old boy, with AOM related acute ataxia. In both cases, the CT scan showed signs of inflammation and fluid accumulation in the middle ear. However, there were no signs of mastoiditis, labyrinthitis or sinus venous thrombosis. In both patients ventilation tubes were inserted and treated with intravenous antibiotics. No microorganism was found in one patient and Streptococcus pneumoniae in the other. Complete resolution of ataxia occurred on the following day.
Conclusion: Ataxia is a well described complication of AOM. The mechanism that leads to balance dysfunction remains unclear. Bacterial labyrinthitis should be thought of in order to prevent severe sequelae. Therapeutic approaches are still being debated. The time course with the rapid restitution of symptoms in the two cases presented speaks in favor of myringotomy as the more relevant therapy compared with antibiotic treatment, considering the fact, that AOM is caused by viral infection as well. Nonetheless, it is imperative that otolaryngologists and pediatricians are aware of the effect of AOM on balance, the management should be discussed interdisciplinary.

P026

Age-specific normal ranges of mannose-binding lectin (MBL), M-, L-, and H-ficolin, and MBL-associated serine protease-2 (MASP-2) in human serum

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Introduction: The lectin pathway of complement activation has just recently been added to the list of pathways being investigated in pediatric patients with infections and immunological diseases. Pediatric reference values are lacking and no consensus exists on what cut-offs should be used to define deficiency. The aim of this study was to establish age-specific normal ranges of serum concentrations of the lectin-pathway components mannose-binding lectin (MBL), M-ficolin, L-ficolin, H-ficolin and MBL-associated serine protease-2 (MASP-2) in preterm and term neonates, children and adolescents, versus adults.
Methods and subjects: Concentrations of lectin pathway components in serum were measured in 141 preterm and 30 term neonates, in 120 children, including infants and adolescents, and in 350 adults (97 for L-ficolin) by in house time-resolved immunofluorometric assays (TRIFMA) or commercially available enzyme-linked immunosorbent assays (ELISA). The adjacent categories method was used to determine between which age categories the respective serum concentrations were significantly different.
Results: Analyzing serum concentration versus age, an inverted-U shape was found for MBL, M-, L-, and H-ficolin, i.e., higher serum concentrations in children than in neonates and adults; and an S-shape for MASP-2. Only M-ficolin in children >1 year and H-ficolin in neonates >37 weeks gestational age and in children were found to be comparable with adult values. Using the 10th percentile found in adults as a measure to define deficiency in neonates and children, the proportion of deficiencies would be underestimated for some (MBL in all pediatric age groups, L-ficolin beyond neonatal age), or overestimated for others (M-ficolin in neonates and infants, L-ficolin in neonates, H-ficolin in preterm neonates, MASP-2 in all pediatric age groups).

Conclusions: MBL, M-, L-, and H-ficolin, and MASP-2 serum concentrations show important changes with age. The respective adult normal ranges should not be used in pediatrics. The age-specific pediatric normal ranges established here may be used in the future.

P027

A pediatric case report combining poststreptococcal reactive arthritis and Kawasaki disease

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A 13 month-old boy came to our emergency ward after a 6 days history of fever up to 39 °C. The first day of fever, he had developed a transient generalized maculo-papular rash. The second day of fever, he had an exudative conjunctivitis treated successfully with the counter eye drops. Over the following days, his general condition declined with marked apathy and loss of appetite. The fifth day of fever, the child developed a very painful swelling of both hands and was markedly irritable and hypotonic. At admission, he was in a poor general condition, with fever and irritability. He had pharyngitis with cracked lips. The back of the both hands and fingers were swollen and hot but without rash. There was no pitting edema. The proximal interphalangeal, distal interphalangeal, metacarpophalangeal joints and the carpus were painfull mobilization. The both feet were discretely swollen and painfull mobilization but it was less marked than in the hands. His laboratory work-up revealed high white blood cell count, platelets, C-reactive protein and erythrocyte sedimentation rate 96. His liver function tests were normal, anti nuclear factors-anticorps Anti Nuclear were negative and rheumatoid factors were in the limit, antistreptolysin was elevated at 300 U/ml. He had a positive Streptococcal rapid test, and his microbiological evaluation for bacterial and viral infection in the blood, urine and cerebrospinal fluid were negative. His spinal tap exam was unremarkable, as well as his abdominal ultrasound and echocardiogram. The working diagnosis was PSRA using the diagnostic criteria of Ayoub and colleagues. The patient was initially treated with antibiotics, antiinflamatories and paracetamol with a good clinical response, although the swelling of his limbs persisted. On the fifth day of his hospital stay, the child presented with desquamation on one finger. This finding associated with the persistence of thrombocytosis and high erythrocyte sedimentation rate suggested to the house staff an atypical Kawasaki syndrome. The child received then one dose of intravenous immunoglobulin and aspirin was also administered starting on the 10th day of fever. This case is interesting in two respects. Firstly, it is a streptococcal infection complicated by poststreptococcal reactive arthritis. Then he could illustrate the theory of superantigens currently reported by the literature.

P028

Food allergy: Evaluation of the quality of life in Swiss children

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Background: Food allergy in children, an increasingly prevalent disease, significantly affects the quality of life. Its impact can be analyzed by the recently validated French version of the Food Allergy Quality of Life Questionnaire (FAQLQ).
Objectives: The aim of our study was to evaluate the quality of life in a small sample of Swiss children with IgE-mediated food allergy.
Methods: Information were collected with the questionnaire among 0–12 years old children and their parents during a scheduled allergy visit, and analysed in term of emotional impact, food anxiety and social and food limitations. Patients were divided according to the questionnaire in three age groups: group 1 from 0 to 3 years, group 2 from 4 to 6 years and group 3 from 7 up to 12 years.
Results: 30 food allergic patients were included, with a girl/boy ratio of 1:1.14. Median age was 6 years. 56% suffered from or had a history of eczema, 23% of rhino-conjunctivitis, 30% of asthma, and 13% reported a drug allergy. None had insect venom allergy. 57% were known to be allergic to one food, 20% to two foods, 20% to 3 foods and 3% had 3 or more food allergies. Tree nuts (51% of all allergies) as well as eggs (28 %) were the major allergies. Emotional impact had a total score of 1.54 but showed differences between age groups. In group 1 it was lower with 0.23, in group 2 the score was 2.03 and 1.77 in group 3. Food anxiety total score was 1.9; 0.76 in group 1, 2.31 in group 2 and 2.23 in group 3. Social and food limitations showed similar results with a total score of 1.73 and 1.23 in group 1, 2.05 in group 2 and 1.68 for group 3.
Conclusion: Food allergy affects the quality of life of Swiss children. Our preliminary results on a small sample are comparable to previously published data. We show that the impact of food allergy on daily life increases when the child starts school and social activities.

P029

Food allergy: Validation of the French version of the FAQLQ-PF Quality of Life Questionnaire

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Background: It has been previously shown with English speaking children that food allergy clearly affects their quality of life. The first allergy quality of life questionnaire has been validated in English in 2008, however to date no questionnaire was available in French.
Objectives: To validate the French version of the Food Allergy Quality of Life Questionnaire- Parent Form (FAQLQ-PF) already existing version developed and validated in English by DunnGalvin et al.
Methods: The questionnaire was translated from English to French by two independent French-speaking translators and retranslated by an independent English-speaking translator.
We then recruited 30 patients between 0 and 12 years with a food allergy. Parents of these children answered the questionnaire during a clinic visit. The results obtained were then analysed and compared with the results provided by DunnGalvin's study and the Food Allergy independent Measure (FAIM).
Results: 27 questionnaires were fully completed and available for analysis. Median age was 6 years with a range from 18 months to 12 years. We had a girl/boy ratio of 1:1.14. A Cronbach's α correlation index of 0.748 was found. Validity was demonstrated by significant correlations between FAQLQ-PF and the FAIM.
Conclusion: The French version of the FAQLQ was validated and will permit to assess degree of Quality of Life for French-speaking children with food allergy. It will be an important tool for clinical research and will allow research collaboration between French and English speaking research teams.

P030

Anaphylaxis in the catholic church

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A 4-year old boy with known atopy and multiple sensitisations to food proteins as well as outdoor and indoor aeroallergens experienced an anaphylactic reaction during attendance of a mass in a Catholic church. He developed acute urticaria, angioedema, cough, dyspnea and pallor minutes after receiving the Holy Communion. There was no emergency medication available; the family had to leave the church immediately. At home the boy recovered spontaneously. What was the responsable allergen? At 2 years of age the child had been referred to our Allergy Unit for assessment of atopic dermatitis and recurrent acute urticaria. Multiple sensitisations to food proteins (egg, peanut, hazelnut and wheat) as well as aeroallergens (cat, grass and tree pollen) were revealed by skin-prick test and in vitro determination of specific IgE antibodies. There was no convincing history of true allergy to these food proteins and aeroallergens. Therefore, food provocation tests were performed which confirmed allergy to wheat. The young boy developed acute urticaria, angioedema, wheeze and rhino-conjunctivitis already after ingestion of 0.5 g wheat protein. The parents were instructed to avoid all foods containing gliadin. Furthermore emergency medications including adrenaline were provided. The boy's anaphylactic reaction in the church could be attributed to the Eucharistic host, which he received for the first time. They were prepared with wheat flour. In order to allow further attendance of the Holy Communion, the family's Catholic community decided to introduce a wheat-free consecrated wafer, made of rice. This new "hypoallergenic" Eucharistic host is currently well tolerated by the boy.
Conclusion: The most important aspect of current management of food allergy is avoiding the allergen and education of children and/or parents. Children with known anaphylaxis to food must always carry emergency medications including an adrenaline auto-injector. Their caretakers must be educated in appropriate management of accidental ingestion, also in places which are considered safe such as a Catholic church.

P031

Change from intravenous to subcutaneous infusion of IgG in children with immunodeficiencies is safe and improves the quality of life of the patients

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Introduction: Subcutaneous immunoglobulin (SCIG) replacement in patients with immunodeficiencies was introduced more than 25 years ago. The subcutaneous route is widely used in most European countries whereas in Switzerland intravenous immunoglobulin (IVIG) is more popular. Pharmacokinetics of IgG differ when smaller doses are given weekly using the subcutaneous route as compared to the large infusions given every 3 to 4 weeks in most IV regimens. SCIG infusions have many advantages like increased patient autonomy with less hospital consultations, decreased systemic adverse effects and no requirement for vascular access. However there are also disadvantages including volume limitation for each infusion and the requirement of a reliable compliance.
Objective: To describe 3 paediatric patients with different immunodeficiencies switched to SCIG therapy after an initial IVIG regimen.
Methods: 3 patients receiving IVIG every 3 to 4 weeks (one patient with congenital heart disease and protein losing enteropathy with hypogammaglobulinemia and two patients with common variable immunodeficiencies such as hypogammaglobulinemia with normal B cells and IgG subclass deficiency with impaired response to polysaccharide vaccination respectively) were placed on a regimen with SCIG administered weekly for several reasons (difficult intravenous access, recurrent infections despite IVIG infusions, anti IgA antibodies and anaphylactic type reactions). We describe the patient's experience more than 2 years after changing the route of immunoglobulin administration.
Results: All three patients had no systemic adverse effects, less recurrent infections, steady IgG values and much less medical consultations. The patients as well as the parents reported a marked improvement of their quality of life. However there were also some limitations of the subcutaneous route as augmented infusion volumes in adolescent patients require two infusions at different sites and hence a longer infusion time.
Conclusions: The subcutaneous administration of IVIG in the paediatric population is safe, efficacious and considerably improves the quality of life of the patients and their families.

P032

Incomplete Kawasaki Disease – Incomplete guidelines?

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Introduction: Kawasaki disease (KD) is an acute self-limiting vasculitis. Children aged 6 month to 5 years are most susceptible. Diagnosis is based on the presence of a set of symptoms listed in several guidelines.
Case presentation: A 14 weeks old boy presented with a history of 2 days of fever and diarroea. Gastroenteritis accompanied by a mild bilateral conjunctival injection and a macular rush on the thighs was diagnosed. Symptoms resolved after 4 days except fever. Chest X-ray showed bilateral patchy pulmonary infiltrates. Antibiotic treatment was started with amoxicillin and clavulanic acid and was extended with clarithromycin after 5 days. When fever did not resolve, differential diagnostic work up was resumed. Echocardiography on day 16 revealed dilated coronary arteries. Based on this finding Kawasaki Disease was diagnosed. Standard treatment with immunoglobulins and acetylsalicylic acid was started. When a giant aneurysm appeared subcutaneous low molecular heparin was instituted.
Discussion: Following the American Heart Association (AHA) guidelines diagnosis of KD should be considered if fever of at least 5 days is accompanied by 4 clinical criteria in case of complete KD, respectively by 2 or 3 clinical criteria in case of incomplete KD. Echokardiography should be performed if fever persists for at least 7 days without other explanation.
Conclusion: We consider the AHA guidelines to be incomplete. Think incomplete KD even though there is another explanation for prolonged fever and do an echocardiography between day 7 and 10.

P033

The changing clinical pattern in celiac disease: a case report

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Introduction: The incidence of celiac disease (CD) has increased in recent years due to the recognition of atypical forms and the identification of silent cases through serological screening.
Case report: We want to report the unusual case of a child that was presented with chronic abdominal pain for almost 1 year and severe constipation with no bowel movement in 10 days. An extensive diagnostic workup was performed, including X rays, sonography, clinical chemical factors, stool calcprotectin. All these examinations were normal, so we decided to involve a child psychiatrist before obtaining the results of Tissue Transglutaminases (tTG IgA). These were elevated showing a value of 40 U/ml. Intestinal biopsy showed total villous atrophy, graded by the Marsh score, and the diagnosis of CD could be made. Gluten free diet was introduced and the patient was seen 4 weeks later in the outpatient clinic for follow up. The patient was asymptomatic and the stool softness could be tapered successfully. The psychosomatic treatment could be stopped.
Conclusion: Although classical CD is seen in most patients referred to our pediatric gastroenterology clinic, CD should also be considered in the presence of atypical presentations, such as severe chronic constipation. Appropriate treatment with a gluten free diet solves the problem in most cases.

P034

Successful initial treatment with Rituximab in severe liver failure due to giant cell hepatitis and autoimmune haemolytic anaemia

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Introduction: Autoimmune haemolytic anaemia (AIHA) associated with giant cell hepatitis (GCH) is a rare and fatal disorder in infants. Early recognition of the disease and prompt institution of immunosuppressive therapy results in clinical remission and prevents liver disease progression.
Case report: A 13 month old previously healthy boy was referred with severe symptomatic Coombs-positive haemolytic anaemia, jaundice and elevated serum transaminases. Initially a transfusion with red packed cells was given. Work-up revealed no serological markers for infection (hepatitis A, B and C, EBV, HIV, Parvovirus B19, HSV, Toxoplasmosis) and there was no evidence of autoimmune hepatitis (SMA/LKM neg). Bone marrow showed hyperplasia of the erythropoiesis and no signs of malignancy. Autoimmune lymphoproliferative disorder as well as severe combined immunodeficiency were excluded. Liver biopsy revealed giant cell hepatitis with giant cell transformation, spotty hepatocyte necrosis, periportal fibrosis and canalicular and hepatocellular cholestasis. Multiple blood transfusions and high dose steroids and IVIG were given. Despite this treatment he developed hepatic failure, with coagulopathy, rising transaminases and severe jaundice. Thus, GCH was considered as severe and potentially lethal. Empiric treatment with IV Rituximab (CD20 monoclonal antibody, 375 mg/m^2, 4 doses/weekly) and Mycophenolate mofetil (MMF, 500 mg/d) was started, on the base of a case report (JPGN 2007; 44:634–636) and review of the literature. On this treatment transaminases declined rapidly, liver function was restored, no further blood transfusion was needed and his condition improved dramatically. 3 months after the initial Rituximab treatment, liver enzymes are continuously decreasing, haemolysis remains mild and the boy is followed as outpatient on dexamethasone pulses (10 mg/3 d) and MMF treatment.
Conclusion: AIHA with GCH is a rare and distinct entity with poor response to immunosuppression and often with fatal outcome. Treatment with immunosuppressant has usually not a sustained effect. We report a case of giant cell hepatitis with acute liver failure and autoimmune haemolytic anaemia with successful initial treatment with Rituximab.

P035

Boerhaave Syndrom: an unusual complication of acute vomiting in a child

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Introduction: Boerhaave syndrome (BS) is a spontaneous esophageal perforation, described in aged, alcoholic males, secondary to forceful vomiting. BS has rarely been described in children.
Case presentation: The patient is a 7-year-old Nigerian girl. She has a past history of clinical gastro-esophageal reflux (treated

conservatively with prokinetics and good evolution), malaria at the age of 3 months and an episode of acute pancreatitis at 5 years. One week prior admission, she had stopped atovaquone-proguanil (AP) prophylaxis after a trip in an endemic area. Two days prior admission, she presented several bouts of isolated acute vomiting, without fever or diarrhea. On admission, she complained of chest pain. Cardiac auscultation revealed crepitus. No subcutaneous emphysema nor respiratory distress was present. Chest radiography and CT-scan confirmed a pneumomediastinum extending to the neck. Esophageal perforation was suspected. An upper gastrointestinal endoscopy was performed and showed a small esophageal tear, grade II–III esophagitis and a single gastric ulcer without any sign of H. Pylori infection. Enteral feeds were stopped and a nasogastric sucking tube inserted. The patient made a full recovery on intravenous antibiotics and conservative treatment. Of note a second episode of subclinical acute pancreatitis, treated conservatively, probably drug-induced.
Discussion: BS is a complete rupture of all layers of the esophagus, secondary to an increased intra-abdominal pressure due to incomplete opening of the cricophayngeal sphincter occurring during vomiting or cough. Rarer causes include eosinophilic or Barrett's esophagitis, HIV and caustic ingestion. Esophageal perforation in children is rare, most of time secondary to necrotizing esophagitis in the newborn, medical intervention (endoscopy, sucking, or intubation) or trauma in the older child. Our patient had none of those risk factors and it is still unclear what predisposed her to this complication. However, we believe that preceding forceful vomiting with increased abdominal pressure acting on a weakened oesophagus due to esophagitis might be responsible. We could not find any association in the literature between AP and BS nor between BS and acute pancreatitis. The origin of her recurrent pancreatitis remains unclear, reason for which genetic testing for mutations in the trypsinogen, trypsin inhibitor and CFTR genes will be performed in case of a third episode.

P036

Ingestion of multiple magnets as an unnoticed cause of intestinal perforation

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Case report: A 23-month-old boy was admitted to our hospital with a four-day history of bilious vomiting and increasing lethargy, no diarrhea or fever. On specific inquiry, the parents mentioned that two plastic-covered magnets were missing. Physical examination of the dehydrated child revealed abdominal distention, dull pain and local tenderness of the upper abdominal quadrants and high-pitched bowel sounds. Inflammation parameters were elevated. Plain abdominal radiography showed distended small bowl loops, no free air. Two foreign bodies in projection of the lumbar vertebra 4/5 were depicted – the missing magnets sticking together. Median laparotomy revealed mechanical obstruction and perforation of the small bowel 40 cm proximal of the ileocoecal valve. Perforation resulted from pressure necrosis elicited by the two adhering magnets. Surrounding the site of perforation, there was a massive intramural haematoma and local peritonitis. Surgical intervention was performed by short-segment resection and end-to-end anastomosis. Antibiotic treatment with Ceftriaxone and Metronidazole was administered intraveniously for 10 days. Adaptation to normal diet was easily attained. Full recovery and discharge from hospital at postoperative day 12.
Conclusions: The majority of magnet ingestions occurs in children aged 1–3 years. Another risk group are older children in context with predisposing health conditions such as developmental delay or psychiatric diseases. The initial clinical symptoms are rather unspecific and parents' awareness of possible ingestion may be absent. Ingestion of a single magnet are usually treated conservatively. If more than one magnet is ingested, early extraction is indicated. This may either be performed endoscopically or by surgical intervention in case of postpyloric location of the magnets. However, severe or even lethal complications of multiple magnet ingestion may occur, e.g. intestinal necrosis and perforation, volvulus, fistula formation, peritonitis and sepsis. When treating a child with an acute abdomen, physicians should be aware of multiple magnet ingestion as a possible cause. Diagnosis is confirmed by plain abdominal radiography. Pediatricians should inform parents about the potential risks of magnets and give advice to remove these out of children's reach.

P037

Gastrointestinal bleeding: a forgotten side effect of NSAIDs in children?

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Introduction: Gastrointestinal bleeding (GIB) is a rare but potentially life-threatening side-effect of nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs are actually very deliberately used in children for fever control in acute infections. This despite the well documented inappropriateness of fever treatment in such circumstances.
Case: We report the case of a 5 1/2 year old boy without any history of former diseases, who developed a severe upper GIB during an infection with H1N1 and pneumonia, after beeing treated with NSAIDs among others. In the week prior to admission he had had episodes of fever, cough and abdominal pain, for which he had been treated with Ibuprofen sirup (10 mg/kg 4x/d) and Acetaminophen. He was hospitalized at a local hospital and started on Cefuroxim i.v. and with Oseltamivir (2x2.5 mg/kg p.o.) for 5 days. With progression of the pleural effusion he was then transfered to our hospital to receive a pleural drainage. Ibuprofen was discontinued and pain therapy was continued with Acetaminophen and Morphin with the help of the Faces Pain Scale (Hicks). Three days later he developed a massive Melena with a drop of Haemoglobin level from 109 g/l to 34 g/l, which needed a transfere to the pediatric intensive care unit, an immediate Transfusion and a therapy with a proton pump inhibitor. The endoscopy showed two duodenal ulcers with active bleeding. Injection was not possible, therefore requiring surgical treatment. The enteral nutrition could be started slowly and after a thoracoscopic revision of a pleural empyema he was discharged after four weeks. He was essentially asymptomatic in the follow up.
Discussion: GIB in Pediatric patients has been reported after uncontrolled stress, but also after NSAIDS or Tamiflu. We assume that our patient was not in stress, since he was under adequate pain therapy and enteral feeds. Tamiflu can cause GIB, but it is described in combination with hemorrhagic colitis, which our patient did not show. In contrast, Ibuprofen is independently associated with GIB due to ulcer in the upper tract; and together with the prolonged intake over 12 days makes it likely to be major cause of the GIB. This case illustrate that NSAIDs may contribute to life threatening side effects, and illustrates that the use of NSAIDs should be restricted.

P038

Aborted sudden death as first manifestation of catecholaminergic polymorphic ventricular tachycardia

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Sudden death is rare in childhood, undiagnosed cardiac disease is the leading cause. Primary electrical disease on a genetic basis (Channelopathies) is one of the causes leading to syncope or sudden death at any pediatric age. We report on 2 children with aborted sudden death as initial menifestation of catecholaminergic polymorphic ventricular tachycardia (CPVT). A 14 year old healthy girl was swimming when suddenly she drowned in the middle of the basin, bystanders took her out and reanimation was started, a professional rescue team wa on place after 8 minutes, she was admitted to the pediatric intensive care unit. Extensive diagnostic work up did not give any pathological result, Echo and cardiac MRI excluded structural heart disease, resting ECG was normal, genetic testing for the main forms of long QT syndrome was negative. On exercise testing she developped ventricular premature beats, genetic testing for CPVT was not done as not being offered by any institution in Switzerland. After several weeks she had completely recovered neurologically. After extensive discussion with the family a defibrillator was implanted and betablocker therapy continued. A 5 year old girl after a heavy debate with her sister had signs of a malaise, then suddenly vomited and went inconscious, later on showed convulsions. Parents started reanimation, a professional rescue team was on spot after 7 minutes and for ventricular fibrillation and torsade de pointes type ventricular tachycardia repetitive electrical cardioversion had to be done. For several hours after admission to the pediatric intensive care unit these ventricular arrhythmias went on with polymorphic premature beats, fibrillation, torsade de pointes and bipolar ventricular tachycardia. Diagnostic work up excluded any other reason for this episode, ECG showed normal QTc. With the suspicion of CPVT betablocker therapy was initiated and despite important neurological sequelae a defibrillator was implanted. Genetic testing is under way and the girl was started in a neurological rehabilitation programme. CPVT is a variant of genetic channelopathies which is rarely encountered before adolescence. Diagnosis is difficult and definite proof of the disease only possible by positive genetic testing. According to the patient's risk profile betablocker alone or with implantation of a defibrillator together with physical restrictions are protective of further cardiac events.

P039

Pericardits constrictiva in a 10-year old boy following Influenza A virus infection

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Introduction: Constrictive pericarditis is defined as an impaired diastolic filling caused by fibrotic pericardium. The diagnosis of constrictive pericarditis remains challenging and often requires a multimodal approach. We present a case of persistent pleural effusion as a sign of cardiac constriction in presence of a pericarditis constrictiva.
Case report: A 10 year old boy suffered since several months from persistent right sided pleural effusion of unclear etiology. 10 months before, he presented with symptoms of fever, diarrhea and fatigue. Drainage of the pleural effusion resulted positive for Influenza A virus (PCR positive). Subsequently pleural effusion persisted as well as dyspnea on exertion. The patient was referred for a cardiac MRI examination, in order to rule out a cardiac cause for the clinical symptoms. MRI demonstrated smallish size of both atria and both ventricles and signs of significant venous congestion. Cine MRI images showed the typical septal flattening during cardiac contraction; the pericardium presented clearly thickened and positive for pathologic late enhancement of contrast medium in the pericardium. These findings were consistent with the diagnosis of pericarditis constrictiva and a pericardectomy was planned. At admission, on physical examination, the boy presented with an attenuated respiratory sound and a hyposonor percussion at the basal area of the right lung, due to a large pleural effusion, a third heart sound with a gallop rhythm and a hepatomegaly. ECG showed right axis deviation and increased p wave amplitudes. Echocardiography confirmed the MRI findings with ventricular septal "bounce" during inspiration and dilatation of the inferior cava vein and of the pulmonary veins. Tissue Doppler Imaging (TDI) parameters were pathologic. Operative pericardectomy was performed without complications. Clinically the patient recovered quickly and 2 weeks later presented no signs of exertional dyspnea anymore. Postoperative echocardiography was almost normalized, without signs of venous congestion or ventricular septal "bounce".
Conclusion: While in most of the cases of pericarditis constrictiva the etiology remains unclear, viral infection is the second most common cause of pericarditis in children. Clinicians should be aware of this complication especially in patients with symptoms of exertional dyspnea and congestive heart failure. Pericardectomy is the therapy of choice in constrictive pericarditis.

P040

Put your hand on the heart of a child with failure to thrive!

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Introduction: In conditions with a wide range of differential diagnoses characteristical clinical signs can provide a clue to an efficient diagnostic work up.
Case report: A girl at the age of four months was admitted to the hospital because of failure to thrive. She had changed weight percentiles from P50-75 to P3-10. During medical history taking parents reported intense crying of the baby, especially after drinking. The mother also mentioned that she was sweating while drinking. On physical examination normal peripheral pulses were palpable. The precordial impulse was impressive both visually and by palpation. ECG was abnormal with positive right precordial T-waves and a negative T-wave in V6. Echocardiography showed a diastolic shunt into the main pulmonary artery, severe impairment of myocardial function, dilatation of the left ventricle, and grade III mitral regurgitation. The girl was mechanically ventilated, and therapy with milrinone and epinephrine as well as furosemide was started. After transfer to the tertiary centre surgical treatment of ALCAPA (anomalous left coronary artery from the pulmonary artery) was performed.
Discussion: ALCAPA is a rare but serious congenital heart defect. If left untreated, mortality is as high as 90% due to myocardial ischemia and mitral regurgitation. Affected babies usually become restless and irritable shortly after birth. Pallor, irritability and sweating (not only after feeding) indicate pain attacks from myocardial ischemia. Furthermore, the babies show symptoms of heart failure, e.g. evidenced by a pronounced apical precordial impact. Fluid intake is inadequate, and failure to thrive ensues.
Summary: A cardiac defect should be considered early in the diagnostic work up of failure to thrive. In the case presented a prominent precordial impact was the clinical diagnostic clue pointing at a cardiac problem.
Literature: M.C. Mancini, Anomalous Left Coronary Artery from the Pulmonary Artery, emedicine.medscape.com/article/893290.

P041

Compartment syndrome after pediatric cardiac surgery: a rare but devastating complication

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Introduction: Compartment syndrome (CS) results when high pressure within a closed fascial space reduces capillarity perfusion below the necessary level for tissue viability. If the pressure remains high for hours, normal function of muscle and nerve is jeopardised and necrosis may result, leading to Volkmann\'s ischemic contracture.
Case report: We report an unusual case of CS in a 14-year-old overweight child with pulmonary atresia intact ventricular septum following a 3rd cardiac surgery for pulmonary homograft replacement. Cardiopulmonary bypass (CPB) was started from the right groin after a difficult bilateral femoro-femoral canulation. Because of mediastinal adherences, a long CPB time of 265 minutes was necessary. The post-operative course was remarkable for persistent hemodynamic instability, capillary leak syndrome and renal failure necessitating increasing inotropic support and hemodialysis. Cardiac catheterization was performed on post-operative day 4 by a left femoral canulation to exclude aorto-pulmonay collaterals. After 8 days of heavy sedation, the child presented predominantly right leg induration and symptoms of nervous injury with bilateral paresia. Doppler echocardiography assessment ruled out a thrombotic lesion and an electromyogram confirmed bilateral sciatic nerve compression. Because of persistent foot drop and inability to walk, physiotherapeutic support was initiated and the patient was discharged home on post-operative day 19. He was readmitted 4 weeks after his surgery in the setting of painful hyperesthesia predominant on the right leg. The magnetic resonance imaging showed bilateral sciatic nerve fibrosis with extended muscular fibrosis and retractions secondary to an undiagnosed bilateral CS. Pain control with gabapentine and clonazepam, intensive physiotherapy and contention were initiated with slow improvement but persistent foot drop and difficulty walking.
Conclusion: CS secondary to femoral canulation for CPB is rare, all the more in children. This case emphasized the difficulty in diagnosing CS in critical care sedated patients. Nevertheless, consequences of a missed CS are serious with subsequent Volkmann\'s ischemic contraction. Awareness and early diagnosis is essential and can be made by the direct needle technique. A compartment pressure >40 mm Hg for >6 hours is an indication to prompt fascitomy and can avoid devastating complications.

P042

Twin pregnancy with heterotaxy and complex congenital heart disease of both fetuses: should hereditary transmission be suspected?

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Introduction: Heterotaxy syndrome is characterized by abnormal left-right axis formation resulting in a complex variety of splenic abnormalities (asplenia/polyspenia), gastrointestinal malrotation as well as complex and severe heart defects. Most cases are sporadic but familial cases with autosomal recessive or X-linked hereditary transmission have been described.
Case report: A 28 year-old gravida 2, para-0 women with a bichorial biamniotic twin pregnancy was referred to our institution for complex heart disease of both fetuses. Familial history was unremarkable. Morphologic echography performed at 18 weeks of gestation showed situs ambiguus with a median liver in both fetuses, with dextrocardia and left-sided stomach in fetus 1 and levocardia, median stomach and polycystic kydneys in fetus 2. Echocardiography performed on fetus 1 showed unbalanced complete atrio-ventricular canal with hypoplastic left atrio-ventricular valve, left ventricle, aortic valve and ascending aorta. Echocardiography on fetus 2 revealed well balanced complete atrio-ventricular canal with normally related great vessels but smaller pulmonary artery and suspicion of total anomalous pulmonary venous return. Amniocentesis was performed and revealed dizygotic XY male fetuses with no chromosomal abnormality. In the setting of heterotaxy syndrome with complex cardiac malformation of both fetuses, therapeutic interruption of pregnancy was performed at 23 weeks of gestation. Anatomo-pathologic evaluation confirmed the findings of heterotaxy syndrome and complex cardiac malformation of both fetuses. Fetus 1 had a median liver, left-sided stomach with a single left-sided spleen whereas fetus 2 had a median liver, median stomach, pulmonary right isomerism with asplenia and right polycystic kidney realizing a complex and different type of heterotaxy syndrome in those dizygotic twin fetuses. Genetic counseling was proposed to the couple and estimated a recurrence risk of 3–5% for monozygotic twins and of 25% for autosomal recessive transmission or 50% for X-linked transmission in successive males in case of dizygotic twins.

Conclusion: Left-right axis malformations are genetically heterogenous and quite variable in their manifestations. When siblings are affected, familial heterotaxy syndrome should be evoked and patients referred for genetic counseling. Fetal echocardiography on the 18–20 weeks gestation fetus is an essential screening and diagnostic method.

P043

Fetal idiopathic constriction of the ductus arteriosus: favorable outcome after delivery

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Introduction: Antenatal constriction of the ductus arteriosus unrelated to congenital heart defect or prostaglandin inhibitors is uncommon, but may result in congestive heart failure, hydrops fetalis and perinatal death.
Case report: We report a case of idiopathic ductal constriction detected prenatally on echocardiography in a fetus presenting with massive right heart dilatation at 36 weeks of gestation. The right ventricle (RV) was severely hypertrophied with fibroelastosis and severe systolic dysfunction. Opening of the tricuspid and pulmonary valves were limited with low velocity flow secondary to poor RV output. There was right to left shunting across the foramen ovale and the valve of the foramen ovale was seen bowing in the left atrium during the whole cardiac cycle. The ductus arteriosus was tortuous with distal constriction seen by pulsed Doppler and a maximal peak systolic velocity of 1.5 m/s. The fetus was closely monitored and congestive heart failure did not develop, allowing for spontaneous vaginal delivery in good condition at term. Neonatal adaptation was good with mild systemic desaturation to 85% related to RV hypertrophy with poor compliance and right to left shunting across the foramen ovale. Direct and indirect signs of high pulmonary vascular resistance were present, and the systolic pulmonary artery pressure was estimated around 50 mmHg from the mild tricuspid regurgitant jet. The saturation improved progressively to reach a normal level at one month of age. The echocardiography showed progressive improvement with normal pulmonary artery pressure, RV thickness and RV systolo-diastolic function at 6 months of age.
Conclusion: In case of antenatal ductal stenosis, the potential risk of congestive heart failure must be considered and lead to emergent delivery whenever necessary. Timely delivery leads to reversal of the pathophysiology providing the potential for a favorable outcome. Some cases of persistence of fetal circulation in newborns may be related to constriction of the ductus arteriosus not diagnosed during intrauterine life.

P044

Ventricular septal defect with massive right heart enlargement revealing a coronary sinus septal defect

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Introduction: Coronary sinus septal defect is rare and difficult to diagnose by conventional echocardiography. Massive right heart dilation with no obvious atrial septal defect or anomalous pulmonary venous return should evoke this diagnosis. Cardiac catheterization has an important role to play to confirm this diagnosis.
Case report: A 19 month-old boy was referred to our institution for surgical closure of a ventricular septal defect (VSD) in the setting of mild symptoms of tachypnea. Pre-operative transthoracic echocardiography revealed a pressure restrictive perimembranous VSD with high velocity left to right shunting and mild left heart enlargement. There was also severe dilatation of the right heart chambers with a small patent foramen ovale. The pulmonary veins appeared to drain normally to the left atrium. The coronary sinus was dilated but no persistent left superior vena cava could be visualized. For this reason, a cardiac catheterization was performed and showed a large communication between the left atrium and the coronary sinus, measuring more than 15 mm, responsible for a massive left to right atrial level shunting and for the right heart volume overload. The child underwent surgical patch closure of the VSD and direct closure of the defect between the coronary sinus and the left atrium with suture of the foramen ovale under cardiopulmonary bypass. The post-operative course has been uneventful allowing for rapid extubation a few hours after surgery. The echocardiography performed 3 weeks after surgery showed normalization of the size of the coronary sinus draining normally to the right atrium and regression of the right heart enlargement with no residual ventricular or atrial level shunting.
Conclusion: Coronary sinus septal defect is characterized by a communication between the left atrium and the coronary sinus responsible for left to right atrial level shunting and for right heart enlargement. In the presence of massive right chambers dilatation without obvious atrial septal defect or anomalous pulmonary venous return, this diagnosis should be suggested and confirmed by cardiac catheterization. Diagnosis is important as undiagnosed defect may lead to pulmonary hypertension if left uncorrected.

P045

Central cyanosis in childhood, think about pulmonary arteriovenous malformations

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Introduction: Central cyanosis is rare in childhood and should make pediatricians think about a pulmonary arteriovenous malformation (PAVM) when the heart structure is normal. PAVMs are abnormal fistulous connections between pulmonary arteries and veins, without intervening capillaries. PAVMs result in direct right-to-left shunt, causing hypoxemia and dyspnea on exertion. Patients may present life-threatening complications as stroke, transient ischemic attack, cerebral abscess, hemoptysis or spontaneous hemothorax. Early diagnosis is essential because these complications can be prevented by PAVM embolectomy and antibiotic prophylaxis.
Case report: We present the case of a 9-year-old girl consulting for progressive worsening of dyspnea, cyanosis, chest pain and palpitations during exertion. A cardiology visit performed two years earlier revealed a normal heart structure and could not find any cause to her symptoms. Clinical exam revealed mild cyanosis with oxygen saturation (SaO_2) of 84% and digital clubbing. Cardiac auscultation was remarkable for a low pitched systolo-diastolic murmur on the left-sided back. The chest radiography showed an opacity in the left hilar region. The ECG was normal. On echocardiography, her heart structure and function was normal with no chamber dilatation. A bubble test showed rapid filling of the left cardiac cavities with contrast after 3 cardiac cycles, suggestive of a PAVM. Three-dimensional reconstructions from a multi-slice CT scan showed an aneurysmal saccular PAVM between the feeding left pulmonary artery and the draining left pulmonary vein. Cardiac catheterization was performed and selective pulmonary angiography revealed a giant aneurysmal sac fed by the left pulmonary artery and draining into the left pulmonary veins. Transcatheter embolization with 2 vascular plugs was performed allowing for an increase in the SaO_2 to 98%. One month later, the girl had no murmur on clinical exam and a SaO_2 of 96% on room air.
Conclusion: PAVMs are well known causes of central cyanosis. Pediatricians should think about it in patients with unexplained oxygen desaturation. The diagnosis can be easily confirmed by contrast echocardiography and the treatment of choice is transcatheter embolization of the PAVM. Early diagnosis is important to prevent the life-threatening complications of this malformation.

P046

Transcatheter closure of muscular ventricular septal defect using Amplatzer Ductal Occluder device in low weight children

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Introduction: Muscular ventricular septal defects (MVSDs) are frequent cardiac congenital anomalies and can lead to symptomatic heart failure in small children. In this condition, surgical closure has been the traditional treatment. Since the introduction of interventional cardiology, muscular VSD occluder devices are increasingly used and considered as well an effective and safe method. We report 2 cases of successful closure of MVSD using a catheter-based approach with Amplatzer ductal occluder (ADO) devices in children weighting less than 10 kg.
Case report: Two children aged 9 and 12 month-old, weighting respectively 5.4 and 9.3 Kg, with significant symptoms of left to right shunt were diagnosed with MVSD. The trans-thoracic echocardiogram revealed a 6 mm conic MSVD distant from the atrio-ventricular and aortic valves for one patient and a 5 mm MSVD nearby the membranous septum for the other one. They underwent right and left cardiac catheterization under general anesthesia. Mean pulmonary artery pressure were 19 and 11 mm Hg respectively with a Qp/Qs of 2.5/1 and 2/1 respectively. The sizes of the MVDS were confirmed by left ventricular (LV) angiogram. After crossing the MVSD from the LV side and establishing an arterio-venous guidewire circuit, a 6F Mullins sheath was advanced from the venous side over the wire across the MVSD. An 8 and 5 mm ADO device were respectively positioned through the MVSD. Trans-esophageal echocardiography and LV angiography were performed to ensure proper positioning of the device. After delivery of the device, appropriate positioning and absence of residual shunting as well as interference with the adjacent cardiac structures were confirmed by echocardiography. No atrio-ventricular conduction disturbances were noted during the procedure or the immediate follow-up. Children were discharged home after 24 hours with anti-platelet therapy for 6 months. The clinical symptoms resolved and the weight increased within 1 month of follow-up.
Conclusion: Trans-catheter closure of symptomatic MVSD is feasible in low weight children and is considered as a safe and effective alternative to surgery. ADO, not originally designed for this procedure, can be well adapted to the anatomic shape of the MVSD.

P047

Severe hypertension of unexpected origin

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Introduction: Prevalence of hypertension (HT) in the adolescent population has increased since 30 years up to 2.2% in Switzerland. Primary HT is frequent in adolescents whereas secondary HT concern 95% of infants and children. Primary HT is also more frequent in obese patients and when there is a positive family history. Common causes of secondary HT are renal, renovascular and endocrine.
Case report: A swedish 12-year old patient fell against a tree while skiing with reception on the right flank. At admission, he had tachycardia (…) and hypertension (…). The urine showed a macrohematuria and the abdominal CT scan a right kidney fracture. Suddenly, he felt bad and his arterial blood pressure (ABP) increased up to 214/135 mm Hg. The patient was not known for primary HT. He had no past history of endocrine or renal disease. HT seemed too high to be related to adrenergism due to pain. HT of renovascular origin due to a lesion in relationship with the trauma would not manifest so quickly. No clear causes were found for this HT and successive antihypertensive as well as sedative drugs were administered. The ABP finally fell to 143/82 mm Hg. Clinical examination was then carefully repeated: heart auscultation showed normal heart sounds but a 2/6 systolic murmur maximal by the aortic valve with irradiation in the back was heard. The femoral pulses were weak and the measure of ABP to the 4 limbs shows a significant difference between upper and lower limbs. Finally, an angio-MRI confirmed the suspected diagnosis of aortic coarctation.
Discussion: As mentioned above, infants and children HT is often secondary to renal, renovascular or endocrine causes. Other rare causes include delayed recognition of aortic coarctation. This malformation accounts for 5–10% of all congenital cardiovascular malformations. It is usually diagnosed and corrected early in life but asymptomatic survival is possible in some patients until the 2nd or 3rd decade because symptoms depend on the severity of the degree of stenosis and the amount of coexisting collateral vessels. Hypertensive crisis leads at that time to the diagnosis in most of the cases. We would like with this case report to emphasize the importance of carefully and extensive examination of the patients in the emergency room even in case of light traumatism and the necessity for the pediatricians of checking ABP following the recommendations of the Swiss Society of Paediatrics.

P048

Kawasaki cardiogenic shock

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We report the case of a patient who developed cardiogenic shock in the context of Kawasaki disease (KD). A twelve year old male with no significant past medical history presented to the emergency room with a 3 day history of fever, left cervical adenopathy, dysphagia, an erythematous maculo-papular eruption, and a left bulbar conjunctivitis. The day before presentation he was treated by his pediatrician with amoxicillin/clavulanate and mefenamic acid. Lab studies revealed an elevated CRP (>200), a leukocytosis with a left shift, and a normal blood chemistry. A neck ultrasound was also performed showing multiple adenopathies without abcedation. The patient was admitted with a diagnosis of cervical adenitis and treated with intravenous amoxicillin/clavulanate. The day after hospitalization and 5 days after symptoms beginning, he developed a cheilitis, bilateral conjunctivitis and symptoms compatible with cardiogenic shock. He was transferred to the intensive care unit where an echocardiogram showed a left ventricular dysfunction with an ejection fraction of 48%, a pericardial effusion, mild mitral insufficiency and coronary arteries at the upper limit of normal. He presented an elevated PCT (9.46 g/l), VS (140 mm/h) and decreased albumin level (16 g/l). At this time, the patient was diagnosed with Kawasaki disease shock syndrome and treated with fluid replacement, dobutamine, one dose of intravenous immunoglobulins and high dose aspirin. The echocardiogram performed one month later showed complete cardiac normalization. A review of the literature revealed 1 case report and 2 studies describing other cases of cardiogenic shock post-Kawasaki disease. These patients showed IVIG resistance. They finally responded to treatment with high dose of anti-inflammatory drugs and repeated IVIG treatment. This treatment led to a good clinical evolution. Cardiogenic shock may be seen in the acute stage of KD in 4–7% of patients needing treatment in an intensive care unit. These cases are reported to have elevated inflammatory markers with important cardiac dysfunction. These patient's illness are often mistaken for toxic or septic shock leading to delay in correct treatment and increasing the risk of more severe coronary artery disease development. The diagnosis of cardiogenic shock post-Kawasaki is a difficult one to make and should always be considered when there is shock with cardiac dysfunction in a patient also with partial KD diagnostic criteria.

P049

Drug management of childhood hypertension: superior palatability of crushed lercanidipine compared with amlodipine

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Aims: To compare the taste of equivalent doses of pulverized amlodipine and lercanidipine, two calcium channel blockers, among children with kidney disease.
Methods: Each child received a test dose of 1 mg of amlodipine besylate and 2 mg of lercanidipine in a single-blinded fashion. Children indicated their preference by pointing to the appropriate face on a visual analogue scale that depicts five degrees of pleasure.
Results: The visual analogue scale palatability score assigned to lercanidipine was higher than that assigned to amlodipine both in nine children 4–7 years of age ($P < 0.005$) and in 10 children 8–11 years of age ($P < 0.005$). The preference for lercanidipine was statistically significant in both girls ($P < 0.02$) and boys ($P < 0.001$) and in both children initially presented amlodipine ($P < 0.005$) and children initially presented lercanidipine ($P < 0.005$).
Conclusions: There is a lack of appropriate formulations for children prescribed drugs originally designed for adults, such as calcium channel blockers. Parents therefore crush available tablets and administer the medication mixed with solid food or a palatable drink. From the perspective of the child, the taste of pulverized lercanidipine is superior to that of pulverized amlodipine.
Appeared As: Milani G, Ragazzi M, Simonetti GD, Ramelli GP, Rizzi M, Bianchetti MG, Fossali EF. Superior palatability of crushed lercanidipine compared to amlodipine among children. Br J Clin Pharmacol. 2010;69:204–6.

P050

Blood pressure measurement in the outpatient clinic: When should it be done?

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Background: Elevated blood pressure has become increasingly recognized as a major health threat in the adult population and among children or adolescents. Screening of high blood pressure is usually performed in a clinical setting; however, the psychological stress during the medical consultation may influence blood pressure assessment. The aim of the present study was to assess when blood pressure should be measured during the medical consultation. We hypothesized that blood pressure values taken after medical consultation are lower compared to values taken just before medical consultation.
Methods: We recorded 146 BP measurements before and after medical consultation in 135 patients (median age 6.9 years, range 0.1–18.8, 48% female) at our out- patient pediatric nephrology clinic. Blood pressure and heart rate were measured with an oscillometric automated device using an appropriate cuff size after 5 minutes of rest in a quiet room.
Results: Systolic blood pressure and heart rate were significantly lower after medical consultation compared to values before medical consultation (systolic blood pressure: 102.9 ± 15.3 vs. 104.2 ± 14.1 mm Hg, $p < 0.02$; heart rate: 96.8 ± 22.2 vs. 102.0 ± 23.2 mm Hg, $p < 0.0001$), yet diastolic blood pressure values were not significantly different. The prevalence of prehypertensive or hypertensive children was significantly lower after medical consultation compared to the prevalence at the beginning of the consultation (29.9% vs. 36.1%, $p < 0.0001$). Of importance, about 1/3 of the initial prehypertensive or hypertensive children become normotensive at the end of the consultation. In contrast, only 1/10 of the initial normotensive children showed prehypertensive or hypertensive systolic and or diastolic blood pressure values at the end of the consultation.
Conclusion: This study suggests that blood pressure measurement in a clinical setting can be optimized by recording blood pressure after consultation, in order to avoid overestimation of hypertensive individuals. Nevertheless, hypertension should be confirmed with ambulatory 24-h blood pressure or home blood pressure measurements.

P051

Recurrent transient renal Fanconi syndrome: Adverse effect of the artificial sweetener cyclamate

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Introduction: We present a 6 year old girl with recurrent episodes of abdominal pain, intractable vomiting, polyuria and renal sodium loss without apparent cause.
Case report: The previously healthy girl presented in April 2008 with abdominal pain, intractable vomiting, polyuria, hypertension (134/70 mm Hg), severe dehydration, impaired consciousness and aggressive behaviour. Laboratory findings included hyponatremia (130 mmol/l), hypokalemia (2.7 mmol/l) and metabolic acidosis requiring massive fluid and sodium supplementation. Plasma creatinine was normal. EEG showed general slowing of background activity; cerebral spinal fluid and MRI of the brain were normal. Within one week, the girl recovered spontaneously and was discharged with the diagnosis of "cerebral/renal salt wasting syndrome". One month later, she presented with a similar episode requiring massive fluid, sodium (up to 40 mmol/kg/d) and potassium (up to 8 mmol/kg/d) supplements. Until May 2009, she sustained 8 further similar episodes: Apart from polyuria and hyponatremia/-kalemia, each episode was associated with various degree of renal loss of bicarbonate, phosphate, uric acid, glucose and aminoacids, consistent with transient renal Fanconi syndrome. Work-up excluded all known metabolic causes; mitochondrial genome analysis was normal, and there was no exposition to Chinese herbs or heavy metals. Urinalysis revealed high amount of cyclohexylamine, a metabolite of the artificial sweetener cyclamate. In July 2009, dietary advice was given to omit all potential sources of cyclamate. So far, the girl has not experienced any further episode. Clinical examination and blood chemistry remained normal; repeated urinalysis revealed either traces or no cyclohexylamine.
Discussion: The initial presentation was consistent with "cerebral/renal salt wasting syndrome", but the further course showed recurrent renal Fanconi syndrome. The long-term remission after omission of cyclohexylamine suggests a causal relationship as reported once in the Lancet 1969. Cause and pathophysiology of "cerebral/renal salt wasting syndrome" are controversial. A recent publication (Bitew S, et al. Clin J Am Soc Nephrol. 2009) reported for the first time an association with the renal Fanconi syndrome. Given the fact that cyclamate is ingested daily by millions worldwide, the observed life-threatening adverse effect is very rare.

P052

Renal agenesis and seminal gland cysts or dysplasia: a rare association

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Background: Cystic lesions of the seminal glands are uncommon, although there is a recognized association between homolateral seminal gland cysts/agenesis and unilateral renal agenesis/dysgenesis. We report 2 such cases, their clinical presentation, and discuss their possible genetic causes.
Cases presentation: Patient 1 is a 15-year-old boy in no distress, who underwent abdominal ultrasonography for fatigue and weight loss. Physical exam was normal. Abdominal ultrasonography revealed a single hypertrophied left kidney, with no cysts, and a right cystic seminal gland, confirmed with abdominal MRI. There was no diabetes, proteinuria, or hypertension. Family history was negative for diabetes or renal diseases. He underwent surgical removal of his right cystic seminal gland without any complication.
Patient 2 is an 80 year-old man with a history of kidney stones, on no medication. His personal or family history is negative for renal failure, diabetes or infertility. His abdominal CT-scan revealed a single left kidney with multiple cortical cysts. There was no visible seminal gland on the right side, whereas it was normal on the left side. His clinical presentation and the presence of multipe cysts on his single kidney makes the possibility of a mutation in HNF1B even more attractive.
Discussion – conclusion: The presence of cystic lesions of the seminal gland, or more rarely absence of the seminal gland, should raise the possibility of an associated homolateral renal agenesis (Zinner syndrome), as reported here (the other differential diagnosis of isolated seminal gland cysts/agenesis/hypoplasia being cystic fibrosis). Hepatocyte nuclear factor-1beta (HNF1B) is expressed in the seminal glands, vas deferens, epididymis, oviducts and uterus, ureteric bud, collecting ducts and kidney tubules. HNF1B plays a major role in ureteric branching and induction of the mesonephros. Therefore HNF1B mutation could explain their unusual clinical presentation. HNF1B mutations are involved in the renal cysts and diabetes syndrome (RCAD), in congenital anomalies of the kidney and urinary tract (CAKUT) and in renal dysplasia/aplasia. We hypothesize that HNF1B mutations in our patients could be responsible for their unusual congenital malformations. Genetic analysis of HNF1B is currently performed.

P053

Uro-radiological investigations in newborns with hypospadias: a systematic literature review

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Background: In patients with hypospadias, the incidence of associated upper urinary tract anomalies has been reported as increased. However this is controversial, some teratology registries showing even less than expected-associated malformations of the upper urinary tract. The need for postnatal urological imaging in children with hypospadias is unclear.
Methods: We searched Medline database from 1966 to present, also including prior articles indexed for Medline, with the following medical subject heading or subheadhings: hypospadias and urination, ultrasonography (US), urinary tract/abnormalities, urinary bladder/radiography, ureteral obstruction, hydronephrosis or vesico-ureteral reflux. Limits were: infant, newborn OR infant OR child OR adolescent.
Results: We found 212 studies. After careful independent reading of the abstracts by 2 persons, 18 studies were kept for further analysis, including 1 prospective study. In that study, 153 children were examined with intravenous pyelography (IVP) and VCUG. The authors found 18 children with VUR (9 needing surgery) and 18 with abnormal IVP (6 ureteral obstruction and 4 duplex ureters, 8 needing surgery). The other 17 retrospective studies showed conflicting results, secondary to marked differences in the characteristics of the studied population and also to the striking absence of any specific indications to uroradiological investigations. The percentage of patients undergoing uroradiological exam as a screening procedure vary from 35% to 100%, so did the percentage of anomalies found, from 1.7% to 25%.
Discussion: There is no agreement in the literature about the benefice of postnatal uroradiologic imaging in newborns with hypospadias. Most of the studies are of poor methodological quality, making them impossible to compare. The types of exam(s) used differed greatly between studies. The patient selection criteria for receiving or not those imaging exams differed greatly within and between studies, with no description of these criteria in many studies. Indication for surgery is often not stated and differs greatly between studies. This makes the interpretation of the clinical significance of the findings extremely difficult to evaluate. We found no study incorporating the data of prenatal ultrasonography in that population. For all those reasons, no clear conclusions regarding the need for postnatal uro-radiological studies in newborns with hypospadias can be drawn at the present time

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P054

A Case of Urinoma Formation after Primarily Conservative Treatment of Traumatic Kidney Laceration

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Introduction: Conservative Treatment of paediatric liver and splenic rupture is well-established and has been practised for several years. There is a growing body of data suggesting that conservative treatment of blunt renal trauma in children is safe as well. We report a case of primarily successful conservative treatment of a kidney laceration in a 4-year old boy with secondary urinoma formation and consecutive surgical intervention.
Case report: On admission, the patient was pale and in reduced general condition. Clinically there was a bruise over the left flank with associated abdominal wall tenderness, reduced bowel sounds and intensive pain on palpation. The initial CT scan showed an extensive hematoma of the left kidney with concomitant retroperitoneal hematoma. Only the upper pole was perfused normally with lacking uptake of contrast agent in the rest of the parenchyma. The classification showed a Grade III lesion with more than 1 cm of parenchymal depth injury without collecting system rupture or urinary extravasation. A conservative treatment was chosen. Over the course of the hospital stay serial abdominal ultrasounds were performed. Repeatedly, perfusion could only be demonstrated in the upper pole. On the third day, an alteration of the lower pole was found which proved to be an extending urinoma in the subsequent CT scan. Furthermore, the ipsilateral ureter showed no contrast agent indicating

a blood clot or an avulsion of the ureter. The patient was then transferred to the paediatric surgery department in St. Gallen for further evaluation where a complete parenchymal rupture as well as an injury of the lower pole vessels could be diagnosed during cystoscopy. A heminephrectomy with ureteropyelostomy was performed. In the end, the initial grading of the injury needs to be changed, turning out to be a grade IV laceration considering the partial devascularisation and rupture of the collecting system. According to the literature, these cases are more likely to require surgery. The question remains if this fact would have excluded conservative treatment at first.
Discussion: Initial conservative treatment proved to be safe for the patient which adds to the preexisting data. Abdominal CT with endovenous contrast is the keystone to diagnosis. Nevertheless, this case demonstrates that the full extent of the injury could only be revealed by pyeloscopy.

P055

Urethral Prolapse: an overlooked diagnosis of uro-genital bleeding in premenarcheal girls

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Introduction: Uro-genital bleeding in pre-menarcheal infants and children is an uncommon problem seen in the emergency department. This pathology has been most cited in children of African descent. With the increasing number of reports of sexual abuse, physicians must keep in mind the importance of excluding an organic pathology prior to considering a possible sexual abuse.
Case report: We report 2 cases of uro-genital bleeding due to urethral prolapse. Both girls (2 ½ and 3 years old) presented to the emergency department of our hospital with an acute history of uro-genital bleeding. The parents were concerned in the first case of possible sexual abuse and in the second case of a self-inflicted trauma. The diagnosis of urethral prolapse was identified after careful physical examination by an experienced paediatrician. Both children were successfully treated by conservative treatment consisting of topical estrogen cream and sitz baths with camomile. The 2 girls were seen regularly by the hospitals' attending surgeons and at 14 months and 8 months follow-up, respectively, both girls have not relapsed, and surgical intervention was not necessary. In both cases, the rapid clinical diagnosis alleviated initial parental concerns.
Conclusion: These cases illustrate the importance of physician awareness of the normal female pre-pubertal genital anatomy in order to avoid serious consequences to the child and family related to an erroneous diagnosis and lengthy examinations often implicated in the case of potential sexual abuse. As this pathology is more frequently seen in children of African descent, a population which continues to grow in Switzerland, the probability of paediatricians to encounter this pathology will increase in the coming years.

P056

Goodpasture's disease presenting with acute renal failure

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A 15-year-old boy was admitted for vomiting, diarrhea, fatigue, crampy abdominal pain and oliguria. A renal failure was diagnosed (creatinine 2523 µmol/, urea 53,1 mmol/l) with severe aregenerative anemia (80 g/l), metabolic acidosis, hyperkalemia, elevated inflammatory markers and normal platelet count. A nephrotic proteinuria was noticed (350 g/mol). Patient's creatinine was normal 4 months before. The diagnosis of rapidly progressive glomerulonephritis was suspected. C3 and C4 were normal, ANA and ANCA were negative; anti-glomerular basement membrane antibody (anti-GBM) was positive (1/320) which lead to the diagnosis of Goodpasture's disease. Chest X-ray showed bilateral hilar infiltration and CT-scan revealed multiple alveolar haemorrhages, confirmed by broncho-alveolar lavage. Renal ultrasound showed swollen and hyperechogenous kidneys with loss of corticomedullary differentiation. Renal biopsy revealed a global extracapillary necrotising glomerulonephritis, with IgG lining the membrane at immunofluorescence. The patient was treated with continuous venovenous hemodia- filtration, plasmapheresis and immunosuppressive therapy (cyclophosphamid and corticoids) which lead to normalisation of anti-GBM level and favourable respiratory evolution with no sequelae. The renal evolution was unfavourable and the patient developed end stage renal disease and was treated with haemodialysis. Goodpasture's disease is an autoimmune process in which anti-GBM are produced against collagen IV present in the kidneys and pulmonary alveolae, resulting in acute or rapidly progressive glomerulonephritis and altering the pulmonary alveolae. It is a rare disease concerning mostly infants and young adults. Clinical presentation consists in an acute renal failure with proteinuria. Pulmonary symptoms (60–70% of the total cases) are dyspnea, cough, and haemoptysis. Diagnosis is made with the dosage of immunological anti-GBM and with renal biopsy. Factors of poor prognosis are initial oliguria, alteration of >50% of the glomerulus, very high creatinine or need of dialysis. Anti-GBM dosage is used for follow up. Patients are treated with immunosuppressive therapy for 6 to 9 months and plasmapheresis. Few recurrences are seen. Goodpasture's disease should be evoqued whenever a young patient is seen with glomerulonephritis, especially if pulmonary abnormalities are present. The disease requires an aggressive treatment in order to prevent respiratory and kidney failure.

P057

ANCA positive vasculitis with rapid progressive glomerulonephritis (RPGN) – a rare disease in children

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Background: ANCA pos. vasculitis with severe renal impairment is rare in paediatric patients. Initial symptoms are unspecific and may delay diagnosis and the induction of an appropriate treatment. We present two children with ANCA pos. vasculitis and RPGN.
Patients: **BOY:** Diagnosis at the age of 13 years. Initially diagnosis of an acute pyelonephritis (leucocyturia, hematuria and slightly elevated plasmacreatinine). Three days thereafter, clinical symptoms of pneumonia (fever, cough and tachypnea). Unsuccessful antibiotic treatment and further impairment of renal function was seen within 3 days (Glomerular filtration rate (GFR) 14 ml/min/1.73 m^2). Additional symptoms: Arthralgia, recurrent epistaxis, petechiae. Vasculitis associated findings: Leucocytosis, anemia, elevated CRP and C-ANCA-titer (1:1280). Renal biopsy: Extracapillary proliferative and necrotizing GN.
Treatment: Nine sessions of plasmaexchange (PEX) within 13 days. Induction therapy with methylprednisolone (M-PDN) i.v. (3 doses of 500 mg/m^2/BS each), thereafter continued with prednisolone (PDN) orally (1 mg/kg/d); cyclophosphamide (CyP) i.v. (3 doses, initially 500 mg/kg/m^2/BS, increased to 1000 mg/kg/m^2 every 4 weeks). Follow up after 3 months: GFR: 62 ml/min/1.73 m^2, proteinuria: 1000 g/mol, C-ANCA-titer: 1:10, blood pressure: 135/90 mm Hg. Current treatment: Daily PDN (tapering, orally), CyP 1000 mg/kg/m^2 every 4 weeks (in total 6 dosis). Thereafter a switch to Azathioprine (AZA) is planed. GIRL: Diagnosis at the age of 13 years. Initially diagnosis of a parvovirus-infection (pos. IgM-titer for parvovirus) with fatigue, gonarthritis, anemia. Symptoms progressed within 8 weeks and renal function decreased (GFR 35 ml/min/1.72 m^2). ANCA-titer (1:640). Renal biopsy: Extracapillary proliferative GN with fibrosis and crescents. Treatment: 14 sessions of PEX within 40 days. Induction therapy with M-PDN i.v (3 dosis of 500 mg/m^2/BS each), thereafter PDN p.os 1mg/kg/d and CyP 2.5 mg/kg/d p.os during 12 weeks. Follow up after 3 months: GFR 60 ml/min/1.73 m^2, ANCA neg. Switch from CyP to AZA 1mg/kg/d p.os and tapering of PDN. Follow up after 2 years: Recurrence of arthralgia and manifestation of cutaneous lesions: Switch from AZA to MTX (15 mg/m^2 weekly). Follow-up after 6 years: In remission with a GFR of 65 ml/min/1.73 m^2, mild proteinuria and borderline ANCA-titer (1:20). Normal blood pressure. Current treatment: Treatment with PDN 2.5 mg every second day and MTX 10 mg/week p.os.
Conclusions: The differential diagnosis of a multi-organ disease should include the diagnosis of ANCA pos. vasculitis. Early and adequate treatment with immunosuppressiva and plasmaexchange may prevent development of rapid progressive glomerulonephritis preserving glomerular renal function.

P058

Long-term consequences of preterm birth

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Introduction: Prematurity or small for gestational age birth are frequently characterized by short-term, neonatal complications (cardiovascular, metabolic or respiratory disorders). Furthermore, these children carry an elevated long-term risk for cardiovascular and metabolic diseases, especially arterial hypertension and diabetes. We describe an unusual long-term complication of prematurity in an adolescent girl.
Case report: A 14 year old girl, born hypotrophic and premature at 30 weeks gestational age due to maternal preeclampsia, was referred to our institution for evaluation of a sustained arterial hypertension with 24-hours blood pressure values around 140/90 mm Hg. The neonatal period was complicated by an E. Coli sepsis accompanied by a

transient impairment of renal function. The development during childhood was unremarkable, without relevant medical issues. Weight, height and BMI are within normal range. The kidney function is normal. Echocardiography excluded aortic coarctation and showed a moderate left ventricular hypertrophy. Neuro-endocrine diseases were excluded by normal urinary cathecholamines and steroid profile. Kidney size was normal on ultrasound and renal artery stenosis was ruled out by angiographic magnetic resonance imaging; however, the vena cava inferior was completely occluded with multiple collaterals that provided a sufficient venous return from the inferior extremities. The etiology of this occlusion remains uncertain; the well developed collateral veins implicate a chronic condition. In this regard, the girl describes frequent leg pain and swollen superficial leg veins. The most probable cause is a post-thrombotic state in the context of possible neonatal iatrogenic complications (umbilical vein catheter). The etiology of arterial hypertension remains unclear, yet, probably related to prenatal or genetic factors.
Conclusion: This case emphasizes that compromised intrauterine fetal growth and prematurity leading to low birth weight and neonatal complications are both associated with life-long consequences on cardiovascular and developmental health. Rigorous follow up of children at risk to develop long term cardiovascular complications, such as arterial hypertension, will improve the prevention of cardiovascular complications in adulthood.

P059

Impaired Neurodevelopmental Outcome in Children with Congenital Diaphragmatic Hernia

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Background: Congenital diaphragmatic hernia (CDH) is a life threatening congenital disease with a prevalence of 1 to 2000–5000 lifeborn per year and an overall mortality rate of 40–60%. It has the power to interrupt normal and mainly cardial and pulmonal organ development and can be associated with genetic disorders or with multiple organ diseases. Multiple long-term morbidities include chronic lung disease, gastroesophageal reflux, growth deficiency, sensoneurinal hearing impairment and skeletal asymmetries. It is unclear whether and in what domains neurodevelopmental impairments may occur and what risk factors are associated with adverse outcome.
Aims: To determine school-age neurodevelopmental outcome in a regional cohort of survivors of surgically corrected CHD.
Methods: We examined 33 children with CDH (85% of the survivors). They were examined clinically and neurologically. Motor performance was assessed with the Movement Assessment Battery for Children 2nd edition (M-ABC-2) in children younger than six years and thereafter with the Zurich Neuromotor Assessment. Intellectual performance was examined with the German version of the Wechsler Intelligence Scale 3th version (WPPSI-III) and with 4th version (WISC-IV) for children older than six years.
Results: Seven (18.2%) children were diagnosed with a comorbidity (either genetic or neurological). In one child, neurosensory deficit (need for cochlea implants) was diagnosed, one child had a cerebral palsy and one child had a myelomeningocele. Children with a genetic comorbidity had lower overall IQ's compared to the norm (median 65, range 49–75; p = 0.04) and to those without a genetic comorbidity (median 103, range 70–121; p = 0.001). Motor performance was lower than the norm for pure motor and adaptive fine motor performance (both p = .06). Also children without a genetic comorbidity had a poorer motor performance in the adaptive fine motor (p = 0.008) and in the adaptive gross motor component (p = 0.001) whereas intellectual outcome was not different from the norm.
Conclusions: Our study provides evidence that long-term neurodevelopmental follow up of patients with CDH is essential for the detection of neuromotor and cognitive impairments in order to provide early therapeutic interventions and parental counselling. Patients with an underlying genetic comorbidity are at particular risk for these deficits.

P060

Cloudy corneas at birth: a case of bilateral Peters anomaly

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Background: Cloudy cornea at birth is rare and raises a differential diagnosis of congenital glaucoma, hereditary corneal dystrophy or metabolic disorders (galactosemia, Fabry disease), amongst other. Prompt treatment is essential in order to prevent deprivation amblypopia. We present such a case.
Case presentation: The patient is a term female baby, born after an uneventful pregnancy. Family history is remarkable for parents' consanguinity (first cousin once removed), severe Hirschsprung disease in the father, and kidney malformations on the mother's side (mother and grand-mother). At birth, physical exam disclosed bilateral buphthalmia, with central corneal opacities, increased corneal thickness and elevated intra-ocular pressure. Ultrasound biomicroscopy showed a central posterior stromal defect connecting the anterior chamber with an intracorneal neo-chamber, as well as irodocorneal adhesions on both sides. Taken together these findings were consistant with the diagnosis of Peters anomaly. Patient's karyotype was normal (46,XX). The patient underwent sclerectomy/ trabeculectomy, which successfully normalized the intraocular pressure and decreased corneal thickness. Cornea transplantation is planned in the near future.
Discussion: Peters anomaly is a rare form of anterior segment dysgenesis in which abnormal cleavage of the anterior chamber occurs. It can be secondary to mutations in PAX6, PITX2 and CYP1B1 genes, the most frequently involved being the first one. Peters anomaly should not be confused with Peters-plus syndrome (OMIM 261540), which includes other systemic malformations, secondary to mutations in the B3GALTL gene. We are currently searching for PAX6 gene mutations in that family.

P061

Severe early lethal course of cystic fibrosis in a boy co-affected by subclinical myotonic dystrophy

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Introduction: Cystic fibrosis (CF) is an autosomal-recessive multisystem disorder caused by mutations in the CFTR-gene. However, there is a considerable variability of phenotype, presentation and clinical course even among carriers of identical genotypes. Modulating co-factors that might account for the phenotypic variability of CF have been proposed. We present the case of an unusual severe course of CF leading to death at the age of 3 years. A possible explanation for this severe disease manifestation was found years later, when two siblings and the mother were diagnosed to have myotonic dystrophy. At a postmortem analysis, the patient was found to carry a myotonin-proteinkinase-1-gene-mutation as well.
Case report: At the age of 4-weeks the boy presented with failure to thrive and persisting diarrhea. Sweat tests were positive and fullsequence analysis revealed heterozygosity for the 3905ins-T-mutation. Repeated severe lung infections and persistent failure to thrive led to several admissions to hospital. At the age of 11 months cultures were positive for P. aeruginosa and MRSA. Parents adhaerence to recommended treatment was poor. However, this was not a sufficient explanation for this rapid deterioration of pulmonary disease and persistent severe malnutrition. At the age 3 years respiratory decompensation due to severe pulmonary infections led to death. Years later, two brothers of the boy presented with mild delay of psychomotor development, myopathic face and subtle bulbar symptoms. Suspected myotonic dystrophy (Curschmann-Steinert) was confirmed in both by genetic analysis revealing a pathological expansion of the myotonin-proteinkinase-gene (DMPK1, 700-900 repeats) inherited by the mother. Accordingly, post mortem analysis of the DMPK1-gene in the index patient was positive for the identical mutation.
Conclusion: Life expectancy in CF has dramatically increased. Our patient had an unusual and severe clinical course leading to death at an extremely young age. A possible explanation for this unexpected outcome is the combination of a subclinical myotonic dystrophy associated with CF. The role of the DMPK-1-gene in the variability of CF-phenotypes seems worthwile to be considered, especially in unexplained severe clinical manifestation of CF in young children.

P062

A patient with Noonan syndrome and a late-onset leg lymphedema

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Noonan syndrome (NS) is a clinically variable and genetically heterogeneous disorder characterized by postnatal short stature, distinctive facial dysmorphism, heart defects (pulmonary stenosis, hypertrophic cardiomyopathy), and variable cognitive deficits. Associated features include, among others, cryptorchidism, bleeding tendencies, and varied lymphatic abnormalities. The latter occur in approx. 20% of patients and can manifest themselves either prenatally (cystic hygroma, chylothorax) and/or in early infancy as dorsal limb

(top of the foot, back of the hand) lymphedema which usually resolves spontaneously during early childhood. NS is caused by autosomal dominant mutations in at least 7 genes (PTPN11, SOS1, KRAS, RAF1, BRAF, MEK1, and NRAS). At present, only PTPN11 can be analyzed in Switzerland, but this analysis is not covered by the health insurance. We report a boy with clinical suspicion of NS who presented at the age of 15 years with a rapidly progressive lymphedema of his left leg. The late occurrence of such lymphatic problem is unusual in NS, as, to the best of our knowledge, only 2 patients have been previously reported in the literature.
Conclusions: albeit unusual in its late presentation, the lymphedema of our patient strongly supports the clinical diagnosis of NS, despite the lack of a current molecular proof.

P063

Antibiotic exposure in children and adolescents with lower respiratory tract infections

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Background and aim: The lack of diagnostic tests differentiating lower respiratory tract infections (LRTI) with bacterial from those with viral etiology and the high morbidity and mortality in children with untreated community acquired bacterial pneumonia (CAP) in the pre-antibiotic era still drive antibiotic prescribing today. Thus, the proportion of antibiotic prescriptions per consultation ranges between 30–50% for LRTI and 80–90% for CAP. However, it is estimated that 45 to 70% of LRTI are of viral origin. The aim of this study was to evaluate the antibiotic (AB) exposure of children and adolescents with LRTI prior to an intervention study investigating Procalcitonin guided treatment of children with LRTI.
Methods: Previously healthy patients treated for LRTI (01/2005-12/2008) were identified by ICD-10 codes and text search of electronic medical records. Cases of LRTI were classified as bronchitis, bronchiolitis, or CAP according to stringent case definitions.
Results: Included were 204 patients; 116 male (57%); mean age 4 yrs (range 0.1–18); mean duration of hospitalisation 4 days (range 1–33). Classified as CAP, bronchitis, or bronchiolitis were 111 (45%), 83 (41%) and 10 (5%), respectively. Of these, 101 (91%), 63 (76%), and 2 (20%) received AB, respectively. CRP values in the 166 patients receiving AB were <40 mg/l in 79 (72%), 40–79 mg/l in 33 (84%), 80–119 mg/l in 22 (96%), and >120 mg/l in 32 (100%). A microbial organism was identified in 88 patients (25 M. pneumoniae, 2 S. pneumoniae, 1 H. influenzae, 2 B. pertussis, and 58 viral pathogens). Mean duration of AB therapy was 11 days (range 1–44), including a mean of 2 days iv treatment (range 1–15).
Conclusions: Antibiotic use in patients with LRTI was higher than expected. Low CRP values (<40 mg/l) were not associated with low AB prescribing rates. Reliable diagnostic tests or clinical criteria guiding confident restriction of antibiotic use are needed.

P064

Central venous catheter-related bloodstream infections – a prospective one year study

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Aim: Our goal was to assess the risk of acquisition of bloodstream infections (BSI) associated with central venous catheters (CVC).
Methods: We prospectively assessed the incidence and risk factors of CVC-related BSI in all patients at our institution with an indwelling CVC either in place or inserted between April 1, 2008 and March 31, 2009.
Results: There were 219 CVC for a total of 14782 CVC days In 162 patients 92 males, 57% including neonates and patients with haemato-oncological, surgical, and other diseases. Mean age at CVC insertion was 1.8 months (Interquartile range 0–51 months). Twenty BSI occurred in 17 CVC in 14 patients (9 males). Overall BSI incidence (per 1000 CVC days) was 1.35 (9.7 for silastic catheters in neonates; 9.5 for conventional CVC; 3.5 for Broviac; 0.4 for Port-a-cath). CVC were in place for <=14 days in 119 (54%) patients, 15–90 days in 45 (21%) patients, and >90 days in 55 (25%) patients. BSI incidences in these 3 categories were 3.2, 4.4, and 0.9, respectively. The results reflect the fact that Port-a-cath CVC usually remain inserted for prolonged periods. The microbial organisms cultured predominantly were coagulase-negative staphylococci (N = 8) and S. aureus (N = 3).
Conclusions: CVC related BSI incidence varies by type of catheter and patients: The highest risk for this complication occurred in neonates where short term silastic catheters are typically used whereas the lowest risk for BSI was observed in chronically ill patients with a Port-a-cath. Prophylactic measures to reduce CVC-related BSI should be individually tailored with respect to catheter type and patient age.

P065

Human parechovirus type 3: a pathogen of infant sepsis-like syndrome

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Aims: To present three infants with clinical sepsis due to human parechovirus-3.
Case series: Three infants between 2 and 7 weeks of age were admitted in late summer with signs of clinical sepsis. One child had diarrhea. They were in poor general condition, had poor peripheral perfusion, were irritable, and febrile at >38.5°. Their vital signs showed normal blood pressure, mild tachycardia and tachypnea and normal oxygen saturation. Complete work-up included complete blood count and C-reactive protein which were normal in all three children. Cerebrospinal fluid (CSF) revealed red blood cells (21 to 1200/mm^3) and few lymphocytes (<30/mm^3), while glucose and protein levels were normal. One child didn't get any antimicrobial treatment; one received intravenous amoxicillin and gentamicin, the third received additionally acyclovir until the results were obtained. Polymerase chain reaction (PCR) on the CSF revealed Human Parechovirus (HPeV) in all three cases. Molecular sequencing confirmed the HPeV type 3. HPeV was also found in the nasopharyngeal secretion of one child, but in none of the stool samples. All other cultures were negative. Clinical outcome was favorable in all three children. Acute phase cerebral magnetic imaging performed in two infants was normal in one case, but showed bilateral frontal T2-hypointense white matter lesions in the other. His neurological evaluation 1 month later was normal.
Discussion: HPeV is a new genus of the Picornavirus family which is not detected by routine enteroviral PCR tests. Currently, 14 serotypes are described. HPeV-1 and HPeV-2 usually cause mild respiratory and gastrointestinal diseases. HPeV-3 is an emerging pathogen with a tropism for the central nervous system. This may explain why it is more likely to be associated with a sepsis-like syndrome in neonates and infants.
Conclusion: During summer season, HPeV-3 should be suspected in infants presenting with sepsis-like disease in addition to other common microorganisms. Specific PCR should be performed to detect HPeV-3. The prevalence and outcome of HPeV-3 disease in infants is unclear and should be studied.

P066

Spinal epidural abscess in a 16 months old boy, an unusual cause of fever of unknown origin

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Introduction: Children with fever of unknown origin present a common challenge to paediatricians. Most causes can be classified into three categories, i.e. infections, connective tissue diseases or malignancy. In the category of infections, localized encapsulated processes pose a particularly difficult challenge because they can present with few and non-specific clinical symptoms.
Case report: This patient was first seen at our service at the age of 9 months because of fever without source of 12 days duration with little response to oral antibiotics. His personal history had been uneventful except for the operation of a pilonidal sinus at the age of 7 months. Radiography of the lungs, abdominal ultrasound and blood cultures were negative. He was discharged after an observational period of three days during which the fever subsided without antibiotic treatment. After a second episode of fever for 14 days he was seen at the Infectious Diseases service at the age of 13 months for re-evaluation. At that point he was afebrile, showed normal growth and psychomotoric development and the inflammatory markers were nearly normal. Again, after 2 months without fever, he presented to our emergency department after a progressive deterioration with loss of the ability to walk and diarrhea. On clinical examination he had nuchal rigidity, diminished tendon reflexes of the lower extremities and urinary retention. An MRI of the spine showed an intraspinal mass dorsal to L1, with extension to L4. During neurosurgery. a spinal epidural abscess was diagnosed with epithelial remnants found on histology, consistent with a dermoid cyst. He was treated with a combination of meropenem and vancomycin, and after cultivation of a fully susceptible Escherichia coli, he was changed to ceftriaxone for a total of 6 weeks. Overall his neurological outcome has been excellent with minimal motor weakness of the left foot remaining.
Discussion: Spinal epidural abscess is rare in children and is frequently associated with pre-existing anatomical defects. In the majority of published paediatric cases a dermal sinus was present and provided the presumed connection with the skin surface. A high index of suspicion is important with spinal epidural abscesses, because early and aggressive surgical management combined with adequate antibacterial treatment prevents long term neurologic sequelae. Dermal abnormalities over the lumbar spine are a red flag, which should prompt appropriate imaging.

P067

The epidemiology and cost of H1N1 epidemic in a small community hospital pediatric department

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Background: In 2009 there was an epidemic of H1N1 influenza. We studied the impact of the epidemic in term of the number of visits to the pediatric emergency department (ED) and estimated its costs.
Methods: All outpatients' visits to the ED were recorded form June, 1, 2009 to January, 31, 2010. The number of ED visit was compared with previous years, and the direct cost for H1N1 was deducted from the hospital billing system.
Results: During the observation period, there were no increased outpatient visits compared to previous years (3516 visits for medical reason, compared to 3723 the previous period). 614 children had fever (17%). Amongst them, 383 (62% of children with fever) had no criteria for potential H1N1 infection (fever, rhinitis, cough, throat pain), which leaves 231 (38% of children with fever) with potential H1N1 infection. 142 children (61% of potential H1N1 infection) had no risk factors for H1N1 infection (chronic heart/lung disease, immunosuppression, age <1 year), were not tested and received no oseltamivir except one. 89 children (39% of potential H1N1 infections or 14% of children with fever) were at risk for complications: 87 had H1N1 PCR test, 38 were positive (44% of tests in that group) and 74 were treated accordingly. 30 subjects were in-hospital patients with potential H1N1 infection. 100% had H1N1 PCR test performed: 6 were positive (20% in that group), and 24 negative. 4 children had a main diagnosis of H1N1 infection (all were H1N1 PCR positive and received oseltamivir). Of the other 26 in-hospital patients, 2 had H1N1 PCR positive results (but not treated), and 2 received oseltamivir (but H1N1 PCR negative). Overall, 117 H1N1 tests were done (37% positive). Costs for H1N1 PCR tests, oseltamivir prescription and protective gowns/gloves/masks amounted 21'060, 900 and 3'093 SFrs, respectively (+ 100%, 100% and 70% compared to previous period, respectively). 172 children were also vaccinated against H1N1.
Discussion – conclusion: We observed no increase in the number of outpatient visits during the study period. Less than half of all children presenting to the ED with fever had criteria for potential H1N1 fever. Similarly, less than half of all H1N1 PCR tests came back positive. The impact of H1N1 epidemic during the 2009 outbreak in our community hospital in Western Switzerland in term of pediatric outpatient visits and cost was modest.

P068

Fungal Ball Expectoration after stem cell transplantation from an alternative donor in a patient with very severe aplastic anemia

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Introduction: Invasive aspergillosis is well known to cause life-threatening infections in immunosuppressed hosts, especially after hematopoietic stem cell transplantation(HSCT).
Case: We describe a case of disseminated aspergillosis, initially located in the posterior wall of the trachea in a patient with very severe aplastic anaemia(VSSA) undergoing HSCT. An 18 year-old male,initially diagnosed with VSAA refractory to immunosuppressive treatment underwent an haploidentical HSCT without engraftment and a rescue double cord blood (UCB) transplant because of persistent aplasia. VSAA had developed 17 months earlier and at the time of transplant,transformation to a myelodysplastic syndrome was diagnosed. After a conditioning regimen of cyclophosphamide, antithymocyte globulin (ATG-Fresenius®) and busulfan,he rejected a T-depleted with Campath-1H haploidentical HSCT from his father. A rescue double UCB transplantation was then performed following a conditioning regimen of cyclophosphamide, fludarabine, antithymocyte globulin(ATG-Genzyme®) with a graft versus host disease prophylaxis of cyclosporine(CSA). In spite of antifungal prophylaxis with voriconazole, he developed fever with a positive galactomannan of 4.57 (nég <0.500) 10 days before UCB transplantation. Computed tomography (CT) showed a para-tracheal lesion,negative on the PET-CT. We strongly suspected Aspergillus infection, posaconazole and liposomal amphotericin B were then introduced. One month after UCB, no engrafment was obtained. Blood chimerism was >97% of donor origin. Bone marrow chimerism was however mixed. Subsequently he suffered from chest pain and fever. A new CT showed the progression of the para-tracheal lesion into an intra-tracheal ball reaching one centimetre in diameter, 5 cm above the vocal cords. He spontaneously expectorated this mass,before performing any surgical removal. Histology of the lesion (Grocott stain) revealed a massive tracheal mycelia infiltration. By culture the presence of Aspergillus terreus was confirmed, sensitive to most antifungal drugs. In spite of intensive treatment with antifungal tritherapy (voriconazole, posaconazole, amphotericine B IV and by inhalation) as well as granulocyte transfusions from a G-CSF stimulated donor, fungal infection disseminated to the lungs and then to the gastrointestininal tract.The patient died shortly of multiorgan failure.
Conclusion: Fungal infections remain challenging in severely immunocompromised patients,especially in the absence of hematopoietic reconstitution.

P069

Salmonella enteritidis hip infection in a healthy child. A case report

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Although Salmonella enteritidis (S. enteritidis) septic arthritis is a typical complication of sickle cell disease, it is rare in children without blood disorder or immune deficiency. Our report deals with a 18 months old boy, previously in good health, who developed septic arthritis two weeks after febrile gastroenteritis. S. enteritidis was isolated from the hip synovial fluid's cultures and synovial biopsies, and favorable clinical response was obtained after arthrotomy and antibiotherapy. The treatment of septic arthritis is a medical emergency and has to be started immediately if this diagnosis is suspected. Even if gram-positive bacterias are the most frequently encountered germs in this disease, 30–50% of cultures don't reveal any pathogen. Therefore antibiotherapy is started on an empirical base. Accurate medical history may give important information whether the antibiotic spectrum should include gram-negative bacterias, like S. enteritidis.

P070

Think of invasive infection with pseudomonas aeruginosa in infancy: treat fast and suspect underlying immunodeficiency!

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Introduction: One of the clinical challenges in paediatrics is the recognition of primary immunodeficiency in children. Literature suggests that diagnosis is often delayed or missed. On the one hand it is not justifiable to screen all children with a confirmed infection. On the other hand, timely diagnosis allows for the initiation of appropriate therapeutic measures, hence reducing morbidity and mortality in these children.
Case presentation: A thus far healthy boy, 3 month old, presents with a septic condition in connection with a bilateral perforated otitis media in the emergency room. A smear test from both ears confirmed growth of pseudomonas aeroginosa (PA). In addition, in the area around the right knee, a pyoderma like skin lesion was present. Despite this severe infection, there were no locally enlarged lymph nodes palpable, giving a first clinical suggestion of underlying defective lymphoid function. Antibiotic treatment with PA coverage for 3 weeks resolved all clinical symptoms. Confirmation of PA together with a family history with two maternal brothers dying of unknown causes during infancy resulted in a further investigation for underlying immunodeficiency. Serum immunoglobulin levels of all classes were nearly undetectable, and lymphocyte characterisation by flow cytometry revealed complete absence of CD19 expressing lymphocytes. This indicates a hereditary B-cell defect, most likely X-linked agammaglobulinemia. Genetic analysis was performed. In order to prevent future invasive bacterial infections, the patient will need lifelong intravenous or subcutaneous supply of human immunoglobulins.
Conclusion: Confirmed or even suspected invasive infections with PA during infancy should lead to rapid antibiotic treatment including PA coverage, and additional investigation for underlying immunodeficiency.

P071

Pediatric A/H1N1 infection in Hôpital Neuchâtelois: epidemiological study using database report

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A/H1N1 virus have infected 1–1.5 Mio inhabitants, and caused 16 deaths in Switzerland according to report of the Swiss Health Office (OFSP). We report our experience with A/H1N1 in the Canton of Neuchâtel. From beginning of the A/H1N1 epidemic, cases tested for A/H1N1 in the out- and in-patient units of the Hôpital neuchâtelois (HNE) were recorded in a database which was sent daily to the office of the State Health Service to facilitate the evaluation of the epidemic. Student's t test and Chi2 test were used for statistical analysis. From May 4th 2009 until Jan. 5th 2010, results from 540 of 545 nasopharyngeal swabs for A/H1N1 tests were known. 30% (162) were done in children. Mean age of infected patients was younger than non infected patients (22.5 ± 16 vs 30.8 ± 19, p <0.0001). Tests were more frequently positive in children compared to adults (71/161 (44%) vs 107/379 (28%), p <0.0003). 84% of pediatric infections were diagnosed between wk 45 and 49 (Nov 2nd- Nov 30th). 29 pediatric patients were hospitalized with clinical suspicion of A/H1N1, mostly because of respiratory distress. A/H1N1 infection was proven in 8 of the hospitalized children, and oseltamivir used in five of them: because of young age (2), immunosuppression (1 renal graft), sickle cell anemia (1), neurological impairment and respiratory distress (1). Two patients had unusual presentation: a 14-year-old boy known for severe epilepsy was hospitalized because of high fever and grand-mal seizures; despite anti-epileptic medication he continued to have intractable seizures and developed respiratory distress with O2 requirement. He received oseltamivir because of proven A/H1N1 infection and slowly recovered from respiratory and neurological symptoms. The second, an 8-yr-old girl with Down's syndrome with flu-like symptoms, was hospitalized on the 4th day of an upper respiratory illness because of macroscopic hematuria. She had a favorable outcome with supportive therapy and IV hydration; although A/H1N1 PCR was negative in her urine, it is likely that A/H1N1 infection has contributed to the hemorrhagic cystitis. Similar to other reports, most of pediatric cases diagnosed in the HNE occurred in young patients, and were mild. Interestingly, two patients had an unusual presentation: one with severe neurological symptoms, and the other with hemorrhagic cystitis. Future epidemiological studies should also help to better define unusual complications of this illness.

P072

Fulminant liver failure following antituberculous therapy: should isonizid still be used?

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Standard treatment for tuberculosis (TB) consists of a tri-or quadri-therapy including isoniazid (INH). INH carries a hepatotoxic risk which can be enhanced by concomitant administration of other drugs. We report the case of a 9-y. old Somalian boy living in Switzerland for 2 years, who presented with anorexia, abdominal pain and weight loss over the past 7 months. His medical history was remarkable for mental retardation and epileptic encephalopathy treated by carbamazepine. Clinical examination revealed a right supraclvicular adenopathy and a lef iliac fossa mass. Investigations demonstrated an inflammatory process (sed rate 107 mm/h, C-reactive protein 86 mg/l), normal liver function test (LFT), discrete leukopenia, retroperitoneal and paravertebral cystic masses, multiple mediastinal and cervical adenopathies and left pulmonary infiltrate. Diagnosis of TB was established by positive tuberculin skin testing, positive M. tuberculosis PCR on the punctured abdominal mass, and detection of acid-fast bacilli on the biopsy of the supraclavicular adenopathy. Immunosuppression and co-infection with HIV, HCV or HBV or lymphoma were excluded. Triple anti-TB therapy (INH, Rifampicine and Pyrazinamid) was started with close follow-up of LFT. Over a few days, he developed decreased level of consciousness, renal and hepatic failure with encephalopathy. Despite supportive treatment, switch of anti-TB treatment to streptomycin, ethambutol and moxifloxacin, his general condition worsened and he eventually died of hepatic failure, cerebral edema with intracranial hypertension leading to cerebral herniation. Although anti-TB therapy, in particular INH, in combination with carbamazepine might be responsible for this catastrophic outcome, clinical presentation and microscopic aspect of the liver biopsy also suggest an underlying chronic metabolic disorder due to the presence of fibrosis and microvesicular steatosis. Urea cycle disorders were ruled out, while genetic for HHH syndrom is still pending. INH is considered as a first line anti-TB therapy. Elevation of LFT is described in up to 13% of patients under INH therapy. Though hepatic failure is rarely encountered in children under INH therapy, it is suggested that patients with metabolic disorders are at higher risk. In patients with a known or susceptible metabolic disorder because of, for example, mental retardation, we caution the use of INH and would recommend its replacement by less toxic agents, such as moxifloxacin.

P073

Kingella kingae primary sternal osteomyelitis in a 13 months old infant

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Kingella kingae is an emerging pathogen responsible for a growing number of paediatric osteoarticular infections, in particular in children less than 5 years old. This gram-negative coccobacillus is difficult to identify with the usual techniques and requires enhanced culture media, prolonged incubation or the use of PCR. Osteomyelitis in children relates mainly to the long bones and less frequently to the flat bones (pelvis and vertebrae). The sternum remains an exceptional localization for a primary osteomyelitis and only twelve cases have been so far described. K. kingae also has been associated with endocarditis in children with underlying heart disease. We present a case of a primary sternal osteomyelitis in a 13 months old girl. Clinical examination was not specific and revealed only a pre-sternal inflammatory swelling (1.5 x 2 cm) which was firm and fixed, with a moderate accompanying pain. A chest x-ray and an ultrasound confirmed the presence of an inflammatory mass associated with an osseous lesion of the manubrium. MRI confirmed that the lesion was encapsulated and located on the manubrio-sternal articulation. The sternal puncture fluid taken under radiological guidance showed the growth of a germ which was identified as being K. kingae thanks to PCR sequencing. An oral antibiotic therapy with amoxicilline-clavulanic acid was given for 5 weeks with a clinical and radiological remission. One week later, a relapse was observed with the same symptoms and an oral antibiotic therapy with Co-trimoxazole was introduced for 3 weeks. This treatment led to a complete cure which was confirmed by MRI after a 3 months follow-up. Literature review of the past 10 years suggests that a sternal osteomyelitis, particularly when located on the the manubrio-sternal joint and the xiphoid apophysis, is often associated to the presence of K. kingae. Bacteriological investigations should include the research of this particular germ because of its difficulty to be identified. The evolution of this infection is generally good. Penicillin is the drug of choice for treatment of invasive infections attributable to beta-lactamase-negative strains of K. kingae, but this germ may occasionally produce beta-lactamases. K. kingae is also sensitive to all antibiotics usually used in paediatrics.
In conclusion, it is essential to underline the importance of K. kingae as a pathogen responsible for osteomyelitis in infants and toddlers because of its increasing frequency.

P074

Visceral leishmaniasis and hemophagocytic syndrome

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A 11 months old female infant from Portugal, free of family history, consults for apathy, weight loss, tachycardia, tachypnea, petechiae, pallor without icterus and hepatoslenomegaly. Seven months earlier, while being in Portugal, she presented a persistent bluish pimple on her buttock. Laboratory results showed anemia (35 g/l), leucopenia (3.3 G/l), thrombocytopenia (13 G/l), impaired coagulation (INR 1.4, PTT 41 sec.), hyponatremia (124 mmol/l), elevated CRP (139 mg/l), high ferritin (34.775 µg/l) and high triglycerides (5.22 mmol/l). After correction of vital parameters, a bone marrow aspiration and biopsy (BMB) revealed both the etiological diagnosis, namely a visceral leishmaniasis (VL) as well as one of its potential complications, the hemophagocytic syndrome (HS). Transfusions of whole blood, platelets and fresh frozen plasma were immediately started. Dexamethasone (10 mg/m^2) and amphotericin B (3 mg/kg/day) have also been administrated. Visceral leishmaniasis is caused by a protozoan (Leishmania donovani) transmitted by the female sandfly. It is endemic in the Mediterranean basin (including France, Italy, Spain and Portugal), South America, sub-Saharan Africa as well as in India and Bangladesh. The parasite infects macrophages and, after

several weeks of incubation, the disease occurs by affection of bloodlines (anemia, leucopenia, thrombocytopenia), hepatosplenomegaly, cachexia, gastrointestinal damage. The complications of the disease may lead to death. Liposomal amphotericin B is the currently recommended treatment. HS is caused by the proliferation and activation of macrophages in the marrow in response to a cytokine storm. It may be of primary cause. When it is secondary, it may be related to infections such as leishmaniasis. Patients present with fever and laboratory diagnostic criteria include cytopenia, hypertriglyceridemia, high ferritin and hemophagocytosis in the BMB. The treatment consists among other in the administration of high doses corticosteroids and, in secondary cases, in the treatment of the underlying cause. In conclusion, the clinical and biological features of VL may mimic haematological disorders as leukemia, but an enlargement of the liver and especially of the spleen should remind in this parasitic infection and its potential fatal complication, the HS.

P075

Typhoid fever in returning travelers could be a diagnostic challenge!

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Introduction: Typhoid fever is endemic in many developing countries and therefore remains an important cause of fever in travelers. However, it sometimes constitutes a challenge for the diagnosis due to the range of the clinical presentations and the difficulties to highlight the pathogen in bacterial cultures at some stages of the disease. Other points of interest are the controversies about the efficiency of the vaccination, especially among travelers, and the outbreak of multidrug-resistant strains of Salmonella typhi, especially in Asia.
Observation: We report the cases of two patients presenting persistent high fever associated with loss of appetite, weight loss and muscular pain as main symptoms after returning from a trip (Egypt and North India). Case 1 had also abdominal tenderness with nausea but no diarrhea; case 2 had no digestive complaints, but nocturnal sudations and a dry cough. In both cases, the blood exams showed increased inflammatory values and the radiological exams highlighted intestinal lesions (ultrasound and computed tomography). In case 1, blood cultures showed a Salmonella typhi. In case 2, cultures were negative. In spite of positive serology for Salmonella typhi (maybe linked to recent Vivotif Berna® vaccine), we did a coloscopy with biopsies to bring to light the nature of the terminal ileitis seen on the CT, that opened the differential diagnosis of another infectious process (Mycobacterium bovis) or an inflammatory bowel disease (Crohn disease). However, the biopsy specimens, positive for Salmonella typhi, were conclusive for the diagnosis of typhoid fever. Consecutive follow up was favorable under antibiotherapy with ciprofloxacin in both cases.
Conclusion: The occurrence of these two cases in our general clinic within 6 months illustrated the importance of always considering typhoid fever in the differential diagnosis of traveler's fever. Furthermore, it showed how blood cultures could be a good way to establish the diagnosis in early stages of the infection, but also how their sensitivity drops in the case of a more advanced disease. On the other hand, many of the travelers were once vaccinated against typhoid fever, hindering the use of serologies. In such cases, specific biopsies could be used to confirm the clinical suspicion and provide the antibiotic susceptibility.

P076

Off-label use of topic Miconazole with systemic side-effects

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A topical therapy with oral topic Miconazole was started for an enoral mycosis in a 15 days old female infant. Immediately after application, the neonate showed systemic side effects in terms of transitory suffocating and inspiratory stridor. The following morning, minute doses were administrated with good tolerance. However, a second episode followed after readministration usual dose of the gel. After a third reaction with apnea, perioral cyanosis, hypotonia and regurgitation the infant was presented in the emergency room. Subsequent neurologic behavior, laboratory testings and a cerebral sonography were normal. The described adverse reactions include eructation and rarely allergic reactions with angioneurotic edema, anaphylactic reactions, asphyxia, nausea, vomiting, diarrhea, hepatitis and dermal reactions. Convulsions are described. The symptoms might be caused by a too large quantity of product with mechanic obstruction of the respiratory pathway, provoking apnea. However the mother was well instructed by her pediatrician and did not use more product than usual. Regarding allergies, the fact, that small quantities were tolerated, argues against an immunoglobulin-modulated pathway. In literature, a capacity to release histamine from mast cells by a non-immunological mechanism is described for Imidazoles (i.e. Miconazole), inducing bronchoconstriction in guinea-pigs after inhalation. We therefore suggest that the reaction could be due to a pseudo-allergic pathway with mast cell release, inducing transitory laryngo- or bronchospasm immediate after application of Miconazole. According to Swiss Medic guidelines, the drug should not be used in children younger than 6 months for precaution. However, it is usually applied even in premature infants without complications. With introducing of drug licensing and the traditional exclusion of children from clinical trials many drugs are used in children with limited information about safety and efficacy in children. Furthermore economic return for industry is often insufficient and research capacity for paediatrics is often limited. So off-label or unlicensed use is common in small children due to limited availability of licensed drugs for infants and small children. It is more common in hospital settings and younger patients. Off-label use varies from alterations of dosage, indications or, as in our case, age. Alertness for side effects or atypical reactions should be high, but even more using drugs off-label.

P077

"When infectious mononucleosis starts in the eye"

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Background: Infectious mononucleosis due to Epstein-Barr virus infection is a clinical diagnosis which presents with fever, fatigue, exsudative pharyngitis and cervical lymphadenopathy. Sometimes the onset, duration or prolonged nature of the pharyngeal-systemic illness presents a diagnostic challenge.
Method: Case report
Results: A previously healthy 2.5 year old boy presented at the emergency department with puffy eyelids and a sleepy look (no conjunctivitis, no watering of the eyes) without fever, no other peripheral edema and normal blood pressure. Family history revealed allergies (father with asthma bronchiale and pollinosis). The signs were interpreted to be most likely allergic and symptomatic therapy was started. Two days later he returned with persistence of periorbital edema, fever up to 39 °C and enlarged lymph nodes in the posterior cervical, retroauricular and nuchal region without further clinical findings. Infectious mononucleosis was suspected after the laboratory tests revealed a leukocytosis with 24.5% atypical lymphocytes. At a clinical check-up two days later the tonsills were found to be coated with a grey, heavy, confluent exudate and there was prominent hepatosplenomegaly. The first urine analysis was normal, specifically without proteinuria. Serologic analysis confirmed the diagnosis of acute Epstein-Barr virus mononucleosis (Viral Capsid Antigen IgM 1:48, IgG 1:20, EBNA-1 negative)
Conclusion: Periorbital edema can be a helpful clue in making an early diagnosis of infectious mononucleosis before the onset of fever, exudative pharyngitis and cervical lymphadenopathy. According to large series it can be found as an early sign in up to 10% of pediatric patients with EBV infection.

P078

Severe deficiency of vitamin B12 in infants breastfed for 10 months: clinical presentation and therapeutic implications

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It is known that vegetarians women may become cobalamine (B12 vitamine) deficient during pregnancy and lactation. Their infants may also be cobalamin deficient if they can not replenish its stocks soon after birth. We report the case of an infant of 10 months only breastfed from birth by a vegetarian mother. After term birth, it presents a normal development of the medical perspective and psychomotor. At the age of 4 months, he has a faltering height and weight with symptoms of vomiting with a decline in general condition and stagnation of psychomotor development as well as fatigue without any other detectable abnormalities. The parents then consulted various doctors who do not identify pathologies. Six weeks before the present hospitalization the vomiting stopped but the general condition of the child deteriorates. A week before his hospitalization, he presented apathy, psychomotor regression of acquired and edema of lower limbs. The laboratory work up carried mainly highlights are generative severe pancytopenia, a severe deficiency in vitamin B12 which are also found in the mother, a clotting disorder likely to vitamin K deficiency and a hypoalbuminemia without proteinuria. An assessment of psychomotor development conducted reveals a delay of 8 months on the mental and motor according to the Bayley scale. The clinical and paraclinical

examinations suggesting a severe deficiency in cobalamin, the child was substituted. Two days later, he developed significant tremors in the mouth, tongue and upper members of preventing food and making it uncomfortable. It is then the benefit of an anti-epileptic medication with slow improvement of symptoms. During hospitalization, he was fed by nasogastric tube and quickly resumed growth height and weight. The neurological status was slightly improved but there was still a delay and blood anormalities being almost corrected when the child is returned home. This case illustrates the clinical and therapeutic implications of severe hypovitaminosis B12 and undernutrition in the context of exclusive breastfeeding of a vegetarian mother. We believe it is important that pediatricians can recognize the symptoms of hypovitaminosis B12 for vegetarian mothers are common in our country. It would be best to anticipate deficiencies and suggest supplementation during pregnancy and lactation to prevent neurological sequelae in infants.

P079

Hyperthyroidism complicated by pseudotumor cerebri – Have a close look at the eye

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Background: Paediatric pseudotumor cerebri (PTC) is frequently associated with identifiable conditions, including drugs and infections. Thyroid hormone replacement and autoimmune hyperthyroidism (M. Basedow) has been associated with paediatric PTC in textbooks, however only few original reports are available. We report of a 13 year-old girl with recurrent bilateral papilledema secondary to hyperthyroidism associated PTC.
Case report: At the age of 13 years, the girl complained of a blurry vision and was diagnosed by an ophthalmologist to have bilateral papilledema and deficits in the visual fields. Exophthalmos was not observed and a history of headaches, nausea or vomiting was denied. However, the mother reported increased nervousness and involuntary weight loss of 4 kg over 6 months. Neurological evaluation revealed PTC with a lumbar opening pressure of 30 cm. Further clinical and laboratory evaluation showed tachycardia, goiter, highly elevated T4 (236 nmol/L, N 60-160) and T3 (6,9 nmol/L, N 1.1–2.8), and completely suppressed TSH values. Autoimmune hyperthyroidism was diagnosed on the basis of elevated TSH-receptor antibodies. Thyroid suppressive therapy with carbimazole subsided initially with propranolol normalized thyroid function rapidly. With acetazolamide therapy papilledema and visual field deficits resolved slowly over 6 months. However, recurrent hyperthyroidism after slow dose reduction of carbimazole after 2 years of therapy was again complicated by PTC relapse with a lumbar opening pressure of 44 cm H_2O water and papilledema associated with bilateral transient optic disc haemorrhages and visual field deficits.
Conclusion: This case report illustrates 1) the need for a detailed diagnostic work-up of children with PTC to identify treatable underlying conditions, 2) the association of hyperthyroidism and severe PCT by simultaneous onset and relapse of both entities, and 3) the importance of close endocrine and ophthalmologic monitoring of hyperthyroid patients with oligosymptomatic PCT to avoid an unfavourable visual outcome.

P080

Pay attention to attention deficit – and the growth curve

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A 14 year old girl was evaluated for Attention Deficit Hyperactivity Syndrome (ADHS) because of a deterioration of her scholastic performance in the course of a year. Fatigue, need for increased hours of night sleep, a short attention span and weight gain without increased caloric intake were the patient's complaints. On physical examination, the girl was overweight (BMI P90), showed a height at P10, below the genetic target height, and a prepubertal Tanner stage. Further, she presented diminished deep tendon reflexes and dry skin without goiter or further abnormalities. Retrospectively, a clear decline of the growth curve from P97 to P10 was seen between 9 and 13 years of age. Clinical biochemical analysis diagnosed a severe primary hypothyroidism (TSH of >375 uU/ml, N 0.6–4.6 uU/ml), fT3 <1.5 pmol/l (N 3–8.5) and fT4 <4 pmol/l (N 9-20). Thyroglobulin and thyroperoxidase specific auto-antibodies were not detected. The ultrasound showed atrophic thyroid loco classico with small nodules representing the end stage of longstanding autoimmune thyroiditis. In accordance with chronic hypothyroidism bone age was retarded by 3.5 years resulting in growth deceleration and delayed onset of puberty. Under substitution therapy with Levothyroxin (L-T4) the girl regained normal physical and intellectual performance as well as regular body weight despite increased appetite. The initially pathological low growth velocity increased to a high normal range and the girl showed a clear catch up growth. She also started pubertal development. The leading sign of school-aged children with severe longstanding hypothyroidism may be unspecific attention-deficit. In conclusion, attention-deficit in the context of weight gain and deceleration of growth velocity should prompt thyroid evaluation.

P081

Screwed up development

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Case report: A 12 month old Swiss-Kirgiz boy was presented with progressive muscular hypotonia, delay of motor development and failure to thrive. He was hardly able to sit or hold his head and only succeeded to lift the arms a few cm from the surface. His speech comprehension seemed normal and he spoke one word ("Mama") with a fable, coarse voice. The child was breastfed for 11 months. During the last 3 months he showed no weight gain at all. Due to progressive vomiting after feeds his formula milk had been changed to soy milk and hydrolysed formula. Laboratory investigations revealed a severe Vitamin B12 deficiency, central hypothyroidism, low IGF-1/IGF-BP3 and low serum total IgA. Chest X-ray revealed a metal screw of 3cm length stuck in the oesophagus, which was removed endoscopically. Vitamin B12 was administered intravenously. The further course was very favourable: The boy began to eat porridge in increasing amounts without vomiting. After 3 months he had gained strength and was able to sit, hold his head, lift his arms even holding toys in his hands, and he started to move forward by rolling. Without further supplementation, the Vitamin B12 level remained stable for 3 months, thus ruling out a hereditary cause like transcobalamin deficiency. Thyroid function normalised spontaneously, and growth hormone parameters increased slowly.
Conclusions: We conclude that the neurodevelopmental delay and failure to thrive in this boy was due to a severe Vitamin B12 deficiency caused by malnutrition, secondary to a screw that had been stuck in the oesophagus for an unknown period of time. Vitamin B12 deficiency in infancy leads to regression in psychomotor and physical development. Substitution of the missing vitamin can lead to (at least partial) amelioration of symptoms.

P082

Neuronal calcium channel mutation in a patient with congenital ataxia and attacks of hemiplegic migraine with cerebral edema

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Background: Familial Hemiplegic Migraine (FHM), characterized by a prolonged unilateral hemiparesis, mainly results from mutations in the alpha-1a subunit of the calcium channel gene CACNA1A that can also cause two other dominantly inherited neurological disorders, Episodic Ataxia type 2 (EA2, with sometimes migrainous headaches) and Spinocerebellar Ataxia type 6 (SCA6, late-onset and progressive). A same mutation can have different clinical expression in a family (hemiplegic migraine, migraine-coma, cerebellar ataxia). CACNA1A mutations in FHM are usually missense, leading to gain-of-function, while truncating mutations leading to loss-of-function are usually associated with EA2.
Case report: This 9-year-old girl was seen as a baby for hypotonia and transient vertical nystagmus. Her first brain MRI was normal. She evolved as a congenital ataxia, but since the age of two, she had attacks of coma, hemiparesis (either side), partial seizures, dystonic movements and fever. Attacks were initially triggered by minor head bumps, subsequently spontaneous. Brain MRIs in the acute stage always showed transient unilateral hemisphere swelling. Follow-up images revealed atrophic lesions in the temporo-occipital regions and cerebellar atrophy. A prophylactic trial with flunarizine was ineffective. Acetazolamide was recently introduced.
Methods: Since our patient shared features of both FHM and EA2, we studied the CACNA1A gene by direct sequencing in the patient's and parents' DNA.
Results: We identified an unreported de novo heterozygous deletion of three base pairs (c.4503_4505delCTT) predicting the deletion of one amino acid (p.Phe1502del). The CACNA1A protein contains 4 domains, each formed by six transmembrane segments. The deletion is located in a highly conserved region in segment 6 (S6) of the third domain. Mutations in S6 segments of calcium channels change single-channel conductance and channel selectivity, most resulting in loss-of-function.
Outlook: In vitro expression studies of the identified mutation are underway, aiming at understanding its functional consequences and finding an efficient treatment.

P083

Hypoglycaemia in children – prone to be misdiagnosed

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Paediatricians are often not aware of the diagnosis of hyperinsulinemic hypoglycaemia beyond neonatal age since the incidence of insulinoma in children is very low. In an attempt to characterize presenting symptoms, diagnostic procedure and to avoid misdiagnoses, two boys with insulinoma are compared to scarce reports on other children and to series of adults with insulinoma. Two unrelated Swiss boys, 11 and 13 years old, were treated for migraine accompagnée and epilepsy respectively. Macrosomy and an impaired school performance were main symptoms. Disorientation during fasting disclosed hypoglycaemia (2.6/2.9 mmol/L) and alleviation of symptoms following carbohydrate intake (Whipple's triad). Pituitary or adrenal diseases were ruled out. Diagnosis of hyperinsulinemic hypoglycaemia was confirmed by neuroglycopenic symptoms, hypoglycaemia (2.6/1.7 mmol/L) and inappropriately elevated insulin (13/6.7 mU/L) and C-peptide (700/840 pmol/L) levels during a supervised 72-h fast. Thus, in addition to undetectable sulfonylurea levels, factitious hyperinsulinaemic hypoglycemia was safely excluded. Low levels of ketones, normal levels of lactate, ammonium and organic acids provided additional evidence for insulin excess. Somnolence or neuroglycopenic symptoms occurred below the threshold of insulin/glucose-ratio characteristic for adult insulinoma patients (29 and 33 versus 37 pmol/mmol) and after an earlier fasting period (4.8 and 12 versus 23 h). Computer tomography scan and MRI were equally sensitive in localizing the tumour. Long term recovery was achieved by laparoscopic distal pancreatectomy in one and conventional enucleation in the other patient. Medical history was shorter, weight gain moderate, glucose threshold of neuroglycopenic symptoms and seizures higher as compared to adults, being explained by smaller glycogen stores in the younger ones. Therefore, adulthood diagnostic criteria for insulin-secreting tumours may not be valid in children.

P084

Idiopathic central diabetes insipidus in a premature newborn successfully treated by sublingual desmopressin

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Idiopathic central diabetes insipidus in the neonatal period is very uncommon. We present a male infant born at 30 gestational weeks (1550 g (–2 SD), 37 cm (–2 SD)) after a pregnancy complicated by threatened preterm labor 48 hours before surgical delivery for placenta abruptio. In the first days of life he demonstrated a 15% weight loss due to polyuria. Hypernatremia (150 mmol/l), high plasmatic osmolality (302 mosmol/l) and low urine osmolality (96 mosmol/l) corrected by intranasal desmopressin confirmed central diabetes insipidus. Imaging studies revealed normal posterior pituitary. No anterior pituitary dysfunction was found. Intranasal desmopressin management led to highly variable natremia, which stabilized after switch to sublingual desmopressin substitution (Minirin Melt®). Follow-up is now uneventful, with normal growth at 7 months of age. A high degree of clinical suspicion is needed in order to diagnose neonatal diabetes insipidus. Rapid management is required to avoid complications such as intracranial bleeding and renal vein thrombosis due to severe hypernatremic dehydration. Sublingual desmopressin seems to represent a safe alternative to intra-nasal substitution in neonatal central diabetes insipidus.

P085

Case study: acute hyperammonemic encephalopathy in an adolescent with ornithine transcarbamylase deficiency (otcd)

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Introduction: Ornithine transcarbamylase deficiency (OTCD) is the most common inborn urea cycle disorder (incidence 1:20,000 live births). Most affected males present as newborns. Females often have partial enzyme deficiency and become symptomatic later due to X-linked inheritance. Untreated OTCD can lead to life-threatening hyperammonemia, chronic progressive encephalopathy, and cognitive deficiencies.
Case report: An 18 year old female adolescent with OTCD, diagnosed at the age of 2 years, was admitted with a history of nausea, fatigue, dizziness and shaking of extremities. Long-term medication at home had included sodium benzoate and L-arginine. History taking and high ammonia level (136 umol/l; <50 umol/l) supported the suspicion of non-adherence to medication and diet prior to admission. Despite of immediate emergency treatment (cessation of protein intake, high intravenous caloric supply to escape catabolism, and ammonia scavenging therapy) the ammonia level rose further to a peak serum concentration of 326 umol/L only 6 hours after therapy onset. Clinically, the patient deteriorated dramatically with signs of hyperammonemic encephalopathy and psychotic features necessitating preparation of emergency peritoneal dialysis. Stabilization was achieved only 24 hours after ICU admission under unchanged therapy. An unexpected long further hospitalization (12 days) was necessary because of persistently elevated ammonia levels.
Discussion: OTCD is rare and our experience with acute OTC metabolic crisis is limited. The initial deterioration after therapy onset was troublesome for family and caregivers. The availability of immediate and repeated expert counseling in the Swiss Metabolic Network as well as ICU standards contributed to managing this challenging situation. The reason for further delay of recovery remains unclear; triggering of catabolism by throat infection is our best explanation. Even though parents and patient had been repeatedly informed on risks of non-adherence, non-compliance was accepted as a seemingly minor sin. The acute crisis could have been anticipated by parents and patient.
Conclusions: 1. Adherence to therapy is an issue in adolescents with OTCD. 2. Both family and medical team should be aware of potential delay of improvement after emergency therapy onset. 3. Treating acute metabolic crisis requires ICU standards as well as expert metabolic counseling. 4. Infection must be considered as cause for delayed recovery from metabolic crisis.

P086

Severe dietary Vitamin D deficiency as cause of apparent life threatening event

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Introduction: We present a boy with severe vitamin D deficiency with rickets, repeated convulsions and long QT syndrome because of lacking substitution in combination with wrong diet.
Case report: A 5 month old boy was admitted to our clinic after an apparent life threatening event (ALTE) with acute cyanosis followed by successful mouth-to-mouth resuscitation by his mother. On admission the boy showed no abnormality in clinical evaluation. A low serum calcium concentration was found in initial blood gas analysis. The diagnostic workup showed normal activity in the electroencephalogram, but a long corrected QT-time of 480 milliseconds in the electrocardiogram. The radiographic findings of the wrists and knees revealed cupping and fraying of the metaphysal region consistent with rickets. Serum level of alcalic phosphatase was high, concentration of Vitamin D2 and D3 were both decreased. The urine sample showed diminished calcium concentration and increased phosphate concentration. The child was monitored and oral supplementation with calcium and Vitamin D2 was started. Because of two more convulsions we administered calcium intravenously, as we did for vitamin K because of simultaneously high INR (International Normalized Ratio) due to refused substitution after birth. Serum Vitamin A level was normal. Pancreas elastase, as a marker of exocrine pancreatic deficiency, in the stool was normal. At the time of discharge long QT time has normalised as well as serum electrolytes. Additional ultrasound of the brain, polysomnography and pH-study showed no further abnormalities. He did neither receive Vitamin D nor Vitamin K supplements since birth and had an inadequate daily intake of calcium due to a special diet.
Discussion: Refusal of vitamin D supplementation and additional wrong diet with cereals prepared with pure water and only small amounts of breastmilk lead to a potentially life threatening condition with convulsions and long QT Syndrome due to profound hypocalcaemia.
Conclusion: In the first year of life refusal of vitamin D supplementation or inconstant administration by parents is not uncommon and can become dangerous if there is an additional dietary lack of calcium intake. Paediatricians should be aware of this problem and advise parents of a healthy diet for the children especially when Vitamin D is refused.

P087

Failure to thrive in a girl born into a family affected by familial dysalbuminemic hyperthyroxinemia

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Autosomal dominant familial dysalbuminemic hyperthyroxinemia (FDH) is characterized by modified human serum albumin (HSA) inducing a substantially higher affinity for thyroxine (T4). Histidin or prolin substitution on residue R218 produces localized conformational changes of HSA creating additional room for T4 binding, leading to 14–20 fold normal total T4 (TT4) levels. Affected individuals are

considered euthyroid. Our patient is an 18 months-old swiss girl born to a mother known for the rare R218P mutation in the HSA gene. She presented with severe failure to thrive (height –2.92 SD, weight –3.6 SD), habitual hip dislocation without anatomical anomaly, late fontanelle closing and protruding ears. Psychomotor development is slightly retarded. Thyroid function testing confirmed extremely high TT4 (1446.0 nmol/l) levels, which are similar to her brother's values (1534.4 nmol/l and 1757.6 nmol/l respectively). Free T4 seems slightly elevated (26 pmol/l), probably due to methodological reasons. TSH (0.92 mU/l), free T3 (4.4 pmol/l) and thyroxin binding globulin (32 mg/l) are within the normal range. Her two half-brothers, affected by the same mutation, are now 18.7 (P1) and 16.6 (P2) years old and were originally described by S. Pannain et al. in 2000. Both were characterized by growth retardation (–2.1 and –2.2 SD) before the age of 4 years. P1 has reached a normal adult height (–0.4 SD) and P2 has caught up to normal growth (–0.68 SD) with moderate bone maturation delay. Pubertal development and anterior pituitary function are adequate. Primary growth and developmental retardation in the first years of life with adequate catch-up seem to be a distinct characteristic in FDH with R218P mutation. Hip dislocation is typically seen in other situations associated to thyroid disorders, like Down syndrome. These findings might be explained by altered early thyroid hormone utilization in children with FDH.

P088

Severe leucodystrophy and coma in the context of glutaric aciduria type II

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Background: Glutaric aciduria type II (GA II) is an inborn error of metabolism resulting from defects in electron transport flavoprotein (ETF) or ETF-ubiquinone oxidoreductase (ETF-QO), which leads to abnormal amino acid, fatty acid and choline metabolism. GA II may present with nonketotic hypoglycemia, developmental delay, muscular weakness and hypotonia. It can be complicated by leucodystrophy – however literature reports concerning neuroimaging findings in GA II are rare. We report on a child with a metabolic crisis due to GA II presenting with coma and severe leukodystrophy.
Case presentation: A 2½ year old boy with a known developmental delay presented with a subacute loss of consciousness (minimal score of 3 on the Glasgow Coma Scale), severe hypoglycemia and insufficient spontaneous respiration needing ventilatory assistance. He had reactive pupils, preserved brainstem reflexes, a generally decreased muscle tone, weak tendon reflexes and bilateral Babinski sign. The cerebral MRI revealed signs of a leucodystrophy with extensive symmetrical signal changes of the supratentorial white matter sparing the U-fibres, swelling of the corpus callosum as well as patchy involvement of the cerebellar hemispheres but unaffected grey matter. MR spectroscopy showed an increase in lactate. Urine analyses revealed an increased excretion of glutaric acid, 3-OH-glutaric acid and fatty acid metabolites, particularly of medium chain fatty acids, thus – together with the cerebral neuroimaging – pointing towards the diagnosis of GA II. On a protein-restricted diet with a for GA II adapted amino acid formula, vitamin B2 supplements, carnitine and maltodextrine, the boy recovered fully to the level of motor function he was before the coma state.

P089

Congenital hypothyroidism escaped from neonatal screening

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Introduction: The neonatal screening program for congenital hypothyroidism was introduced 1977 in Switzerland to prevent mental retardation due to late thyroid hormone therapy. We describe a case of congenital hypothyroidism due to thyroid dysgenesis with diagnostic delay despite pathological neonatal screening.
Case report: A male term newborn was delivered after unehventful pregnancy and birth with normal weight (3250 g) and length (49 cm). Slightly elevated thyroid stimulating hormone (TSH) value (18.3 mU/L Blood) at neonatal screening in the asymptomatic child prompted a recall testing. On the 15th day of life, a second test was collected which was unfortunately not done on the specifically signed Recall Card aimed to control TSH and total thyroxine (T4). The reported TSH was falsely considered adequate (<15 mU/L Blood) and the mother received the information not to pursue thyroid investigations. At 6 months of age, thyroid function was checked again because of failure to thrive: slightly elevated TSH of 4.1 mU/L (N 0.1–3.7) and lowered total T4 [60.6 nmol/L (N 65-165)] were found. Further work-up at 8 months of age confirmed hypothyroidism [TSH 14.04 mU/L (N 0.5-4.5), free T4 9.0 pmol/L (N 9-25)] due to absence of the left thyroidal lobe and a proximally localized functional right lobe at echography and Technetium 99m Pertechnetat scintigraphy. Levothyroxine substitution was initiated. At the age of 13 months, neurodevelopment is normal. Retesting of the second screening card by the Swiss Neonatal Screening Laboratory showed still normal TSH 5.8 mU/L Blood (N <10) and low total T4 104.9 nmol/L (N 123-170). The diagnosis could therefore have been confirmed earlier if the adequate Recall Card had been used, if the birth date had been checked or if the appropriate norm value for age would have been used.
Discussion: Internal procedures at the Swiss Neonatal Screening Laboratory have been modified in order to identify control demands. Our case illustrates the need of using the appropriate Recall Cards in order to prevent escape from neonatal screening and possibly catastrophic outcome. Appropriate interpretation of results remains primordial.

P090

Standardized Family-Based Behavioural Therapy in Obese Adolescents and Their Parents: a Swiss experience

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Introduction: Adolescent obesity is a major public health issue in Switzerland. A new policy with strict criterion was enacted for the reimbursement of childhood and adolescent obesity treatment up to 18 years of age. In this context, we are developing and evaluating a multidisciplinary program for obese adolescents (BMI >97th percentile).
Methods: One year Family-Based Behavioural Treatment (FBBT) with psycho-educational group sessions and physical activity (84 hours) was implemented in 2009. To be developmentally appropriate, the patients are oriented in two groups depending on their age: younger adolescents (YA) aged 11–14 years and older adolescents (OA) aged 15–18 years. These two programs differ in the number of sessions and the choice of themes. It address three axes: diet (choices, quantities, taste education, sensations), psychology (emotional eating, self esteem, stress and conflict management) and physical activity. Techniques include self-awareness, goal setting, cognitive behaviour strategies and coping skills training. Participation rate, psychosocial parameters, anthropometrics measures and quality of life (Kidscreen questionnaire) are assessed at baseline and six months.
Results: As the result of the limited available places in the program (12 adolescents per group), only 25 adolescents on the hundred of new adolescents' patients consulting our clinic in 2009 were able to benefit for the program. The YA group includes 13 patients (4 girls and 9 boys), mean age 13.3 years, and BMI 28.7 kg/m² (BMI Z-score 2.8). The OA group includes 12 patients (2 boys and 10 girls), mean age 16.0 years, and BMI 32 kg/m² (BMI Z-score 2.5). These two groups are on-going. The preliminary results for the OA group at 4-months show a participation rate of 79.8% and 80% in the parents group. A mean BMI of 0.6 kg/m² was observed. 6-month Anthropometric parameters, participation rate and quality of life will be presented for both groups during the meeting.
Conclusion: Few adolescents consulting our centre could benefit from the program, as a result of the limited available places. This pilot study will allow us to evaluate the acceptability of a standardized FBBT in two groups of adolescents and the weight and quality of life outcomes.

P091

Case study: pitfalls in evaluating and treating bone disease in a female adolescent with anorexia nervosa

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Introduction: Anorexia nervosa (AN) is detrimental for bone mass accrual and a risk factor for later osteoporosis (OP). However, there is little agreement on how to identify and treat pediatric osteopenic bone disease. Dual energy x ray absorptiometry (DXA) is increasingly used to evaluate children for OP even though the method in this population implies some unanswered questions. Bisphosphonate (BP) use in adolescence is controversial (lack of longterm and safety data) and should be reserved to specific indications.
Case presentation: A 16 year old female adolescent with longstanding AN and secondary amenorrhoea was referred from a general practitioner for BP treatment after assessment of bone mineral density by DXA had seemingly rendered the diagnosis of OP. Reevaluation showed that criteria for diagnosis of OP were not met, and that treatment criteria for BP use were not met either.

Discussion: Pediatric DXA interpretation is complicated by 1) lack of standard reference data; 2) necessity of Z-scores (standard deviation score compared with same age) in addition to T-score; 3) influence of bone size, skeletal maturity and body composition. In paediatric patients diagnosis of OP should not be made on grounds of DXA alone; in addition to DXA criteria (Z-score < –2.5) pathological fractures are a required diagnostic criteria. Our patient had a Z-score of –2.3 and no pathological fractures. She thus did not meet any of the criteria of paediatric OP. BP therapy for paediatric OP is generally reserved for patients with clinically evident bone fragility, which we did not find in our patient.
Summary: Our patient was incorrectly evaluated by overriding age-specific normative DXA values and neglecting Z-scores; in addition she was over-diagnosed with OP by uncritical application of adult diagnostic criteria; finally she was about to be over-treated (notably with a highly controversial intervention) by uncritical application of adult therapeutic indication criteria.
Conclusion: Evaluation and treatment of pediatric bone disease including DXA and BP therapy requires involvement of the specialist. This case highlights yet again that children and adolescent are not merely small adults and – if treated as such – are at risk of receiving inadequate and potentially harmful treatment.

P092

Levothyroxine ingestion with suicidal intent

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Background: Eltroxin intoxication in children and teenagers is an occasional and rarely severe event. The most serious complication is thyrotoxicosis.
Case report: A 14 year old and previously healthy girl (body weight: 54.5 kg) ingested 96 tablets of Eltroxin-LF® 0.1 mg (Levothyroxine – Natrium free from lactose) with suicidal intent. This corresponds to a total amount of levothyroxine of 9.6 mg or 0.18 mg per kg body weight. The patient was brought to the emergency room 24 hours postingestion. Emesis was not induced and no activated charcoal was administered. After consultation with the Swiss Toxicological Information Centre, we installed a monitoring and determined thyroid hormone levels on the third day after the intoxication: TSH basal: 0.03 mU/l (standard range: 0.4–4.0 mU/l); fT3: 20.1 pmol/l (range: 2.4–6.4 pmol/l); fT4: >77.2 pmol/l (range: 2.4–6.4 pmol/l). Neither complications nor signs of thyrotoxic crisis were observed.
Discussion: A review of the literature shows, that accidental or intentional exposures with levothyroxine are frequent. Severe courses are rare and no lethal case after monoingestion of levothyroxine (T4) is described to our knowledge. Serum half-life of T4 and T3 is 7d and 1d, respectively. Plasma peak concentration is reached within 12 h for T4 and in 24 h for T3. Ingestion of levothyroxine (T4) causes a delayed occurrence of symptoms (several days), because T4 has to be converted to T3 to be effective. Mild symptoms are expected after ingestion of 2,0 mg/kg bodyweight. A total dose greater than 5 mg levothyroxine can lead to more severe symptoms. The clinical signs may include: tachycardia, increased blood pressure, vomiting, increased body temperature, headache and agitation. Hospital admission should be considered if the T4 concentration 6 h after ingestion is >160 pmol/l, if the patient is symptomatic or if there is a pre-existing cardiopulmonary disease. Treatment with propranolol is recommended if the heart rate is over 120 bpm in the sleeping patient. The administration of activated charcoal is controversial.
Conclusion: Levothyroxine (T4) overdose in children is well documented and is rarely associated with major toxicity. Administration of activated charcoal should be considered after ingestion of 5 mg of levothyroxine. Patients with symptoms, pre-existing cardiopulmonary disease or a fT4 value >160 pmol/l need to be hospitalized for monitoring. Discharged patients must be controlled for 10 days.

P093

Eating and physical activity habits of overweight children attending a specialized childhood obesity clinic: The Geneva experience

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Introduction: Childhood obesity represents a major public health burden. In order to improve the management of children with this condition, we aimed to describe the eating and physical activity habits of patients attending our specialized Obesity clinic.
Methods: This was a retrospective study including 211 new patients (2.3 to 15.3 years, mean 9.6 ± 2.7) attending our Obesity clinic between January 2008 and December 2009. Subjects visiting the Adolescent medicine clinic were not included. We focused on body mass index (BMI), eating patterns, quantity of food ingested and speed at which our patients ate. Also, we assessed their physical activity habits and sedentary behaviours (screen time).
Results: The mean BMI was 25.2 ± 3.7kg/m² and BMI z-score was 2.71 ± 0.98. Regarding their eating habits, 76% of our patients ate 3 meals a day and 22% did not eat breakfast. Forty-five percent had one afternoon snack, 38% had morning and afternoon snacks and 15% had none. We observed that 69% admitted to eating too much, 54% were eating fast (<15 minutes/meal) and 73% were nibblers. Regarding their physical activity habits, 32% had no afterschool activity, 36% engaged in 1–3 h/week of sport and 13% in >3 h/week. Fifty-five percent were described by their parents as active and 63% liked to play outside. Thirty-seven percent spent less than 1h30/day in front of television or computer and 17% spent more than 3 h/day. We found that the patients eating quickly ate more (88 vs. 25, p = .008). Those who did not play outside nibbled more (62 vs. 9, p = .003) and those who did not nibble were more often playing outside (35 vs. 9, p = .003). Spending more than 3 hours in front of television or computer was inversely related to the amount of afterschool activity (p = .007).
Conclusion: Overweight children who eat quickly are significantly eating a greater quantity of food and those who engage in outdoor playing nibble significantly less than those who have an indoor lifestyle. A large amount of time in front of television or computer is inversely related to physical activity. Therefore, we recommend to paediatricians to assess carefully eating and physical activity habits of overweight children. They should encourage them to eat slowly, have an active lifestyle and decrease sedentary behaviours.

P094

National survey on abdominal trauma practices of pediatric surgeons

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Introduction: Pediatric blunt abdominal trauma is a frequent reason for hospital admission, but there are no established guidelines to assess these patients. Our study aims to evaluate the diagnostic process of pediatric surgeons in Switzerland.
Methods: Scenario-based survey among Swiss pediatric surgeons. Respondents were asked to report on their management of children with blunt abdominal trauma.
Results: The response rate was 46% (26 of 54). The clinical signs considered as most important are abdominal examination and palpation (100%), auscultation (81%), genital exam (77%) and Glasgow Coma Scale (77%). The most frequent laboratory exams requested are urine analysis (100%), complete blood count (96%), liver function tests (85%) and coagulation tests (77%). 42% of the physicians ask for an abdominal ultrasound for every patient with blunt abdominal trauma. 58% report that some patients do not need a CT scan despite anomalies in the initial workup. There were significant variations in the clinical assessment of patients with minor blunt abdominal traumas. Abnormal ultrasounds, but not abnormal liver functions tests, prompt clinicians to obtain CT scans. When evaluating the probability of organ injury after a full workup, clinicians rely on the results of the ultrasound but not on the liver function tests. A normal CT scan does not appear to reassure physicians if the patient still presents mild abdominal pain.
Conclusion: There is a wide variation in the clinical assessment, request of laboratory tests and use of radiological exams among the Swiss pediatric surgeons. Further studies are required on the evaluation of abdominal organ injuries in children.

P095

Vipera aspis bites: what to do?

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Background: There are three different kinds of poisonous snakes with a similar venom in Switzerland: Vipera aspis, Vipera berus and Vipera ammodytes. Although they are not aggressive against humans, a viper bite can have serious consequences. The venom is a composite of proteins with enzymatic activities, resulting in a destruction of endothelial cells with increased transendothelial permeability and extravasation of electrolytes, albumin and erythrocytes. Consequences may be hemolysis, edema, hemoconcentration, hypovolemic shock, lactic acidosis, destruction of tissue and increased coagulation. Local symptoms can include swelling, compartment syndrome or rarely gangrene. Also, systemic symptoms and allergic reactions are observed. In Switzerland about 10–20 patients a year are asking for medical help after a viper bite. The incidence of serious reactions (grade 3) is 10–14%.
Case 1: A 5-year-old boy was bitten in the right thumb. He was admitted to the hospital for observation. In the course of hospitalization he developed increasing edema with livid discoloration of upper limb without spread to the chest, vomiting and nausea. Because it was a grade 2 reaction, no antivenom was administered. The boy was discharged home in a good general condition after 24 hours and was doing well one week later.

Case 2: An 8-year-old boy was bitten in the right index finger. During hospitalization increasing edema with crossover to the chest was observed. Because of a grade 3 reaction, antivenom was administered. While the edema significantly decreased, the livid discoloration of the arm initially increased. He was discharged after 48 hours. One week later he had complete resolution of edema and discoloration.
Recommendations after Vipera aspis bites: keep calm, immobilize the affected limb and go to the hospital. Observe in the hospital for at least 24 hours. There is no evidence in the literature that antihistaminics, steroids or epinephrine are of benefit for grade 2 reactions (local edema of the limb, moderate systemic reactions like hypotonia, vomiting and/or diarrhea). Nor is there evidence for the benefits of preventive treatment with antibiotics or heparin. Grade 2 reactions resolve spontaneously. Antivenom is the therapy of choice for grade 3 reactions (trunk oedema, anaphylactic reactions and/or circulatory shock) with good prognosis. Single cases with hypersensitivity reactions as side effects have been documented. Don't forget tetanus vaccination.

P096

Miracles Don't Always Come in Bottles …

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We report the case of a twelve year old female who after drinking a homeopathic medication, Miracle Mineral Solution (MMS), presented with a caustic gastric burn. Our patient presented to the emergency room with abdominal pain, vomiting, dysphagia, and cough 4 hours after ingestion of 10 ml of pure MMS (pH 11.6). The patient took the medication to relieve a sore throat. 15 minutes after ingestion, the patient began vomiting at home at which time her parents contacted poison control and were advised to come to the emergency room.
A naso-gastric tube was placed, blood gas analysis and electrolytes were performed showing no electrolyte imbalance, acid-base disturbance, or increased methemoglobin level. The patient was kept fasting with a gastric aspiration, and was treated with intravenous administration of a proton pump inhibitor (2 mg/kg/d). An upper endoscopy was performed 12 hours after ingestion, showing a severe, erosive, caustic gastritis, stage garden II-III. The patient was progressively refed and was able to be discharged symptom-free 5 days later. MMS is a 22.4% solution of sodium chlorite in distilled water primarily intended for water purification, bleaching, and stripping of textiles or papers. When this strong oxidant comes in contact with an acidic environment chlorine dioxide is produced, a highly endothermic compound. Alternative medicine promotes the use of MMS to cure a large number of illnesses such as AIDS, tuberculosis or cancer. Instructions available on the internet advise patients to make an oral solution by mixing 1 drop of MMS with 5 drops of lemon juice and 10 ml of water. The information available on the internet even advises patients to NOT stop the treatment although the patient experiences diarrhea or vomiting. A review of the literature revealed no case of intoxication with MMS, but two cases of sodium chlorite poisoning leading to breathing difficulties, renal failure, and death. The lethal dose of sodium chlorite is 10 to 15 grams. Our patient ingested 2.24 g. Caustic gastroesophageal lesions in childhood are very common with a large range of lesions, ranging from minor burns to severe necrosis. Complications such as esophageal stricture, perforation or gastric outlet obstruction may occur. An early endoscopic evaluation is necessary to adapt treatments and to reduce morbidity and mortality. Risks of certain alternative medicine use have to be well explained to parents to prevent the consequences of caustic agent ingestion.

P097

A male newborn with Netherton syndrome

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Introduction: Netherton syndrome (NS) is a rare autosomal recessive disease characterized by congenital ichthyosis and erythroderma, hair shaft abnormalities (trichorrhexis invaginata or "bamboo hair") and immune dysregulation. Mutations in SPINK5, encoding the serine protease inhibitor LEKTI, result in reduced expression or loss of LEKTI in epithelial cells of skin and mucosa.
Case report: A one-month old boy was admitted with irritability and generalized erythroderma with extensive skin scaling. A skin infection was initially suggested because of fever and increased inflammatory markers. Intravenous antibiotic therapy was started. The boy did not tolerate oral feeding (vomiting, diarrhea) and his general condition worsened including hypernatremic dehydration (maximal plasma sodium 156 mmol/L), hypoalbuminemia (19 g/l) and eosinophilia (1.3 G/l). Thus, differential diagnosis was extended to immunodeficiency syndromes incl. NS. Immunhistochemistry of skin biopsy demonstrated complete loss of LEKTI in epidermal keratinocytes consistent with NS. Extensive immunological analysis did not reveal any immunodeficiency. Increased insensible cutaneous losses required high fluid intake (200 ml/kg daily). Severe failure to thrive (4.17 kg at 2 months; birth weight 4.23 kg) led to parenteral nutrition via centrally placed venous catheter until the age of 4 months. Endoscopy showed chronic inflammation of the duodenum. Oral nutrition was switched to amino acid based formula because of the high risk of atopic diathesis in NS. The patient suffered from recurrent systemic infections incl. catheter infection with septic thrombosis of the right Aa. subclavia and axillaris and septicemia with S. aureus and MRSA. A monthly therapy with intravenous immunoglobulin (IVIG) was started at the age of 3 months based on a previously published study (J Allergy Clin Immunol 2009; 124;536–43). There were no further systemic infections and feeding was markedly improved; parenteral nutrition could be stopped after 2 doses of IVIG. The boy was discharged with a nasogastric tube at the age of 4.5 months.
Conclusion: NS is a rare multisystem disease with potentially life-threatening complications during the first weeks and months of life incl. neonatal erythroderma, severe hypernatremic dehydration, systemic infections and severe failure to thrive. We report the case of a young boy with early diagnosis of NS and clinical improvement after IVIG substitution.

P099

Alloimmune anaemia and neutropenia induced by maternal anti-Kell antibodies in a newborn

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Introduction: Maternal alloimmune antibodies to the Kell antigen can cause severe anaemia in the Kell positive fetus and newborn. In contrast to intrauterine fetal care, few literature exists about the postnatal course and management.
Case report: We describe the postnatal course of a second child of a Kell negative and previously not transfused mother with known anti-Kell antibodies whose alloimmune anaemia lasted until the seventh postnatal week. A hydrops fetalis was noticed at 22 1/7 gestational weeks. Intrauterine management consisted of eight erythrocyte transfusions. Directly postnatal his haemoglobin was stable. Immunoglobulins (IVIG) were given prophylactical once. Phototherapy was necessary for three days (Bilirubin max. 223 umol/l, 3 day p.p.). Three weeks postpartum his haemoglobin dropped to 69 g/l, with normal bilirubin, negative Coombs test, very low reticulocytes and neutropenia. Two erythrocyte transfusions were given. Additionally IVIG was administered four times in order to influence the likely anti-Kell mediated inhibition of the erythroid and myloid progenitor cells. At age of five weeks his reticulocyte count began to raise, the haemoglobin became stable, and for the first time his own blood group became detectable in parallel to the group of the transfused erythrocytes as sign of own haematopoiesis.
Pathophysiology: In anti-Kell alloimmune anaemia of the fetus and the newborn haemolysis is less or even absent in comparison to anaemia caused by Rhesus- or ABO-incompatibility. The cause is the quasi-aplastic phenotype of the affected individuals caused by direct inhibition of erythropoiesis and partially myelopoiesis due to the expression of the Kell-antigen on immature precursor cells. In vitro the progenitor cells are inhibited in further development.
Conclusions: In cases of Kell-alloimmune anaemia suppression of erythroid progenitor cells, not haemolysis is the leading cause for anaemia. a) Haemoglobin should be monitored for two months as a late decline can occur. b) Serum bilirubin is not a reliable marker for the residual activity of the anti-Kell antibody. c) Coombs test can be negative in transfused babies due to the absence of own blood production. d) The reticulocyte count will rise as the first sign of restored own haematopoiesis. e) Neutropenia is caused by myloid progenitor inhibition. f) Immunoglobulins are a sensible measure to increase own haematopoiesis by slowing the inhibition of precursors.

P100

Hemophagocytic Lymphohistiocytosis (HLH) as the initial presentation of Hodgkin lymphoma (HD)

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Aims: Atypical presentation of a Hodgkin lymphoma.
Case report: We report the case of a 14 year old female, admitted with a 2 week history of fever, wrist pain, a 3 kg weight loss and a rash on hands and feet. At admission, she was febrile at 39 °C, was in an excellent general condition with a maculopapular rash on the back of both hands, and the rest of the physical exam was normal. Laboratory investigations showed bicytopenia (white blood cells 1,9 G/l and platelets 100 G/l), hyperferritinemia (1080 mcg/l), liver dysfunction with

cytolysis, hypertriglyceridemia (2.2 mmol/l), LDH of 1155 U/l and low natural killer (NK) cell numbers (27/mcl). However, inflammatory markers and fibrinogen levels were normal and the abdominal ultrasound showed no hepatosplenomegaly. A bone marrow biopsy was performed and showed massive hemophagocytosis and erythrophagocytosis. This patient therefore fulfilled the criteria for hemophagocytic lymphohistiocytosis (HLH). A late-onset familial HLH seemed unlikely, and the investigations showed no signs of an infectious or rheumatologic etiology. However, a PET-CT showed multiple hypermetabolic axillary and thoracic lymphadenopathies. Histological examination of an axillary lymph node yielded the diagnosis of a Hodgkin lymphoma, stage 2B. The fever stopped spontaneously and the biological exams normalized without treatment. She then received chemotherapy according to the children's oncology group AHOD0031 protocol with 4 cycles of chemotherapy (Doxorubicin, Bleomycin, Vincristine, Etoposide)+/-radiotherapy.
Discussion: HLH is a rare but severe disease caused by dysregulation in NK T-cell function and characterized by fever, hepatosplenomegaly, cytopenia, liver dysfunction, hyperferritinemia, hypofibrinogenemia and bone marrow evidence of hemophagocytosis. HLH can be primary (genetic) or secondary (in the course of infections, autoimmune diseases, or malignancies etc.). Cancers most commonly associated with this syndrome are leukemias and lymphomas. The latter are usually non-Hodgkin lymphomas. HLH has also been described in Hodgkin lymphoma, but usually it occurs in patients having an advanced stage of disease.
Conclusion: In the setting of hemophagocytic lymphohistiocytosis, oncologic causes, including Hodgkin lymphoma, should be investigated.

P101

Is Acute Fibrinous and Organizing Pneumonia the mirror of an immune dysregulatory syndrome?

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Introduction: Acute fibrinous and organizing pneumonia (AFOP) is a recently described histological entity associated with a clinical picture of diffuse pulmonary disease. In children, clinical course is always fatal. We describe here the first case of non-fatal AFOP in a child with very severe aplastic anaemia (SAA). We hypothesize that AFOP may be part of an immune dysregulation syndrome.
Case report: A 10-year-old boy, initially diagnosed with fulminant hepatic failure of unknown etiology, with spontaneous recovery, further developed a SAA. He presented fever with cough and chest pain. Pulmonary CT scan revealed multiple small nodules disseminated in both lungs. Infectious investigations remained negative. Histological evaluation of the lung was consistent with AFOP.ATG (antithymocyte globulin, ATG Genzyme®) and cyclosporine (CSA) were started.
A week later he developed a serum sickness syndrome that responded to corticosteroid therapy. As the immunosuppressive therapy did not improve the SAA, CSA was stopped. One week later, there was a dramatic increase in aminotransferase levels, responding rapidly to high dose corticoids. A follow-up CT scan showed favourable evolution of the lung consolidation images. Hematopoietic stem cell transplantation (HSCT) with a HLA fully matched unrelated donor was performed with ATG- Fresenius®, fludarabine and cyclophosphamide with no major complications. At 17 weeks post-transplantation, he is free of any symptoms with a normal bone marrow and full chimerism.
Conclusion: AFOP is considered a variant of acute lung injury, and possibly a fibrinous type of diffuse alveolar damage. The literature reveals 11 cases of AFOP in children, all fatal, and provides the following differential diagnosis: infectious agents, drug-induced reactions, inhalation of toxic products, connective tissue diseases, altered immune status. This case raises the question whether AFOP is part of a multisystemic immune dysregulation or autoimmune syndrome because of the other organs (liver, bone marrow) involvement or because of the fact that the use of aggressive immunosuppressive therapy and eventually HSCT altered the fatal outcome. Further follow-up will show if HSCT will be successful in correcting the hypothesized immune dysregulation.

P102

Nutrient deficiency dermatitis in Cystic Fibrosis

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Cystic Fibrosis is the most common severe hereditary disease in Caucasian population. Typical presenting symptoms include meconium ileus, failure to thrieve and respiratory problems. Furthermore, atypical presentations with a great variety of symptoms are also known. Cutaneous manifestations are one of these rare primary manifestations of Cystic Fibrosis, most of them consistent with nutricient deficiency due to malabsorption. We report on a female infant presenting with severe seborrheic dermatitis. Primary findings induced anemia, hypoproteinemia and zinc depletion. Further investigation revealed the diagnosis of Cystic Fibrosis with a positive sweat test and genetic heterozygosity for F508del and 2347delG.

P103

Reliability & validity testing of a simplified version of the Seattle Pulmonary Exacerbation Score in patients with Cystic Fibrosis

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Background: Lung disease in Cystic Fibrosis (CF) is characterized by recurrent pulmonary exacerbations (PE). Nevertheless, there is a lack of a consensus how to define a PE in the paediatric as well as in the adult population of patients with CF. As a uniform outcome measure of clinical data would allow meaningful comparison in CF clinical trials across studies or centres, and since modalities of CF treatments are changing and new treatments are under investigation, applying a consistent definition of PE would be even more important for use as an outcome measure in clinical trials as repeatedly stated. We analysed the reliability and validity of a simplified version of the Seattle Pulmonary Exacerbation Score1 (SPEX), and compared its performance with the original score.
Methods: Cross-sectional observational case-notes review of paediatric CF patients in an outpatient setting. The Kappa – coefficient of agreement (definition < .40 poor, .40-.59 fair, .60-.74 good, >.74 excellent) was used to assess interobserver reliability, whilst analysis of the intraobserver reliability was assessed following re-evaluation 21 months later. Validity was analysed using the independent clinical assessment as "gold standard".
Results: Data from 39 consecutive consultations in 32 patients (13 males) were included. Age was from 4 months to 16 years (median age 8.7). In total 10 PE were diagnosed by the physician. Nine pulmonary exacerbations were identified using the SPEX, 8 of which were also diagnosed by the physician. In 26 consultations neither the score nor the evaluation by the physician identified a PE. In 4 cases, there was divergence between the 2 observers. The inter-observer reliability testing showed discordance in 4 of 39 consultations (10.1%) with a Kappa coefficient of 0.75. Intra-observer reliability 21 months later showed an intra-observer concordance of 97% (38 out of 39 consultations, Kappa coefficient of 0.94). Validity testing showed a Kappa coefficient of 0.92. The sensitivity and specificity of this score compared with the clinical judgement of the physician as gold standard was 100% and 96.30% respectively. Both the original and the simplified score performed equally.
Conclusion: The simplified SPEX could act as a consistent definition of a PE in clinical trials due to its excellent inter- and intraobserver reliability and validity.

[1] Rosenfeld, et al. Defining a pulmonary exacerbation in CF. J Pediatr. 2001

P104

Arterial Stiffness and body composition in children with cystic fibrosis

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Background: Increased arterial stiffness is an independent risk factor for cardiovascular disease. It occurs in inflammatory diseases indicating an ageing of the vasculature. In the present study we aimed to assess arterial stiffness and body composition in children with cystic fibrosis (CF).
Methods: Digital volume pulse analysis, with the computation of the stiffness index (SI) and pulse wave velocity between carotid and femoral artery (PWVcf), were determined in 20 CF children (7 female, median age 12.3, range 7.9–17.0 years) and in 49 healthy children, matched for age and gender. Body composition was assessed using a bioimpedance spectroscopy device (BCM-Monitor, FMC). Lean and fat mass were expressed by the Lean Tissue Index (LTI) and the Fat Tissue Index (FTI), and the hydration status as 'fluid excess' relative to the fluid content of healthy children. Reference data of body composition were obtained in 607 healthy children and adolescents.
Results: SI was significantly higher (6.4 ± 0.9 vs. 5.9 ± 0.8, p = 0.004) and there was a trend towards PWV increase (6.3 ± 1.5 vs. 5.7 ± 0.7, p = 0.12) in CF children compared to controls. Mean LTI was 13.8 ± 1.7 kg/m² and mean FTI was 3.8 ± 2.1 kg/m²; 20% of the CF children showed a reduced lean mass, however the fat mass was similar to controls. FTI and LTI displayed a strong linear relationship with BMI (r2 = 0.55, p = 0.0002 and r2 = 0.27, p = 0.02; respectively). PWV but

not SI was significantly correlated with LTI (r2 = 0.33, p = 0.01). PWV was increased in CF children positive for Pseudomonas aeruginosa or Stenotrophomonas maltophilia (7.2 ± 1.8 vs. 5.6 ± 0.8, p = 0.004) compared to the non-infected ones.
Conclusion: SI, indicating central arterial stiffness is increased in children with CF. Arterial stiffness in children with CF seems to be associated with Pseudomonas aeruginosa or Stenotrophomonas maltophilia colonization. Normal fat tissue distribution and reduced lean tissue are characteristics of children with CF. These findings have important implications for the management of cardiovascular functions in patients with CF and require further exploration so that cardio-vascular health can be maintained.

P105

Low immunoglobulin levels in patients with cystic fibrosis: reduced inflammation or sign of common variable immunodeficiency syndrome?

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Introduction: In children with cystic fibrosis (CF), low immunoglobulin (IgG) levels have been reported to be associated with significantly less severe lung disease. However, decreased IgG can be a sign for common variable immunodeficiency (CVID) and affect clinical outcome. The aim of this study was to analyze clinical and serological data of patients having low IgG levels in routine blood tests at annual assessment, particularly their antibody response to polysaccharide antigens.
Method: Retrospective chart review of demographic data of CF patients followed at the pediatric CF clinic throughout 2009. Clinical parameters (genotype, pancreas sufficiency, FEV1), presence of Pseudomonas aeruginosa (PA) and number of exacerbations per year were correlated with immunoglobulin and vaccination antibodies levels (antibodies to pneumococcal serotypes 14, 19, 23, 1, 5 and 7F measured by enzyme-linked immune-sorbent assay).
Results: 4 out of 60 patients (6.7%) had lower IgG-levels for age. Ages ranged from 1 year 8 months to 11 years, 2 boys, 2 girls. Three patients were delF508 homozygotes, one heterozygote composite delF508/G542X. All were pancreatic insufficient. FEV1 ranged from 74 to 108%. One patient never had colonization by PA, 2 had intermittent PA colonization and one was chronically infected. After conjugated vaccination all patients had protective antibodies against serotypes 14, 19, 23F. For serotypes not included in the vaccine, only one patient had protective titers for 1 out of 3 serotypes. None of the patients had received unconjugated pneumococcal vaccine. There was no significant clinical difference in FEV1, PA colonization or number of exacerbations according to IgG and vaccination antibody levels.
Conclusion: Cystic Fibrosis patients with low immunoglobulin levels have normal antibody response to protein antigens. However, despite recurrent infections, there seems to be delayed or deficient antibody response to polysaccharide antigens. Prospective studies are needed to evaluate the development of polysaccharide antibody responses in CF-patients to monitor for CVID. With early detection of CF by newborn screening program, long term follow up could be started early in childhood.

P107

Acute respiratory distress after working in a silo: a case report of silo-filler's disease

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Background: In adults, silo-filler's disease is an occupational lung disease which may occur during the harvest months of September and October. It is associated with toxic gas inhalation while working in a silo which has been filled with grass just previously. The disease presents as pneumonitis and bronchiolitis caused by inhalation of nitrogen oxides (NOx). Clinical signs include acute respiratory distress due to pulmonary edema. Later on, patients may develop bronchiolitis obliterans with rapid deterioration. Outcome depends on the duration of exposure and varies from death, chronic restrictive pneumopathy to complete recovery.
Case report: A 14-year-old farmer boy with well controlled asthma was working for a short time in a silo which had been filled with freshly cut grass three days ago. After leaving the silo, he developed acute severe dyspnea and was taken to the family doctor (GP). Peak flow, heart rate, blood pressure and oxygen saturation were normal. On chest auscultation there were no rales or wheeze. Acute asthma exacerbation was diagnosed by the GP. The patient was treated with intravenous steroids and discharged home. During the following night, respiratory distress increased despite maximal bronchodilator treatment. The boy was again presented to the GP's practice where oxygen saturation was still normal. Anti-asthma treatment with oral and inhalant steroids as well as bronchodilators were continued. The patient was referred to our pulmonology unit 11 days after the incident only, due to persistent dyspnea and fatigue. Assessment revealed mild tachypnea, but no abnormalities in lung function, chest x-ray and oxygen saturation. However, elevated methemoglobin level was measured. Silo filler's disease was diagnosed retrospectively. Specific treatment was not started at this late stage. The patient recovered spontaneously.
Conclusion: Silo-filler's disease is a rare incident occurring in farmer populations. Preventive strategies are crucial and include silos with good ventilation systems. Nevertheless, adolescents have to be briefed and smaller children to be kept away from silos by their parents. In case of an incident, rescuers have to be protected from inhaling the gases. Patients need to be treated with oxygen, systemic corticosteroids and in any case admitted and monitored in hospital for at least 48 hours. A normal oxygen saturation can mislead the diagnosis because of false normal values due to methemoglobinemia.

P108

Near fatal pneumococcal pneumonia in a 5 year old boy: Tension pleurothorax

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Background: Every child with clinical suspicion of a pleural effusion should have an ultrasound control and eventually a diagnostic puncture. But even after several days of minimal effusion this may suddenly accumulate and develop a major pleural effusion presenting as pleurothorax with cardial impairment which needs an emergency puncture.
Case report: A 5 year old boy is referred to the ER with a history of recurrent cough, fever and anorexia. He presents with minor respiratory distress and tachypnoea. Thoracal imaging shows a consolidation in the right lower lobe but only minor effusion. The boy is treated for pneumonia with pleural effusion with co-amoxiclav. No diagnostic puncture was done and the thoracal ultrasound was repeated on day 4 showing again minimal effusion. On day 6 the boy complained about thoracal pain and within 6 hours he showed severe respiratory distress. He was pale, short of breath and developed a remarkable tachycardia and low blood pressure. The x-ray showed a pleuropneumonia with major effusion of the right lobe with severe midline shift to the left. An emergency puncture was performed and 1000 ml of clear fluid evacuated over the following 2 days. All cultures remained negative but pneumococcal antigen in the urine and the effusion was positive.
Discussion: Children with severe pneumonia should be checked regularly for the development of an effusion. In the situation of a major effusion, an immediate diagnostic and therapeutic drainage must be performed and the child carefully observed.

P109

Deterioration of an adequate treated pneumonia – not always a pleural empyema

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Background: Compared to developing countries, community acquired pneumonia are less frequent in Switzerland, but they are still a challenge for paediatricians. Most of the pneumonias are viral induced, but many are due to bacteria. Treated with adequate antibiotical therapy, children generally recover within a few days. If there is no improvement within 2 to 3 days, pleural effusion and empyema have to be excluded. Rarely, other complications can occur.
Case report: A 14 months old boy with severe pneumonia was admitted to our hospital for parenteral antibiotic treatment. Despite adequate treatment, the child has deteriorated and pleural effusion was diagnosed and treated with a pleural drain. The laboratory findings showed a decreasing CRP but a haematocrit of 13%. Further diagnostics revealed a positive direct Coombs test, thrombocytopenia and fragmented red blood cells. Subsequently, the child developed renal insufficiency with anuria, and peritoneal dialysis was necessary. Renal markers improved gradually and dialysis could be stopped after 10 days. Pneumococcus serotype 3 was isolated from pleura's puncture liquid and the diagnosis of a pneumococcal-associated haemolytic uremic syndrome (P-HUS) was made. After two pneumothoraxes, the child slowly recovered and could be discharged after 5 weeks. Due to a persistent arterial hypertension, the child was treated with a beta blocker, which could be stopped 4 months later.
Conclusions: P-HUS, defined as microangiopathic haemolytic anaemia (Hb <100 g/l with fragmented red blood cells), thrombocytopenia (platelet count <130 G/l), acute renal impairment with oliguria and elevated plasma creatinine) is a rare event after a pneumococcal infection. HUS usually occurs after gastroenteritis with E.coli. Compared with E. coli gastroenteritis-associated (D+) HUS, patients with P-HUS are younger, have more severe renal and hematologic disease (more dialysis, more platelet- and red blood cell-transfusions), and a poorer clinical outcome.

P110

Discrepancy between clinical and radiological presentation of pneumonia in a 6-year old boy

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History: A 6-year old boy presents with cough and low fever (38.5°C). At the age of 2 years he was hospitalized with a pleural empyema and consecutive need of prolonged intubation and i.v.-antibiotics (bronchoscopy was performed to exclude a foreign body).
Clinical findings: Signs of upper respiratory tract infection. Oxygen saturation 98%, respiratory rate 26 per minute. On auscultation marked hypoventilation and on percussion marked hyposonority of the entire left hemithorax. No wheezing, no retractions and no nasal flaring.
Diagnostic investigations: laboratory findings: CRP 35 mg/l, total white blood cells 4.8 G/l, platelets 320 G/l, band neutrophils 2%, segmented neutrophils 46.5%, monocytes 8%, lymphocytes 41.5%. Radiography of the thorax: "white lung" on the left with mediastinal shift to the left. CT scan of the thorax: complete atelectasis of the left superior lobe, in a subsequent angio-CT scan detection of the aortic arch on the right, the brachiocephalic trunk originating on the left and agenesis of the left pulmonal artery.
Diagnosis: Vascular and parenchymal malformation of the lungs
Discussion: Unilateral lung agenesis or hypoplasia may have few symptoms resulting in only 1/3 of the cases being diagnosed. However, it has to be considered in the differential diagnosis of radiological "white lung". Radiological findings of unilateral lung or lobar collapse with a mediastinal shift toward the affected side may also refer to suspected foreign body aspiration. Pulmonary hypoplasia is usually secondary to other intrauterine disorders that produce an impairment of normal lung development. Conditions such as deformities of the thoracic spine and rib cage, pleural effusions with fetal hydrops, cystic adenomatoid malformation, congenital diaphragmatic hernia and oligohydramnios lead to diminished parenchymal growth and diminished vascular branching. In the case of few symptoms but impressive clinical findings in patients with a pleuropneumonia it is important to complete the diagnostic by further investigations.

Free communications

CL01

Auditory event-related response in newborns: a discrimative parameters for prediction of early cognitive development in preterms?

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Aim: Infants born before 32 weeks of gestational age (GA) have a higher risk of developmental retardation. No tool exists for early prediction of outcome. The aim of our study is to examine a simple non-invasive bedside investigation set for the early prediction of mental development of preterm infants.
Methods: 16 preterm infants (mean age at birth: 27.4 weeks; range 25.0–31.3, mean weight 884 g range 470 g–1530 g) were examined at the gestational age of 40.7 weeks (38.4–43.0). In a passive oddball paradigm, evoked brain potentials to pitch change detection will be recorded. The auditory event-related potentials (ERP) was registered with electrodes attached to frontal (Fz), central (Cz) and parietal (Pz) scalp sites according to the International 10–20 system. In the experimental setting, the silent awake or sleeping infants will be presented two tones with different frequencies. The standard tone is 1000 Hz, the deviant tone 1500 Hz. The standard tone occurs with a probability of 85%, while the deviant tone occurs with a probability of 15%. Three blocks of 500 stimuli will be presented to each newborn via headphones. Mismatch negativity (MMN) is a neurophysiological feature elicited by a discriminable change in some repetitive aspects of auditory stimulation. It is an auditory event-related potential, which is defined as the difference between the potentials from standard and rare tones in the time window between 150 and 300 ms after stimulus presentation. The development of the children was examined by Bayley Scales of Infant Development II at a mean age of 21.7 months (range: 18–25). MMN and developmental quotient was correlated.
Results: First: The difference between MMN in the first and the third block, demonstrating a habituation effect at Cz ($r = -0.659$, $p = 0.014$) is negatively correlated with birth weight. Infants with higher birth weight showed a more pronounced habituation (learning) effect. Second: The mental developmental index value is significantly negative correlated with the mean MMN about all three blocks at Pz ($r = -0.561$, $p = 0.046$). Infants with higher developmental quotient show a more pronounced neurophysiological differentiating reaction.
Conclusion: To detect differences between two tones are interpreted as a pre-attentive cognition. In preterm infants MMN as one of the ontogenetically earliest cognitive processing in the prefrontal cortex seems to have a predictive value for the mental development.

CL02

Neonates born to syphilis positive mothers: management and outcome

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Introduction: Acquired syphilis has re-emerged in Western Europe in the last decade, mainly due to immigrated cases. As a consequence, the nationwide mandatory laboratory notification system has been re-established in Switzerland in 2006. In contrast to worldwide guidelines, screening for syphilis in pregnancy is not generally recommended in Switzerland and usually only performed in pregnant women considered at high risk. There has been an increasing trend in the incidence of laboratory confirmed syphilis among women (2006: 185 cases; 2009: 263 cases), with the highest proportion among women in childbearing age (70%). Until now, national data of syphilis in pregnant women is missing.
Methods: To provide first data in Switzerland, we conducted a retrospective study at our hospital with a large maternity unit to evaluate the total numbers of pregnant women with positive syphilis (TPPA test positive) and the trend of confirmed diagnosis over the last 10 years. Additionally, we evaluated the clinical management and analyzed the outcome of the newborns through Captia-IgM measurements.
Results: Positive syphilis serology was noted in 9 out of the 13968 pregnant women. Four women had residual antibody titre and 5 were diagnosed for syphilis (re-)infection during pregnancy. Out of these 5 women, 4 were adequately treated. Regarding their offspring, 8 of the 9 newborns were tested serologically. In 2 of the newborns with adequately treated mothers, a single dose Penicillin i.m. was administered directly after birth. There was 1 newborn of the affected women diagnosed maternal syphilis with congenital syphilis (CS) that was treated according to international guidelines (Penicillin i.v. for 10 days).
Conclusion: CS is a preventable disease with pregnancy screening being a simple, cost-effective and effective measure, both for prevention of the disease as well as for treating the pregnant women and their partners. Our study shows that CS exists in Switzerland, too. As the total number of conducted syphilis serologies in pregnancy in our study is not known, the number of syphilis positive mothers is highly underestimated. It could also be possible that cases of CS remained undetected and untreated during the study period. The persistence of CS in Switzerland reflects a gap of prenatal care and syphilis control programs. An effective assessment and management of syphilis in pregnant women and their newborns is mandatory and requires an interdisciplinary approach.

CL03

Cell death and autophagy after severe hypoxic-ischemic encephalopathy in term newborns

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Introduction: Various studies from hypoxic-ischemic animals have investigated neuroprotection by targeting necrosis and apoptosis with inconclusive results. Three types of cell death have been described: apoptosis, necrosis and more recently, autophagic cell death. While autophagy is a physiological process of degradation of cellular components, excessive autophagy may be involved in cell death. Recent studies showed that inhibition of autophagy is neuroprotective in rodent neonatal models of cerebral ischemia. Furthermore, neonatal hypoxia-ischemia strongly increased neuronal autophagic flux which is linked to cell death in a rat model of perinatal asphyxia. Following our observations in animals, the aim of the present study was to characterize the different neuronal death phenotypes and to clarify whether autophagic cell death could be also involved in neuronal death in the human newborns after perinatal asphyxia.
Methods: we selected retrospectively and anonymously all newborns who died in our unit of neonatology between 2004 and 2009, with the following criteria: gestational age >36 weeks, diagnosis of perinatal asphyxia (Apgar <5 at 5 minutes, arterial pH <7.0 at 1 hour of life and encephalopathy Sarnat III) and performed autopsy. The brain of 6 cases in asphyxia group and 6 control cases matching gestational age who died of pulmonary or other malformations were selected. On histological sections of thalamus, frontal cortex and hippocampus, different markers of apoptosis (caspase 3, TUNEL), autophagosomes (LC3-II) and lysosomes (LAMP1, Cathepsin D) were tested by immunohistochemistry.
Results: Preliminary studies on markers of apoptosis (TUNEL, caspase 3) and of autophagy (Cathepsin D, LC3II, LAMP1) showed an expected increase of apoptosis, but also an increase of neuronal autophagic flux in the selected areas. The distribution seems to be region specific.
Conclusion: This is the first time that autophagic flux linked with cell death is shown in brain of human babies, in association with hypoxic-ischemic encephalopathy. This work leads to a better understanding of the mechanisms associated with neuronal death following perinatal asphyxia and determines whether autophagy could be a promising therapeutic target.

CL04

Benign neonatal sleep myoclonus: a systematic review of the literature

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Objective: Neurologically normal term infants sometimes present with repetitive, rhythmic myoclonic jerks that occur during sleep. The condition, which is traditionally resolved by 3 months of age with no sequelae, is termed benign neonatal sleep myoclonus. The goal of this review was to synthesize the published literature on benign neonatal sleep myoclonus.
Methods: The US National Library of Medicine database and the Web-based search engine Google, through June 2009, were used as data sources. All articles published after the seminal description in 1982 as full-length articles or letters were collected. Reports that were published in languages other than English, French, German, Italian, Portuguese, or Spanish were not considered.
Results: We included 24 reports in which 164 term-born (96%) or near-term-born (4%) infants were described. Neonatal sleep myoclonus occurred in all sleep stages, disappeared after arousal, and was induced by rocking the infant or repetitive sound stimuli. Furthermore, in affected infants, jerks stopped or even worsened by holding the limbs or on medication with antiepileptic drugs. Finally, benign neonatal sleep myoclonus did not resolve by 3 months of age in one-third of the infants.
Conclusions: This review provides new insights into the clinical features and natural course of benign neonatal sleep myoclonus. The most significant limitation of the review comes from the small number of reported cases.

CL05

The Grischuna autism experience: A retrospective study over the last 10 years

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Introduction: Some years ago autism and autism spectrum disorders (ASD) were regarded as very rare disorders with a prevalence of 3–4/10000 children. Today the prevalence is about 1/150 children or about 0.6%, nearly that of epilepsy. In 2005 we started with a screening program for autism and ASD in the neuropediatric outpatient clinic with nearly 700–800 admissions a year. From 2006 we started also with the diagnosis of these disorders with the ADOS (Autistic diagnostic observation schedule) and the ADI-R (Autistic diagnostic interview), the so called diagnostic goldstandard. We used the FSK (Questionnaire social communication) and the CBCL (Child behaviour checklist) for children at the age of 4 or older and the CHAT (Checklist for autism in toddlers) for younger children. We reviewed our cases from 2000–2004 without screening and from 2005 till today (March 2010) with screening.
Results: From 2000–2004 we saw only 1–2 children every year with the new diagnosis of autism, most of them with the early infantile type (Kanner). From 2005 till today we made the diagnosis of autism or ASD in 53 children and adolescents, 7 girls and 46 boys. Autism, mostly of them with the Kanner-type in 13 children, Asperger also in 13 children and adolescents and ASD in 27 cases. Many of the children with Asperger or ASD had a diagnosis of ADHD and came to the neuropediatric evaluation cause of persisting behaviour- and schoolproblems.
Conclusion: By screening for autism or ASD we found a five-to sixfold increase of these cases, otherwise missed. The diagnostic criteria for ADHS (Attention-deficit-hyperactivity disorder) are wellknown to all pediatricians, but they should also consider the possibility of an ASD in their investigations for these children, otherwise they will miss them. Today we have good screening instruments for these conditions, but you have to use them.

CL06

Long-term pulmonary outcome of bronchopulmonary dysplasia

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Aim: To study the longitudinal changes of lung function from adolescence to mid-adulthood in subjects who were born prematurely, and who had been diagnosed with bronchopulmonary dysplasia (BPD) in infancy.
Methods: A cohort of 14 individuals with BPD (gestational age 31.8 ± 2.9 weeks, birth weight 1795 ± 456 g) were followed longitudinally by lung function testing. Five of the 14 subjects had been tracheotomized in early childhood.
Results: Patient characteristics in 2008: 3/14 had persisting upper airway obstruction (2 from subglottic stenosis, 1 due to vocal cord paresis). 7/14 were smokers and/or atopic. 6/14 had current respiratory complaints (exercise intolerance, chronic cough, or asthma).

Lung function:

Year of study	1983	1987	2008	p (1987 vs. 2008)
Age (years)	14.9 (3.6)	18.4 (3.2)	38.1 (3.2)	
TLC (%predicted)	94.6 (9.5)	95.9 (12.5)	113.2 (19.0)	0.02
RV/TLC (%)	23.7 (4.9)	26.1 (7.3)	39.4 (8.7)	< 0.001
FEV_1/VC (%)	73.8 (12.8)	72.2 (9.3)	69.7 (10.9)	not sign.

Means (SD). TLC = total lung capacity; RV = residual volume; normal value for RV/TLC ratio <30%; FEV_1 = forced expiratory volume in 1 second; VC = vital capacity; normal value for FEV_1/VC >75%.

Conclusions: Mild airway obstruction remains stable through early adulthood, represented in the table by only minor changes of the FEV1/VC-ratio. A significant increase of the TLC and the RV/TLC-ratio, however, indicate increasing hyperinflation. This suggests that aging may be associated with early emphysematous changes in a significant proportion of BPD-survivors.

CL07

Chest physiotherapy in bronchiolitis: a randomised trial assessing passive expiratory manoeuvres

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Introduction: Chest physiotherapy is not recommended as routine care by most international guidelines for the management of infants with bronchiolitis due to the lack of proven benefits. We undertook an open randomized trial to evaluate the effectiveness of chest

physiotherapy using passive acceleration of expiratory flux in infants hospitalized for bronchiolitis. We compared the daily improvement of a severity score, the length of hospital stay and the occurrence of complications between patients with and without physiotherapy.
Methods: Children less then 1 year admitted for bronchiolitis in a tertiary hospital during 2 consecutive RSV seasons. All children received standard of care (minimal handling, oxygen therapy for saturation SpO2 ≥ 92%, fractionated meals and rhino-pharyngeal suctioning). Children were randomized to group 1 with physiotherapy (Prolonged Slow Expiratory technique PSET, Slow Accelerated Expiratory technique ASET and Coughing Provoked CP) or group 2 without physiotherapy.
Results: 99 eligible children (mean age 109 months, 44 girls), 50 in group 1, 49 in group 2. All baseline variables were comparable between groups. The severity score (general well being items and respiratory items) was similar between groups. The mean respiratory rate, the mean SpO_2 and the change in clinical score over time did not improve faster in the group with physiotherapy. Overall complications were rare but tended to occur more frequently in the group without physiotherapy ($P = 0.21$).
Conclusion: This study shows the absence of effectiveness of physiotherapy using passive expiratory maneuvers in infants hospitalized for bronchiolitis. It seems justified to recommend against the routine prescription of physiotherapy in these patients. Further work is needed before extending this finding to patients with bronchiolitis treated as outpatients.

CL08

Curcumin inhibits deleterious effects of respiratory tract bacteria on human oropharyngeal cells – potential role in chemotherapy-induced mucositis?

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Purpose: The dietary spice curcumin exerts its anti-inflammatory activity via inhibition of nuclear factor-kB. Oropharyngeal epithelia and residing bacteria closely interact in inflammation and infection. This in vitro model investigated the effects of curcumin on bacterial survival, adherence and invasion of upper respiratory tract epithelia and studied its anti-inflammatory effect. We aimed to establish a model, which could offer insights into the host-pathogen interaction in cancer therapy-induced mucositis.
Methods: Moraxella catarrhalis (Mcat) and the oropharyngeal epithelial cell line Detroit 562 were used. Time-kill curves assessed the inhibition of bacterial growth, adherence assays and gentamicin protection assays determined the effect of curcumin-preincubation of cells on bacterial adherence and invasion. Curcumin-mediated inhibition of pro-inflammatory activation by Mcat was determined via interleukin-8 concentrations in the supernatants. The synergistic role of secretory IgA (sIgA) on adherence was investigated.
Results: Curcumin was bactericidal at concentrations >50 µM. Pre-incubation of Detroit cells for 60 minutes demonstrated that concentrations >100 µM inhibited bacterial adherence. Together with sIgA, curcumin inhibited adherence at concentrations ≥50 µM. Both 100 and 200 µM curcumin significantly inhibited Mcat cell invasion. Curcumin inhibited Mcat-induced pro-inflammatory activation by strongly suppressing IL-8 release. At a concentration of 200 µM, 10 minutes of curcumin exposure inhibited IL-8 release significantly, complete suppression required a pre-exposure time of ≥45 minutes.
Conclusion: Curcumin – in clinically relevant concentrations for topical use - displayed a strong antibacterial effect against a facultative upper respiratory tract pathogen by inhibiting bacterial growth, adherence, invasion and pro-inflammatory activation of upper respiratory tract epithelial cells in vitro.

CL09

Pulmonary function test decline in patients with post-infectious bronchiolitis obliterans despite treatment

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Rationale: Post-infectious bronchiolitis obliterans (PBO) is a rare form of chronic obstructive lung disease that follows a severe insult to the lower respiratory tract, resulting in fibrosis of the small airways. It has been suggested that PBO is a non progressive disease; however, there is limited information supporting this statement or the evolution of PBO with anti-inflammatory and intravenous immunoglobulin (IVIG) therapy. The aim of this study was to determine the change in pulmonary function tests over time in patients with PBO treated with inhaled corticosteroids (ICS), and macrolides and/or IVIG.
Methods: Six children with PBO, ages 6 to 15 years, were retrospectively studied between 1999 and 2009. All the patients received inhaled corticosteroids. In addition, three patients received IVIG therapy and two received macrolide therapy. Spirometry, lung volumes, and the carbon monoxide lung diffusion capacity (DLCO) were performed in accordance with the ATS guidelines. Lung function was monitored over time and the average rate of change was calculated using a linear regression model.
Results: All the patients showed data consistent with mild to severe obstruction and air trapping. The average values at baseline for forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1), FEV_1/FVC ratio, and forced expiratory flow 25–75 (FEF25-75) were 58%, 44%, 86%, and 28% respectively. FVC increased at a rate of 2.4% per year ($p > 0.05$). The forced expiratory volume in 1 sec (FEV_1) did not change significantly over time ($p > 0.05$). However, The FEV_1/FVC decreased at a rate of 5% per year ($p < 0.05$). The forced expiratory flow 25-75 (FEF25-75) fell at a rate of 3.5% per year ($p < 0.05$).
Conclusion: Pulmonary function in childhood PBO is characterized by significant airway obstruction which worsens over time despite anti-inflammatory and immunomodulatory therapy. FEV_1 remained stable and FEV_1/FVC ratios declined, suggesting impaired airway but not lung growth. Further studies will be needed to validate these observations with this small group of patients.

CL10

Does this child have a foreign body aspiration?

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Context: Foreign body aspiration (FbA) is a serious problem in children. Accurate clinical and radiographic diagnosis is important because missed or delayed diagnosis can result in respiratory difficulties ranging from life-treatening airway obstruction to chronic wheezing or recurrent pneumonia. Bronchoscopy also has risks and accurate clinical and radiographc diagnosis can support the decision of bronchoscopy.
Objective: To rewiev the diagnostic accuracy of clinical presentation (CP) and pulmonary radiograph (PR) for the diagnosis of FbA. There is no previous rewievMethods: A search of Medline is conducted for articles containing data regarding CP and PR signes of FbA. Calculation of likelihood ratios (LR) and pre and post test probability using Bayes theorem were performed for all signs of CP and PR.
Inclusion criteria: Articles containing prospective data regarding CP and PR of FbA.
Exclusion criteria: Retrospectives studies. Articles containing incomplete data for calculation of LR.
Results: Five prospectives studies are included with a total of 585 patients. Prevalence of FbA is 63% in children suspected of FbA. If CP is normal, probability of FbA is 25% and if PR is normal, probability is 14%. If CP is pathologic, probability of FbA is 69–76% with presence of cough (LR = 1.32) or dyspnea (LR = 1.84) or localized crackles (LR = 1.5). Probability is 81-88% if cyanosis (LR = 4.8) or decreased breaths sounds (LR = 4.3) or asymetric auscultation (LR = 2.9) or localized wheezing (LR = 2.5) are present. When CP is anormal and PR show mediatinal shift (LR = 100), pneumomediatin (LR = 100), radio opaque foreign body (LR = 100), lobar distention (LR = 4), atelectasis (LR = 2.5), inspiratory/expiratory abnormal (LR = 7), the probability of FbA is 96–100%. If CP is normal and PR is abnormal the probability is 40–100%. If CP is abnormal and PR is normal the probability is 55-75%.
Conclusions: This rewiev of prospective studies demonstrates the importance of CP and PR and an algorithm can be proposed. When CP is abnormal with or without PR pathologic, the probability of FbA is high and bronchoscopy is indicated. When CP and PR are normal the probability of FbA is low and bronchoscopy is not necessary immediatly, observation should be proposed. This approach should be validated with prospective study.

CL11

Asthma education in canton Valais

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Asthma is the most common chronic disease in childhood, with a 10% prevalence. Passive smoking and allergen (dust mites) eviction as well as patient education are the most effective, evidence-based non pharmacologic interventions to improve disease control, quality of life and long-term prognosis of these children. In and out pediatricians already invert a considerable time to inform individual patients and parents about asthma, but lack of time and stress related to practice and emergency settings limit the efficiency of such a teaching approach. Moreover there is no doubt that parents and patients

interactions and support improve the outcome of asthma teaching. Therefore, we developed a new teaching concept especially tailored for children and parents, including action plan, asthma quality of life questionnaire and a booklet. It explains in an easy and illustrative way the various symptoms and the classification of asthma. It also advices how to avoid common triggers. Antiasthmatic drugs are described, with emphasis on difference between acute and chronic medication, as well as different inhalation techniques. The teaching sessions for asthmatic children and their parents last 2x90 minutes. It has been worked out by hospital and practice pediatricians, pediatric and specialized nurses, and a physiotherapist to better answer personal needs of children and parents with the following objectives: recognition of asthma attacks, adequate use of medications to avoid emergency visits, hospitalizations and school absences. During teaching sessions, the interaction between families is stimulated and allowing also teaching by peers, which confers a membership and support feeling. Our presentation will detail the working-out and the first experiences with asthma education in Valais. Such an education programme is important to decrease morbidity of asthma in children.

CL12

Recurrent spontaneous pneumothorax: treatment by simple talc poudrage under videothoracoscopy and local anesthesia

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Patient 1: A 14-year-old boy presented with left complete pneumothorax which was drained by a chest tube. However, the pneumothorax recurred every time the drain was clamped. After 8 days of unsuccessful attempts, a videothoracoscopy was performed under local anesthesia. Surprisingly, many blebs and bullae were discovered on both the apical and basal regions of the lung parenchyma. Talc (1 g) was gently sprayed over the visceral pleura. The patient was discharged after 4 days but relapsed 8 days later and was treated by surgical pleurectomy. No skin lesions or signs of Marfan syndrome were observed and alpha 1-antitrypsin deficiency was also excluded. Despite a negative family history for recurring pneumothoraces or renal cancers, Birt-Hogg-Dubé syndrome is suspected and results of FLCN gene analysis are pending.
Patient 2: A 15-year-old boy suffered from left complete neumothorax, successfully drained by a chest tube. Five months later a new pneumothorax occurred controlaterally, on the right lung, and was successfully treated by the same technique, which showed again bullae on the lung parenchyma. Unfortunately, after 11 months the left pneumothorax recurred, requiring wedge resection of the left superior lobe with mechanical pleural abrasion. 3 months later, a third partial left recurrence of pneumothorax happened, successfully controlled by a chest tube. Physical examination suggested Marfan syndrome, no skin anomalies were noted and family history was non inductive for any known relevant predisposing disease. Alpha 1-antitrypsin levels were normal. Echocardiography revealed mitral valve prolapse, furthermore supporting the Marfan syndrome hypothesis. FBN1 and FLCN gene analysis was negative and TGFBR1/2 mutation search is ongoing.
Take home message: Simple talc poudrage under videothoracoscopy is a safe mininvasive technique to control persistent or recurrent pneumothorax, allowing, in case of relapse, to perform surgical pleurectomy with or without bullectomy. Recurrent spontaneus pneumothoraces in children should make one consider a genetic etiology, such as Marfan syndrome or the cancer-prone Birt-Hogg-Dubé syndrome.

CL13

Association between breastfeeding and lung function in childhood

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Aim: It has been postulated that breastfeeding may influence lung development in children, but findings are inconclusive. Some studies reported even a reduced lung function effect in school-age children of asthmatic mothers (Guilbert, AMJRCCM, 2007). We examined this relationship in a large population-based cohort.
Method: Breastfeeding and its duration was recorded at recruitment in 1998 in children from Leicestershire, UK. We performed spirometry (FVC, FEV_1, and FEF50) after several years in a nested sample (N = 1005) of children aged 9–13. Lung function in breastfed and non-breastfed children was compared using linear regression adjusting first for anthropometric factors (height, weight, age, and sex) and then also for potential confounders (birth weight, ethnicity, maternal asthma and parental smoking). Cut-offs of 3 months and 6 months for breastfeeding duration and effect modification by maternal asthma were also tested.
Results: Of the 1005 children in the sample 673 (67%) children were breastfed, 363 (36%) for over 3 months and 222 (22%) for over 6 months; 176 (17%) children had asthmatic mothers. We found no difference between children who were breastfed or not breastfed when adjusting for anthropometric factors: FVC(L) 2.58 vs. 2.62 (p = 0.06); FEV_1 (L): 2.24 vs. 2.27 (p = 0.19); FEV_1/FVC(%): 86.9 vs. 86.3 (p = 0.18) and FEF50(L/s): 2.92 vs. 2,88 (p = 0.45). Results remained similar after adding the confounders to the model (all p >0.37) or when looking at children breastfed for >3 months or >6 months.
There was little evidence for effect modification by maternal asthma (all p-interaction >0.09).
Conclusion: In our dataset breastfeeding was not associated with lung function assessed by spirometry at school age. Importantly, we found no evidence for a harmful effect of breastfeeding in children with asthmatic mothers.
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CL14

Use of NSAIDS compared to paracetamol as potential risk factors for asthma

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Introduction: Use of paracetamol has been associated with an increased risk of asthma in several epidemiological studies. In contrast, it has been suggested that non-steroidal anti-inflammatory drugs (NSAIDs) might be protective (Kanabar, Clin Ther 2007), but data relating to these drugs are scarce.
Methods: Prevalence of asthma and intake of analgesics in the past 2 years were assessed by questionnaire in 2008 in young adults (≥;16 years) diagnosed with cancer between 1976 and 2003 (Swiss Childhood Cancer Survivor Study). In a multivariate logistic regression we analysed the association between asthma and intake of paracetamol only, NSAIDs only or their combination, adjusting for age, sex, cancer diagnosis, cancer therapy and time since diagnosis.
Results: Of the 1293 participants (response rate 68%), 83 (6%) reported asthma and 845 (65%) intake of analgesics in the past 2 years. Of these, 257 (29%) took paracetamol only, 224 (25%) NSAIDs only, 312 (35%) a combination of both and 52 (6%) other analgesics. Adjusted Odds ratios for asthma were 2.2 (95% CI 1.0-4.7; p = 0.04), 1.9 (0.9–4.3; p = 0.12) and 2.9 (1.4–6.1; p <0.01) in those using paracetamol only, NSAIDs only or their combination respectively.
Conclusion: These cross-sectional data in a selected population do not support a protective effect of NSAIDs against asthma, neither taken alone nor in combination with paracetamol. All analgesics were positively associated with reported asthma episodes in the past two years. This can be explained by reverse causation, with intake of analgesics being a result rather than a cause of asthma events. Randomised controlled trials in unselected populations are needed to clarify the direction of causation.

CL15

Validating of the Tucson asthma predictive index in an independent cohort

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Introduction: The loose and stringent asthma predictive indices (L_API and S_API; Castro-Rodriguez AJRCCM 2000), very popular clinical decision rules for children, need external validation. We assessed the predictive performance of the API in an independent cohort and compared it with the simple predictor "frequency of wheeze".
Methods: 3155 3-year old children from a population-based cohort study in Leicestershire (UK) were classified as being at no, medium (L_API) or high (S_API) risk for later asthma. We then compared odds ratio (OR), positive predictive value and specificity of these indices at 7 and 10 years with results from Tucson. Predictive performance was then compared to predictions based only on frequency of wheeze (any wheeze, ≥4 attacks).
Results: Prevalence of L_API and S_API were 33% and 13% in our cohort vs. 24% and 6% in Tucson. In Leicester, children with L_API had an increased risk of asthma (OR 5.2 and 6.3 at ages 7 and 10 respectively). For children with S_API, ORs were 7.7 and 6.7 for ages 7 and 10. These results were comparable to those published for Tucson (OR 5.5 and 2.6 for L_API; 9.8 and 4.3 for S_API). The positive

predictive value for asthma at age 10 was 26% in our cohort vs. 27% in Tucson for L_API, and 37% vs. 42% for S_API. Specificity of S_API was above 90% at both ages in both cohorts. Risk prediction based on frequency of wheeze yielded similar results to L_API and S_API.
In conclusion, performance of the API in the validation cohort was comparable to that in the original study. However, a simpler risk classification based only on frequency of wheeze performed comparably in our population. This highlights the need for improved clinical decision rules.
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CL16

Liver transplantation for inborn errors of metabolism in children: the Geneva experience

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Background: Liver transplantation (LT) is accepted as the treatment of choice for inborn errors of metabolism (IEMs) that are difficult to manage medically or are associated with end-organ damage secondary to toxic metabolites.
Aim: The aim of this study was to evaluate retrospectively the outcomes of the pediatric cohort transplanted in Geneva for IEMs.
Methods: The Geneva transplant registry was queried for LT and IEMs in children. The cohort was then analyzed for demographic parameters, pre- and post transplant variables, and long term outcomes including actuarial survival, associated renal transplant, and special diet post LT.
Results: 16/100 patients required LT for IEMs (16%). Indications were similar to published series from other centers (4 had Wilson's disease = 25%). Median age at transplant was 9 years [0.5–17] in contrast to 1.5 years for the overall cohort. No living-related transplants were performed for IEMs. Actuarial survival was 90 % for the overall cohort (n = 100) and 88% for the IEM cohort (p = ns). There were 2 early deaths owing to acute, non-metabolic complications (12.5%). Median follow up was 8.9 yrs. 2/16 patients with oxalosis (12.5%) required associated renal transplantation. Patients with oxalosis or OTC deficiency were maintained on specific diets post LT with the view to optimize metabolic stability during growth and development. No patient required re-transplantation. Patients requiring phototherapy pre-LT for Criggler Najjar were weaned post LT.
Summary and conclusion: LT for IEM is an acceptable therapeutic option offering good actuarial survival in our center. Further studies are required 1) to determine optimal timing for transplant to minimize the need for combined transplants 2) to establish the necessity for post LT dietary restrictions in patients with IEMs.

CL17

Psychomotor evaluation of pediatric liver transplant recipients and parental assessment before and after transplantation

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Increasing evidence points to psychomotor deficits in pediatric liver transplant (LT) recipients. Parental involvement and family dynamics are important for psychomotor development, and both are challenged in the families of children with life-threatening disease.
Aims: 1) to assess children and parents individually, 2) to assess the parent-child relationship 3) to look for correlations between parental functioning and patient outcome.
Methods: Patients, parents and the child-parent pair were assessed using age-appropriate scales before transplant, 1 year- and 2-years-following transplant. Written and spoken French or German was required. The study was approved by the institutional ethics committee.
Results: Subjects: 21/80 patients participated in the study over 2 yrs. 57% of families were Swiss. Indications for LT were similar to those reported previously. 4 patients were not evaluated pre LT. 19 mothers and 16 fathers were evaluated pre-LT, while only 8 fathers were seen post-LT. Development quotient (DQ): No subjects scored in the 'very good' range. There was an increasing proportion of children with deficits from LT to 2 yrs: 17.6% vs 28.6%. Subjects 0–2 yrs were more likely to have normal DQ at transplant (66.7% vs 50% for older children). Abnormal development was more prevalent 2 yrs post-LT among patients transplanted in the older age group (p = 0.02). Mother-child relationship was measured as normal in 59% of families pre-LT, increasing to 67% at 2 yrs. The trend was more favourable when the child was transplanted as an infant (p = 0.014 at 12 months post LT, P = 0.022 at 24 months post LT). Protective factors for normal DQ: a) higher maternal score pre-LT (p = 0.03), b) diagnosis of biliary atresia at all time points, and c) German or French mother tongue pre-LT. Parents: Mothers' performance score improved from a mean of 59% pre-LT to 71% post-LT. Positive predictors of normal functioning included siblings and a diagnosis of biliary atresia. Employment was predictive of better adaptation at 2 yrs. Fathers scored higher than mothers for performance at all time points.
Conclusions: In this representative cohort, we show that there is a trend toward increasing psychomotor impairment post LT, confirming the findings of others. Novel findings include: parental education has unpredictable effects on DQ peri-transplant, maternal functioning is more severely affected than paternal, and employment and siblings aid in the recovery of maternal functioning.

CL18

A successful intervention to increase immunization and protection in liver transplanted children: tailored recommendations based on serologies

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Despite well established vaccine recommendations for solid organ transplanted patients, children referred for orthotopic liver transplantation (OLT) in Geneva, Switzerland, were not vaccinated optimally. In 2002, new guidelines recommended to base catch-up immunization schedules on serum antibody titers against vaccine-preventable diseases assessed before and after OLT. We measure here the results of this intervention by comparing vaccine coverage and antibody titers in the pre- (1990–2002, P1) and the post- (2003–2008, P2) intervention cohorts. P1 children (n = 44, 57% female, mean age at OLT 4.4yr, range 0.6–16.8yr) and P2 children (n = 30, 47% female; mean age at OLT 4.5yr, range 0.5–16.5yr) were evaluated. At the pre-OLT visit, DT, Streptococcus pneumoniae (SPn) and MMR serologies were checked more frequently in P2 than P1 children (P = 0.001, <0.001 and 0.021 respectively). More P2 than P1 patients were up-to-date for DTaP (70% versus 43%, P = 0.023) and MMR (74% versus 44%, P = 0.049) or had received at least one dose of HBV, HAV, SPn and VZV vaccines (P <0.001, 0.011, <0.001 and 0.029 respectively). In patients to whom pre-OLT catch-up immunizations were recommended, HBV, HAV, SPn, MMR and VZV serologies were assessed more frequently in P2 (P <0.001, <0.001, 0.001, 0.013 and <0.001 respectively). Pre-OLT antibody titers were higher in P2 patients for D, T and Hib (P = 0.007, 0.011 and 0.016 respectively). One year post-OLT, DT, SPn, MMR and VZV serologies were more frequently checked in P2 children (P <0.001, <0.001, <0.001 and 0.159 respectively). Antibody titers were higher in P2 for D, T and HAV (P <0.001, 0.008 and 0.009 respectively). Confounding factors such as gender, age at OLT or diagnosis did not explain these differences. Among P2 patients, pre- and post-OLT titers for D, T, Hib, HBV, SPn14 and SPn19 were correlated (P = 0.025, 0.005, <0.001, 0.005, 0.045 and 0.013 respectively); however, there was no influence of pre- or post-OLT titers on titers after post-OLT booster immunization. We couldn't demonstrate an influence of gender, diagnosis, number of vaccine doses before OLT on titers, either after OLT or after post-OLT booster immunization. Protection against vaccine-preventable diseases of high-risk children such as OLT patients may be significantly improved by tailored recommendations using serologies to vaccine-preventable diseases.

CL19

Assessing Accuracy of Interpretation of a Rapid Celiac Assay in a Ward Setting

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Celiac Disease(CD)is a autoimmune condition that can cause several manifestations largely underdiagnosed. To allow faster counseling and treatment, a prospective study has been conducted from April 2008 to December 2009 in a Gastroenterology consultation ward to evaluate the clinical accuracy of screening CD in high risk populations (HRP) using a new point-of-care device.
Methods: Patients were enrolled at the pediatric Departement of the Hospital of Geneva.Local ethical committee approval was granted. Criteria for inclusion, apart from signed informed consent,were clinical symptoms suggestive of CD, known CD under gluten-free diet (GFD) and first degree relatives of CD patients. Intestinal biopsy and genetic profile were performed in all CD patients. A multi-analytic lateral flow immunochromatographic assay (CD-LFIA) based on the detection of both IgA and IgG anti-transglutaminase and total IgA was evaluated. Whole-blood sample results were compared to anti-transglutaminase enzyme linked immunoabsorbant assays (ELISA) and total serum IgA determination.
Results: A total of 122 patients were sequentially submitted for CD testing using ELISA and CD-LFIA devices. A positive CD seroprevalence was found in 17 patients (13.9%) of wich 10 were new CD patients and 7 were known CD with poor GFD. CD-LFIA results

were read by two independant observers (IO). Using binary scores, an excellent concordance between IO was found with an inter-class correlation coefficient k of Cohen of 0.93 (0.84–1.00). The sensitivity of CD-LFIA compared to that of of ELISA assays was 94.1% (71.3-99.9) and 88.2% (63.6–98.5) for each IO respectively. Two false negative results (15/17) belonged to CD patients under poor GFD with mean values (48U/ml) close to the threshold level. However,all new CD patients were correctly diagnosed with CD-LFIA test for each IO with 100% sensitivity (10/10) for both IO. The specificity of the CD-LFIA test for each IO was 99.1% (94.8–100.0) and 98.1% 93.3–99.8).
Conclusion: CD-LFIA have the potential to be used outside routine laboratories and in less sophisticated clinical facilities. Results interpretation was unambiguous for all new CD patients for both observers. The difficulties appeared in interpreting samples of CD patients under GFD. For this specific group, another approach could be preferred using an automated, self-timed reader. However, with a very high negative predictive value of 99.1% (94.8–100.0), the CD-LFIA test is highly suitable to rule out CD in screening HRP.

CL20

International consensus conference on PFAPA syndrome: Evaluation of a new set of diagnostic criteria

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The PFAPA syndrome is characterized by periodic fever, associated with pharyngitis, cervical adenitis and/or aphtous stomatitis and belongs to the auto-inflammatory diseases. Diagnostic criteria are based on clinical features and the exclusion of other periodic fever syndromes. An analysis of a large cohort of patients has shown weaknesses for these criteria and there is a lack of international consensus. An International Conference was held in Morges in November 2008 to propose a new set of classification criteria based on a consensus among experts in the field. We aimed to verify the applicability of the new set of classification criteria. 80 patients diagnosed with PFAPA syndrome from 3 centers (Genoa, Lausanne and Geneva) for pediatric rheumatology were included in the study. A detailed description of the clinical and laboratory features was obtained. The new classification criteria and the actual diagnostic criteria were applied to the patients. Only 43/80 patients (53.8%) fulfilled all criteria of the new classification. 31 patients were excluded because they didn't meet one of the 7 diagnostic criteria, 8 because of 2 criteria, and one because of 3 criteria. When we applied the current criteria to the same patients, 11/80 patients (13%) needed to be excluded. 8/80 patients (10%) were excluded from both sets. Exclusion was related only to some of the criteria. Number of patients for each not fulfilled criterion (new set of criteria/actual criteria): age (1/6), symptoms between episodes (2/2), delayed growth (3/3), main symptoms (21/0), periodicity, length of fever, interval between episodes, and length of disease (19/0). The application of some of the new criteria was not easy, as they were both very restrictive and needed precise information from the patients. Our work has shown that the new set of classification criteria can be applied to patients suspected for PFAPA syndrome, but it seems to be more restrictive than the actual diagnostic criteria. A further work of validation needs to be done for this new set of classification criteria in order to determine if these criteria allow a good discrimination between PFAPA patients and other causes of recurrent fever syndromes.

CL21

Febrile seizures in children during the influenza A (H1N1) pandemia 2009/2010

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Introduction: In children neurologic complications associated with influenza virus infection frequently present as febrile seizures (FS) with or without further signs of central nervous system involvement. It's a question of whether there was an increase of FS during the 2009 influenza A (H1N1) pandemia. We assessed the incidence of FS during the pandemia in a pediatric emergency unit in Zurich. We further investigated the frequency of FS among patients with suspected influenza A (H1N1) infection focusing on the difference between patients with positive versus negative H1N1-test results.
Patients and methods: Retrospective study in a pediatric secondary care center in Switzerland. The observation time comprises the pandemia period in Switzerland from July 1st, 2009 until January 31th, 2010. To assess the overall incidence of FS during the influenza A (H1N1) pandemia we compared the data of our emergency register from 2009/2010 with those of previous years. There was no routine testing for influenza A (H1N1) in all patients with influenza-like illness presenting to our emergency unit. Only those patients were tested, that had to be hospitalized because of disease severity. H1N1 tests were performed by polymerase chain reaction using a nasopharyngeal swab specimen.
Results: During the pandemia period 2009/2010 there were 3238 pediatric emergency consultations (surgical patients excluded) with 43 FS (overall incidence 1.33%). Data from the same period (july to january) of pervious years were as follows: 2008/2009 3325 patients with 47 FS (1.41%); 2007/2008 2994 patients with 46 FS (1.54%); 2006/2007 2941 patients with 27 FS (0,92%). Between July 2009 and January 2010 42 pediatric patients with suspected pandemic influenza A (H1N1) infection were hospitalized, including 7 patients with FS. In 13 cases the H1N1-test was positive (31%), 29 cases were negative for H1N1 (69%). Seizure rate among those with proven influenza A (H1N1) infection was 31% (4/13), while seizure rate in the H1N1-negative group was only 10% (3/29). Severity of neurological manifestations did not differ between the two groups.
Conclusion: Overall amount of patients as well as overall incidence of FS did not increase during the influenza A (H1N1) pandemia 2009/2010 in our hospital. Both were within the range known from pervious years. Although the rate of FS was higher among patients with proven influenza A (H1N1) infection, this criterion cannot be used for a clinical discrimination. With regard to FS, influenza A (H1N1) infection seems not a "particular" form of influenza virus infection.

CL22

Globalizing allergy: From "palapalam-fruit allergy" to molecular diagnosis of food allergy – an instructive case-report

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Background: The investigation of allergy to a "strange" food allergen is often difficult. Typical symptoms shortly after its consumption are suggestive for an IgE-mediated allergy. Symptoms on first contact favour cross reactivity rather than primary sensitization to the eliciting allergen. The growing knowledge on the molecular structure of the different food allergens improved diagnosis, treatment and advice for prevention substantially.
Case: 11 2/12 year old girl has a "filthy" sensation in her throat while eating for the first time "palapalam"-fruit. Thirty minutes later, facial angioedema, difficulty to swallow and generalized itching exanthema appear, responding well to standard emergency treatment. The following day, an upper respiratory infection is diagnosed. The girl suffers from seasonal rhinoconjunctivitis in spring and summer with oral allergy syndrome after prune- and pear-ingestion. Only several weeks after consultation, "palapalam" could be identified as a Jackfruit (Artocarpus heterophyllus).
Test results: Skin-Prick-Test (SPT) were positive for grass, tree and weed pollen as well as house dust mite, hazelnut and cat. Serology screen for 103 allergen components (microarray-chip ISAC, Phadia, Uppsala, Sweden) revealed positivity for nearly all tested PR-10 homologues, including Bet v1 (birch pollen), but not to other food allergens. In our case, only a western blot with Jackfruit extract demonstrating monosensitization to the Bet v1-homologue protein could prove the causal relationship.
Discussion: Birch pollen-associated food allergy is based on cross reactivity between the major allergen of birch (Bet v1) and its homologue in fruits, e.g. Mal d1 in apple. In our case, a Bet v1-homolog protein contained in jackfruit might have been responsible for the reaction. Usually, birch pollen-associated food allergy is mild and limited to the oral cavity. The more severe symptoms in our case may be attributed to an upper respiratory infection as an aggravating co-factor.
Conclusion: First, systemic allergic reactions on initial contact with a new allergen are possible, if the patient has been sensitized to another allergen with a similar protein structure. Second, sensitization to common molecular structures like PR-10 homologues (Bet v1) or lipid transfer proteins can only be shown in serology. Cross reactivities may reach far across botanical borders. Knowledge of these food allergen families is essential to advise the patients correctly.

CL23

VlsE contribution in the early diagnostic of Lyme borreliosis presenting with facial palsy in children

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Background: Erythema migrans is a pathognomonic sign of Lyme borreliosis. Facial nerve palsy can be a symptom of Borreliosis but is unspecific. Serologic markers may be negative at the beginning of the disease and remain negative if antibiotic therapy is prescribed. In these cases, etiologic diagnosis may be missed. Recently, a protein named VlsE (Variable Like protein Sequence Expressed) has been proposed as a new Borrelia infection marker expressing the current replication of the bacteria.
VlsE: The quantitative Borrelia IgG VlsE LIA has proven to have a good specificity, much better than any Borrelia IgM ELISA, and

sensitivity equal to these ELISA. Within an interval of 7 to 10 days, the Borrelia VlsE test demonstrates rapid increase of titers in the acute phase of infection and also a clear decrease after treatment. After 3 to 6 months the test becomes negative in most patients. This test seems to follow the activity of Borrelia in the host.
2007–2009 experience in canton: Valais
VlsE test was proposed in patients with facial nerve palsy with or without tick bite notion between 2007 and 2009. In most of the cases, the Western Blot IgG and/or IgM for Borrelia were not conclusive and diagnosis of Lyme borreliosis could not certainly be established. In approximately ¾ of our cases, the VlsE test was positive. Initial negative VlsE test can't exclude a definitive diagnostic, consequently ulterior serological follow up must be proposed.
In conclusion, VlsE test bring a new contribution to the early diagnosis of Lyme borreliosis. It can allow to treat more selectively patients with unspecific signs of Lyme borreliosis as those with facial nerve palsy, and at the same time, avoid overtreating those non infected by Borrelia. Furthermore, it could be used as a follow up marker, reflecting the treatment response. Nevertheless, complementary studies should be done in the future to confirm these data.

CL24

Comparison of clinical presentation of febrile respiratory tract infections in H1N1 positive and negative patients

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Background: In spring 2009, a new human influenza A H1N1 virus appeared and was initially identified as the virus of the "Swine flu". In Switzerland we faced 2 waves of infections with this new virus. During the second one, we conducted a prospective descriptive study.
Objectives: To describe the clinical presentation of infections with influenza A H1N1 virus and to compare it with infections related to other virus in children consulting at the emergency department of the Universitary Children Hospital of Geneva. METHODS Children presenting with a febrile respiratory tract infection or a febrile seizure were eligible for participating to the study. All patients had an influenza PCR.
Results: 109 patients were recruited, between October 1st, 2009 and February 10th, 2010. Median of age was 7 years (range 0.1–18). Five patients presented with a febrile seizure. Among them, 4 were H1N1 positive. There were 75 H1N1 positive patients (69%). Thirty-two of them had identified risk factors (43%) among which asthma or a wheezing history was most frequent. Fever (91%), cough (93%) and rhinitis (87%) were the most frequent reported presenting symptoms. Five patients (7%) received a diagnosis of otitis media, 7 (9%) of pneumonia and 7 (9%) of obstructive bronchitis or asthma. When compared with H1N1 negative patients, H1N1 positive patients were older (median of age 8.2 vs 4.6 years, p = 0.002), more likely to have risk factors (43% vs 37%, p = 0.04), muscle pain (41 vs 25%, p = 0.04) and to have used non-steroidal anti-inflammatory drugs (NSAID) for the present illness (48 vs 41%, p = 0.04). There were more cases of bronchospasm among non-H1N1 patients (15 vs 9%) and median of oxygen saturation was lower (97 vs 99%, p = 0.001), proportion of dyspnea observed by parents (26 vs 20%, p = 0.05) and rate of hospitalizations 35 vs 16%) higher among those patients.
Conclusions: Clinical presentation of H1N1 patients is marked by an older age and a higher proportion of muscle pain, risk factors and use of NSAID when compared with H1N1 negative patients. Severity appears lower with H1N1 positive (lower proportion of reported dyspnea and hospitalization, higher oxygen saturation), than with H1N1 negative patients probably related to a higher proportion of asthma/wheezing episodes among H1N1 negative patients.

CL25

Altered Surfactant Protein Metabolism due to NK2 homeobox 1 (NKX2-1) Mutations cause Interstitial Lung Disease in "Brain-Lung-Thyroid Syndrome"

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Background: NKX2-1 (NK2 homeobox 1) / TITF1 (Thyroid transcription factor 1) is a critical regulator of transcription for the surfactant protein (SP)-B and -C genes (SFTPB and SFTPC) in the lung and for thyroglobulin and thyroperoxidase in the thyroid. Mutations in this transcription factor are associated with a triad of specific diseases of the brain (hypotonia evolving to benign hereditary chorea), the lung (surfactant deficiency syndrome and interstitial lung disease) and the thyroid (congenital hypothyroidism).
Aim: The effect of NKX2-1 mutations has been studied for thyroid specific target genes of NKX2-1, but not yet for surfactant protein expression.
Results: We identified and functionally characterized two new de novo NKX2-1 mutations c.493C<T (p.R165W) and c.786_787del2 (p.L263fs) in infants with severe interstitial lung disease (ILD), hypotonia, and congenital hypothyroidism. Functional analyses using A549 and HeLa cells revealed that NKX2-1-p.L263fs induced neither SFTPB nor SFTPC promoter activation and had a dominant negative effect on wild-type (WT) NKX2-1. In contrast, NKX2-1-p.R165W activated SFTPC to a significantly greater extent than did WT NKX2-1, while SFTPB activation was only significantly reduced in HeLa cells. In accordance with our in vitro data, we found decreased amounts of SP-B and SP-C by western blot in bronchoalveolar lavage fluid (patient with NKX2-1-p.L263fs) and features of altered surfactant protein metabolism on lung histology (patient with NKX2-1-p.R165W).
Conclusion: We show for the first time, that ILD in patients with NKX2-1 mutations was associated with altered surfactant protein metabolism, and that both gain and loss of function of the mutated NKX2-1 genes on surfactant protein promoters were associated with ILD in "Brain-Lung-Thyroid syndrome".

CL26

From central diabetes insipidus to SIADH (syndrome of inappropriate antidiuretic hormone): check co-medication

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Background: Among other drugs, carbamazepine is known to cause hyponatremia due to a vasopressin- like effect. We describe occurrence of carbamazepine-induced SIADH in a girl with central diabetes insipidus.
Case: Following resection of a desmoplastic astrozytoma of the left hemisphere at the age of 3 months our patient became panhypopituitaric and requires replacement of hydrocortisone, L-thyroxin, desmopressin and growth hormone. Concomitant epilepsy was treated initially with phenobarbital, then phenytoin and from the age of 6 years with carbamazepine (starting dose 7 mg/kg/d). At the age of 7 years mild asymptomatic hyponatremia (sodium 129 mmol/l, osmolality 272 mosmol/l) was observed. Overdosage of desmopressin was suspected and the dose was adjusted from 5 to 3 g/d. The hyponatremia (minimal sodium 123 mmol/l, osmolality 266 mosm/l) however persisted despite further dose reduction and finally ceasing vasopressin replacement. Other hormonal replacement appeared to be appropriate, i.e. glucocorticoid deficiency or hypothyroidism could be excluded as a cause for hyponatremia, as well as renal disease, intestinal sodium loss or cerebral salt wasting. A careful review of the girls additional medication revealed that the dose of carbamazepine had been increased to 17 mg/kg/d at the time when hyponatremia occurred. Hence drug-induced SIADH was suspected. After changing the anticonvulsive treatment to levetiracetam, sodium and osmolality levels returned to normal, and vasopressin substitution had to be initiated again.
Conclusion: A drug side effect is not an uncommon etiology of hyponatremia/SIADH.
Since carbamazepine is often used as an anticonvulsive drug in children, its vasopressin-like effect should be known to prescribers. In a patient with central diabetes insipidus and vasopressin replacement, the diagnosis of SIADH is a special challenge and can cause critical hyponatremia.

CL27

Effect of iron deficiency without anemia and its treatment on cognitive and physical performance in children: a systematic review of the literature

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Background: Iron deficiency without anemia (ID-A) is a common condition encountered mostly in children of developing countries, of low socio-economic classes and in young menstruating women. The effects of chronic ID-A and especially its treatment on cognitive and physical development are controversial, and the role of intravenous (IV) iron supplementation unknown.
Methods: We systematically searched Medline database from 1966 to present with the following Mesh subject headings: Iron AND Randomized Controlled Trial AND (Infant OR child OR Adolescent).
Results: 507 studies were retrieved. After careful reading of the abstracts by 2 independent reviewers (FC, MD), 15 studies

(9 randomized controlled trials (RCT), 2 cross-sectional studies and 4 case series/cohort studies) reporting the effect of ID-A and its treatment on academic/cognitive performances in children were analyzed. Baseline assessment: before intervention, 6 studies found significant differences in test scores between ID-A patients and controls, whereas 9 found no difference. Intervention: in the 9 RCT, treatment varied in term of elemental iron dose (from 2 to 6 mg/kg/dose) and duration (from 1 week to 6 months). Outcome evaluation: Bayley Scale of Infant Development was the most frequently used test (7 studies, including 5 RCT). The type (Bayley-, Wechsler scale, others) and timing (weeks to years after intervention) of psychomotor/developmental tests varied greatly, making comparisons between studies extremely difficult. Outcome: after intervention, 2 RCT found some benefits of iron supplementation, whereas 6 RCT found none. The report or not of confounding factors had no impact on the outcome results at baseline (p = 1, Fisher's test). We found no studies reporting the effect of ID-A and its treatment on physical performances in children. We found no studies reporting the effect of IV iron on ID-A in children.
Discussion: The effect of iron therapy in children with ID-A on academic/cognitive functions seems at best controversial. The differences in the age of the subjects, the duration of the ID-A, the iron therapy dose and duration, and the confounding factors make the results extremely difficult to evaluate and compare. The severity of iron deficiency seems to play a major role, the children with iron deficiency and anemia being more affected than children with ID-A or control patients. Further studies are needed in children to evaluate the best way to treat ID-A in that population.

CL28

Cardiorespiratory arrest and vitamin D deficiency rickets: A case report

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Vitamin D deficiency rickets became a rare disease in industrialized countries due to vitamin D supplementation in infants and nutritional guidelines. Symptoms of hypocalcemia due to vitamin D deficiency rickets may be life threatening. We report a case of a 16 months old infant who initially presented with stridor that was misdiagnosed as viral laryngitis. He presented, two weeks later, a cardiorespiratory arrest related to a laryngospasm secondary to severe hypocalcemia (ionized calcium level: 0.42 mmol/l,total calcium level: 1.15 mmol/). He was successfully resuscitated and vitamin D deficiency rickets was diagnosed. The medical history revealed that the infant was exclusively breast fed without vitamin D supplementation till the age of 10 months and also deprived from other milk products intentionally by the parents due to cultural habits. The laboratory investigations showed an elevated alkaline phosphatase level at 577 U/l, a normal phosphatemia level at 2 mmol/l, a decreased 25 (OH) cholecalciferol at 5.7 mcg/l,a normal calciuria level at 0.35 mol/mol of creatinine and an increased parathyroid hormone level at 325 ng/l. Cardiocirculatory arrest secondary to vitamin D deficiency rickets is very rare. The aim of this presentation is to highlight the symptoms of vitamin D deficiency rickets and to raise pediatricians' awareness to the necessity of including the diagnosis of hypocalcemia in case of stridor especially if the nutritional history or ethnic origin of the infant predispose to vitamin D deficiency. Vitamin D supplementation is important for some ethnic minority population, whom are faced with the risk of developing this disease

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CL29

Body dissatisfaction on top of depressive mood among adolescent with severe dysmenorrhea

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Purpose: Dysmenorrhea is the leading cause of recurrent short-term school absenteeism among adolescent girls. Yet, studies of menstrual symptoms in the light of adolescent psychological background seldom appear in the recent literature. This study aims to determine whether adolescent girls with severe dysmenorrhea (SD) have different body perception on top of poorer psychological health.
Methods: We analyzed data from the Swiss Multicentre Adolescent Survey on Health (SMASH 2002) among a nationally representative sample of adolescents (n = 7548; 3340 females) aged 16 to 20 years attending post-mandatory education. Dysmenorrhea was defined as presence of abdominal or back pain during menstruation on the last 12 months. The severity of dysmenorrhea was defined according to the impact on daily activity and was assessed by 3 questions on the way menstruations interfere with daily life: 1) "You feel well and have normal activities", 2)"you must stay at home" and 3) "you feel restricted in your school or professional activities". Studied variables were: depressive symptoms, suicidal attempt, sexual abuse, health perception in general, body satisfaction, desire to modify body shape, and disordered eating behavior (DEB) with restrictive or bulimic tendency. Controlling variables included socio-economic status (SES) as measured by both parent's level of education, gynecological age (age-age at menarche), academic track (student/apprentice) and age.
Results: 12.4% (95% CI: 11.0–14) declared severe dysmenorrhea, 74.2% (95% CI: 71.8–76.5) mild to moderate dysmenorrhea and 13,4% (95% CI: 11.5–15.5) had no dysmenorrhea. Compared to their peers, controlling for confounding variables, subjects with SD were more numerous to report depressive symptoms (AOR: 1.73; 95% CI: 1.39–2.15), to feel in poor health (AOR: 1.44; 95% CI: 1.14–1.81). Moreover, the proportion of those reporting dissatisfaction with their body appearance was higher (AOR: 1.48; 95% CI: 1.00–2.18).
Conclusion: Patients with SD not only show a different profile than their peers in terms of their mental health and health perception, but also a distinct relation to their body. Therefore clinicians should pay particular attention to patients with SD and offer them a global evaluation keeping in mind what can be associated with SD.

CL30

Characteristics and evolution of children attending a specialized childhood obesity clinic

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Introduction: Childhood overweight is a major public health issue that concern 20% children. We aimed to describe the population attending a specialized obesity clinic and to determine changes in body mass index (BMI) during individual obesity therapy.
Methods: This was a retrospective study including 130 new patients (2.3 to 15.3 yrs, mean 9.5 ± 2.9) attending the paediatric obesity clinic of the Geneva University Hospitals between January 2008 and December 2009. We assessed medical history, anthropometrics, clinical symptoms and signs of complications, resting blood pressure and lipids.
Results: There were 57% of girls and 65% of patients were referred by their health practitioners. Mean BMI and BMI z-score were 25.2 ± 3.9 kg.m-2 and 2.8 ± 0.9, respectively. The majority of patients (54%) attended the clinic regularly, 43% of them consulting every 2 to 4 months. At first visit, 2 (2%) had normal weight, 14 (11%) were overweight, 72 (56%) were obese and 42 (32%) were morbidly obese. Mean follow-up time: 8.9 ± 6.4 months and mean visit number: 3.5 ± 2.7. Age at weight gain in years, N(%): <3: 44(34); 3-6: 39(30); 6-10: 36(28); >10: 8(6). Triggering factors, N(%): No explanation: 76(59); Life change/parents separation: 37(29); Medication/disease: 7(5); Other: 10(8). Presence of, N(%): Systolic hypertension: 14(11); Dyslipidemia: 10(8); Hyperlordosis: 37(29); Genu valgum: 44(34); Acanthosis nigricans: 31(24).
Complains of, N(%): Their weight: 88(68); Mockery: 43(33); Breathlessness: 57(44).
Beneficial changes in BMI z-scores (mean: –0.14 ± 0.36) were dependant of age at weight gain (p = .013), follow-up duration (p = .042) and presence of hyperlordosis (–0.40 ± 0.6 vs. –0.15 ± 0.3, p = .038), but not of initial BMI z-score, age, or any other factors listed in table 1. The BMI z-score was: 1) reduced in 42% (mainly if weight gain at 3–6 or >10 yrs); 2) stable in 37% (mainly if weight gain at <3 yrs) and 3) increased in 21% of patients (mainly if weight gain at 6–10 yrs). The majority of patients remained in their initial adiposity category, 13 (10%) changed to the category below and only 4 (3.1%) passed to the one above.
Conclusion: Most obese children gain weight before 6 years old and present early signs of complications. They usually complain about their weight excess. We demonstrate that individual obesity therapy in a specialized paediatric centre leads to beneficial BMI changes in the majority of overweight patients. Age at weight gain influences treatment outcomes.

CL31

Playing with fire: the chocking game

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Introduction: The chocking game's primary goal is to produce a euphoric sensation through brief hypoxia. The compression of the carotid arteries by strangulation combined with breath holding leads to a reduced cerebral blood flow and oxygenation. Although this game can cause long-term disability and death, it seems to be of increasing popularity.

Methods: Case report and review of literature.
Findings: This otherwise healthy 12-year-old boy was found unconscious hanging with his neck on a cord tied about 40 cm over the floor. There was no suicide note or other sign of a voluntary death. His father started with cardiopulmonary resuscitation. 15 minutes later health care professionals find a boy with a Glasgow Coma Scale (GCS) of 3 without heart activity. Resuscitation with epinephrine finally was successful and the boy was transported to our hospital. GCS remained 3. Consistent with strangulation, the physical examination revealed the typical distribution of petechiae over his neck and palpebrae. The EEG showed a severely altered activity and the evidence of repetitive seizures. MRI of the brain 48 hours after the accident showed severe damage consistent with hypoxic ischaemic encephalopathy. Somato-sensoric evoked potentials over the Medianus nerve lacked any cortical response. With regard to the very bad prognosis therapy was discontinued and the boy died a few minutes after extubation.
Discussion: Familiarity with chocking games seems to be low about healthcare professionals. The medical literature, especially in Switzerland, is very poor. The highest prevalence of this game is found at the age of 13 years. Parents are mostly not aware about their children's activity. Substance abuse and mental health risk factors predispose for chocking game participation. Clinical signs like frequent headaches, tinnitus, marks on the neck, bloodshot eyes or a history with suspicious ropes and belts in the bedroom or insinuations of strangulation activities should rise the attention of paediatricians and other health care providers. Addressing the topic with potentially concerned adolescents may be a life saving strategy.
Conclusion: It is extremely important to recognize the chocking game as a potentially life-threatening activity in adolescents. Health care providers should look for signs of strangulation activities and integrate basic factual information about the dangers of the chocking game in their prevention activities.

CL32

Are adolescents aware of adverse consequences of their illegal psychoactive substance use?

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Background: As adolescents using illegal psychoactive substances are thought to minimize the consequences of their consumption, some physician may be reluctant to address such behavior. The present study explores adolescents' perceptions of problems linked to their illegal psychoactive substance use, identifying their magnitude and what characterizes adolescents who report the most.
Methods: This study was based on a nationally representative sample of adolescents aged 16 to 20 pursuing post mandatory education in Switzerland (SMASH02). Using self-administered questionnaires, 2515 adolescents (male n = 1621, female n = 894) reporting illegal psychoactive substance use in the last month were assessed, further separated in 3 exclusive groups on their consumption: occasional consumers (reporting cannabis use once or twice but no other illegal drugs), regular consumers (reporting cannabis use 3 times or more but no other illegal drugs) and polyconsumers (reporting cannabis use and at least one other drug). Problems adolescents perceived as linked to their consumption were grouped (school, individual, relationship and sexual) then compared, using bivariate analysis, according to substance use modalities. Multivariate analysis were performed, using occasional consumers as the reference category, controlling for several personal characteristics and alcohol consumption (results given as relative risks ratios: RRR [95%CI]).
Results: On bivariate analysis, groups significantly differed ($p < 0.05$) with 26.9% of occasional consumers, 53.8% of regular consumers and 73.3% of polyconsumers reporting at least one type of problems related to their consumption. Increasing in numbers along consumption, types of problems were all more likely reported by polyconsumers (school: 4.65 [3.12–6.92], individual: 3.78 [1.56–9.09], relationship: 6.67 [4.48–9.93], sexual: 6.06 [3.46–10.63]). Adjusted for substance use modalities, having higher depressive symptoms was the characteristic most frequently associated with reporting problems.
Conclusions: Our findings show that many adolescents have drug related problems and, more importantly, that most are aware of them. Physicians should therefore feel confident inquiring adolescents on problems linked with illegal substance use as they are likely to be responsive on that issue. In addition, special attention should be oriented towards depressed adolescents using illegal substances as they seem more prone to drug related problems.

CL33

Fatal attraction: smoking among adolescents with chronic pulmonary conditions

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Objective: To study tobacco use among adolescents with chronic respiratory problems and their perception of smoking as a problematic behavior.
Methods: Data were drawn from a nationally representative sample of Swiss adolescents aged 16 to 20 years in post mandatory education having completed a self-administered survey (SMASH 2002). Subjects were divided in 3 groups: those reporting a chronic condition and frequent respiratory problems in the last year, such as asthma or hay fever (chronic pulmonary conditions: CPC, n = 251); those reporting a chronic condition but no respiratory problems (non pulmonary chronic conditions: NPCC, n = 459); and healthy controls (no chronic condition: NNC, n = 5466). Those without a chronic condition reporting respiratory problems in the last year were excluded from the analysis (n = 1056). Bivariate analysis comparing groups on daily smoking, identification of tobacco use as a problem for which they needed help, and consultation in the prior year with a physician regarding tobacco were performed. Using multivariate analysis, groups were further compared using NCC as the reference category and several personal characteristics as cofactors. Results are given as relative risk ratios (RRR [95%CI]).
Results: In bivariate analysis, groups differed significantly ($p < 0.05$) on daily smoking (CPC: 50.8%, NPCC: 36.2%, NCC: 29.8%), identification of tobacco use as a problem for which they needed help (CPC: 27.8%, NPCC: 28.3%, NCC: 17.4%), and consulting a physician in the prior year regarding tobacco, although few adolescents reported so (CPC: 2.1%, NPCC: 1.2%, NCC: 0.5%). In multivariate analysis, CPC were more than twice as likely to be daily smokers (2.51 [1.68–3.78]). However, adjusting for their smoking status, CPC did not identify more frequently tobacco use as a problem for which they needed help (1.04 [0.45–2.39]), while it was the case for NPCC (1.99 [1.22–3.25]). No differences were found on having consulted in the last year regarding tobacco.
Conclusions: Despite the well-known adverse health effects of smoking, adolescents with chronic pulmonary conditions were more likely to be daily smokers than their peers. Unfortunately, unless brought up by professionals, discussion about smoking is not likely to happen. Therefore, as adolescents with chronic conditions consult physicians frequently, every opportunity should be taken to address smoking, especially among those with chronic respiratory problems who seem to minimize its burden.

CL34

Childhood obesity therapy in Switzerland – where are we? *

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Overweight affects approximately 250000 children in Switzerland and represents a major public health burden in so far as early signs of chronic diseases develop during childhood. Efficacy of multiprofessional group programmes, including diet counselling, behaviour therapy and exercise training for the treatment of overweight children has been demonstrated in randomized controlled trials, but the translation into clinical practice is difficult. Certified multidisciplinary group programs, but not in an individual or in-patient setting, are now reimbursed by Swiss health insurances. In this multicentre study, we aim to determine the feasibility and acceptability of such programmes* and to identify socio-economic and psychosocial predictors of beneficial changes and long-term health maintenance.
Methods: To date only 220 patients can be treated in such programs and we expect a total of 1200 until 2013. Group therapy is performed during 12 months according to identical quality criteria and includes overweight or obese children aged from 6 to 18 years. Nationwide, valid questionnaires are used at baseline, 12 and 24 months to assess changes in body mass index (BMI), fat distribution, blood pressure, quality of life, eating and family habits, nutrition, physical activity, mental health, eating disorders, parenting skills and parents' weight. Preliminary results indicate that only 66% of families applying for treatment fulfil criteria for group therapy. Overweight children and families have an average to lower educational level and 45% are migrants. Their mean age is 12.4 + 2.2 year old and mean BMI is 28.5 kg/m^2 (range 21.8–39.0). Main co-morbidities or risk factors observed are musculoskeletal problems (74%), elevated blood pressure (26%), increased fasting glucose (19%) and dyslipidaemia or hyperuricaemia (each 16%), as well as suspicion for ADHS in 37% of the boys and headaches in 36% of the girls.

Conclusions: A great proportion of overweight children suffer from co-morbidities. Longitudinal data of new multidisciplinary programs will provide important clinical information on obesity therapy and support the continuation of reimbursement of multiprofessional therapy after 2013. Great efforts still have to be made to reinforce the network of health professionals to ensure adequate follow up after group therapy or to develop individual therapy according to the special needs of multi-morbid children who cannot participate in group settings.

CL35

Comparison of early markers of atherosclerosis between pre-pubertal obese children and their mother

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The aim of this study was to compare early markers of atherosclerosis and cardiovascular diseases (CVD) risk factors between pre-pubertal obese children and their mother. This was a cross-sectional study including 27 pre-pubertal obese children (age 9.6 ± 1.1 year, 51% female) and their mother (39.5 ± 4.8 yr). Outcome measures included: intima-media thickness (IMT) and stiffness (incremental elastic modulus) of the right common carotid artery, and endothelial function (flow-mediated dilation – FMD) of the brachial artery using high resolution ultrasound; cardiorespiratory fitness (VO2max); body mass index (BMI); abdominal fat by DXA; fasting blood lipids, glucose, insulin and HOMA-IR (homeostasis model of insulin resistance). Results showed that 67% and 18% of mothers were overweight and obese, respectively. Children had higher abdominal fat (51.3 ± 6.1 vs 47.7 ± 7.7 %, p = .03) and HOMA 2.1 ± 1.0 vs 1.6 ± 1.0, p = .03), compared to mothers (mean ± SD). Arterial stiffness (8.9 ± 4.3 vs 25.6 ± 15.9 mm Hg.10 2, p = <0.0001) and IMT (0.53 ± 0.06 vs 0.56 ± 0.04 mm, p = .03) were greater, and VO2max (38.1 +/- 7.3 vs 32.3 ± 8.9 ml. kg-1.min-1, p = .02) was lower in mothers than children, though IMT remained within the normal range. Interestingly, children had reduced FMD likewise to mothers (5.9 ± 3.3 vs 5.7 ± 2.8 %, p = .79). Blood lipids were similar. We demonstrate that impaired vascular reactivity appears before puberty in obese children and the reduction of FMD is of similar magnitude compared to their mother. Central adiposity and insulin resistance indexes are even greater in obese children than mothers. Early family behavioral therapy might be a promising approach to reduce CVD risks in both children and mothers. Research relating to this abstract was funded by the Swiss National Science Foundation # 3200B0-120437 and supported by the Research Platform of the Department of Child and Adolescent.

CL36

High incidence of childhood hemolytic uremic syndrome in Switzerland is associated with indicators of livestock farming intensity

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Background: Hemolytic-uremic syndrome (HUS) is a multisystem disorder associated with significant morbidity and mortality. Typically, HUS is preceded by an episode of (bloody) diarrhea mostly due to Shiga-toxin (Stx) producing Escherichia coli (STEC). The main reservoir for STEC is the intestine of healthy ruminants, mostly cattle, and recent studies have revealed an association between indicators of livestock density and human STEC infection or HUS, respectively. Nationwide data on HUS in Switzerland have been established through the Swiss Pediatric Surveillance Unit (SPSU) [Schifferli et al. Eur J Pediatr. 2010; 169:591-8].
Aims: Analysis of age-specific incidence rate of childhood HUS and possible association of Shiga-toxin associated HUS (Stx-HUS) with indicators of livestock farming intensity.
Methods: Epidemiological and ecological analysis based on the SPSU data (1997–2003) and the database of the Swiss Federal Statistical Office (data on population and agriculture).
Results: One hundred-fourteen cases were registered, 88% were ≤5 years old. The overall annual incidence rate was 1.42 (0.60–1.91) and 4.23 (1.76–6.19) per 100000 children ≤5 and ≤16 years, respectively (P = 0.005). Stx-HUS was more frequent compared to cases not associated with STEC (P = 0.002). The incidence rate for Stx-HUS was 3.85 (1.76–5.65) in children ≤5, compared to 0.27 (0.00–0.54) per 100'000 children 5-16 years (P = 0.002), respectively. The incidence rate of cases not associated with STEC infection did not significantly vary with age (P = 0.107). Compared to data from Scotland, Canada, Ireland, Germany, England, Australia, Italy, and Austria the annual incidence rate of HUS in young children is highest in Switzerland. Ecological analysis revealed strong association between the incidence rate of Stx-HUS and indicators of rural occupation (agricultural labourer / population, P = 0.030), farming intensity (livestock breeding farms / population, P = 0.027) and cattle density (cattle / cultivated area, P = 0.013).
Conclusions: Alike in other countries, HUS in Switzerland is mostly associated with STEC infection and affects predominantly young children. However, the incidence rate is higher compared to countries abroad and is significantly correlated with indicators of livestock farming intensity. The present data support the impact of direct and indirect contact with animals or fecal contaminants in transmission of STEC to humans.

CL37

Developmental and social outcome of children born to opiate-dependent mothers

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Introduction: Care of children born to opiate-dependent mothers is a growing social and health. In 1995, a program was established in our primary health care centre offering a multidisciplinary approach for the children born to opiate-dependent mothers and their families. In this study we seek to analyze the neonatal period for possible risk factors to the long term care and development of these children.
Methods: Retrospectively, data were analyzed for children born to opiate-dependent mothers between 2000–2008. Follow-up data were obtained through structured one-to-one interviews with the children's legal guardians.
Results: A total of 73 neonates were included. At the time of delivery, 10% of their mothers were exclusive methadone users and 4% exclusive subutex users. In 59% additional heroin or polydrug abuse was detected in the meconium. Median gestational age was 38.3 weeks (33–42) with 8 (11%) being premature; and 17 (23%) having intrauterine growth retardation. The median time for abstinence syndrome therapy was 35.3 days (13–87, one missing value). No significant difference was seen between mother's type of drug abuse and duration or severity of the neonatal abstinence syndrome. In 29 (40%) of the children a monotherapy with morphine was used, while 3 (4%) necessitated a combination therapy (morphine and phenobarbital). The remaining 41 (56%) were included in a national double-blind randomized study (2000–2004), therefore no data for therapy are available. At total of 29 (40%) were discharged to parental home, 20 (27%) to a mother and child welfare institution, 22 (30%) to child welfare institution and 2 (3%) to a foster family. The child protective services were involved in 68 cases (93%), in 16 (22%) parental authority was withdrawn. Preliminary data suggests that children discharged to parental home are at increased risk for neglect and a subsequent placement in a child welfare institution or foster family was needed in some cases. Furthermore, children with an unstable family environment have higher degree of developmental impairment.
Conclusions: Our study emphasizes the importance of a careful evaluation of social resources, not only during hospitalisation, but ideally already during pregnancy and after discharge, with long term follow-up by child protective services. While support provided to the children and their families is important, child neglect may be underestimated, and infant safety should be assessed from early on.

CL38

Neurodevelopmental outcome of neonates treated with nitric oxide for persistent pulmonary hypertension

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Persistent pulmonary hypertension of the newborn (PPHN) is a life threatening condition associated with an increased risk of neurodevelopmental impairment. The recommended treatment for this condition is inhaled nitric oxide (iNO) and has been used in our Neonatal Intensive Care Unit since 1998. We prospectively offered neurodevelopmental follow-up to children treated with iNO for PPHN, including extensive neurological evaluation, developmental/cognitive evaluation at 18 months and 3.5–5 years old, and evaluated the rate of severe and moderate handicap and normal neurodevelopmental outcome, compared to a control group and the literature. Population consisted of 29 patients treated only with iNO, born between 01.01.1999 and 31.12.2005 (study group), and 32 healthy term infants born in 1998 in our maternity (control group). During those seven years, 65 infants were admitted in our Unit with PPHN, of whom 40 were treated with iNO alone. 34 children survived (85%) and were offered neurodevelopmental follow-up, 7 children were lost to follow-up due to various reasons. 22 children were examined at the age of 18 months (76%) with a rate of moderate handicap of 22% (2 with expressive language delay, 2 with

difficult behavior, and 1 child with moderate hearing loss), and a rate of major handicap of 4.5% (1 child with cerebral palsy due to perinatal stroke, and moderate hearing loss). At preschool age, 17 (50%) were examined, the rate of moderate handicap was 22% (4 borderline intelligence, 1 hearing loss), and the rate of major handicap was 4.5% (one child with cerebral palsy and hearing loss), compared to 26.9% and 0% in the control group. Mean developmental quotient at 18 months was 100.3 ± 8.7 (control group 118.3), and at preschool age mean cognitive indices were within normal limits for the 2 tests performed at 3.5 or 5 years (108 ± 21, 94.4 ± 17). Most of the children with a less favorable neurodevelopmental outcome suffered from birth asphyxia (ruptured uterus, placental abruption, maternal hypotension, diabetic cardiomyopathy), and notably, the 2 children with sensorineural hearing loss both suffered from severe hypoxic-ischemic enkelopathy. Treatment with iNO was not the direct cause of the neurodevelopmental impairments observed in children treated for PPHN.

CL39

Functional modification of the CXCR4 chemokine receptor function by targeting phosphorylation of its intracellular tail in leukemic cells

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Background: An important feature of leukemic and solid cancer cells is their migratory potential. The chemokine receptor CXCR4 is a key regulator in cell migration, and its overexpression has been associated with a poor prognosis in acute myeloid leukemia (AML). We have recently shown that the PIM1 serine/threonine kinase plays a role in phosphorylation of the serine residue 339 in the intracellular C-terminal tail of CXCR4 that is known to be important for internalization and recycling of the receptor upon CXCL12 (ligand) stimulation.
Aim: To evaluate the role of Ser339 phosphorylation in CXCL12/CXCR4 mediated homing and migration of leukemic cells.
Methods: We have established cell lines stably expressing wildtype CXCR4 (WT) or CXCR4 mutants that abrogate phosphorylation (S339A) or imitate constitutive phosphorylation (S339E) using HEK293 cells and the Kasumi-1 human AML cells both lacking endogenous expression of the receptor. The impact on CXCR4 function of S339 phosphorlyation was studied by following the migration capacity towards CXCL12 in Transwell assays and by measuring receptor internalization/recycling as well as downstream signaling by live cell imaging and flow cytrometry.
Results: Only cells expressing CXCR4-WT or CXCR4-S339E were able to migrate towards CXCL12 as determined by Transwell assays. These findings were also reflected by the homing capacity of these cells in vivo as assessed in preliminary transplantation experiments. Moreover, PIM1 overexpression modulated the migration capacity of the cells confirming its role in regulating CXCR4 function. In the presence of CXCL12, although showing different patterns, normal and mutated receptors were all internalized confirming that S339 phosphorylation is important for CXCR4 recycling but not for its internalization. Interestingly, treatment of these cells with small molecule PIM inhibitors rapidly decreased CXCR4 surface expression and impaired migration towards CXCL12.
Conclusion: Our data strongly suggest that CXCR4 S339 phosphorylation is likely to fine-tune CXCR4 recycling, an important process for cellular homing and migration of leukemic and solid cancer cells most probably through regulation the of recycling of the CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 function in malignant cells.

CL40

Predicting Adverse Events in Children with Fever and Chemotherapy-Induced Neutropenia. Results of the Prospective Multicenter SPOG 2003 FN Study

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Purpose: To develop a score predicting the risk of adverse events (AE) in fever and neutropenia (FN) for pediatric cancer patients, and to evaluate its performance.
Patients and methods: Pediatric cancer patients presenting with FN induced by non-myeloablative chemotherapy were observed in a prospective multicenter study. A score predicting the risk of future AE (serious medical complication, microbiologically defined infection, radiologically confirmed pneumonia) was developed from a multivariate mixed logistic regression model. Its cross-validated predictive performance was compared to that of published risk prediction rules.
Results: An AE was reported in 122 (29%) of 423 FN episodes. In 57 (13%) episodes the first AE was known only beyond reassessment after 8–24 hours of inpatient management. Predicting AE at reassessment was better than prediction at presentation with FN. A differential leukocyte count did not increase the predictive performance. The score predicting future AE in 358 episodes without known AE at reassessment used four variables: preceding chemotherapy more intensive than ALL maintenance (weight, 4), hemoglobin ≥90 g/L (5), leukocyte count <0.3 G/L (3), and platelet count <50 G/L (3). A score (sum of weights) ≥9 predicted future AE. The cross-validated performance of this score exceeded the performance of published risk prediction rules: At an overall sensitivity of 92%, 35% of the episodes were classified as low risk, with a specificity of 45% and a negative predictive value of 93%.
Conclusion: This score, based on four routinely accessible characteristics, accurately identifies pediatric cancer patients with FN at risk for AE after reassessment.

CL41

Quality of life in the aftermath of child maltreatment

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Objective: In the aftermath of child maltreatment or neglect, the quality of life in children is likely to be affected. However, research on quality of life in maltreated children is lacking. The aim of this study is to describe the health-related quality of life (HRQoL) in a follow-up sample of children referred to an interdisciplinary hospital child protection team (CPT).
Method: Of the 704 children referred to the CPT at University Children's Hospital Zurich between 2005 and 2006 a sample of 182 children was drawn to contact for a follow-up. HRQoL was assessed in 42 children participating in a face-to-face interview at the University Children's Hospital Zurich using the Kidscreen-27 for children over the age of six years and the TAPQOL parent report for children younger than six years. Study non-participation resulted because no contact or adequate communication in German, French or English could be established (n = 51) or because the parents or children refused to participate (n = 50). In 39 cases only a short telephone interview with the parents could be done without assessment of child HRQoL.
Results: HRQoL in maltreated children over the age of six years was significantly impaired compared to Swiss norms, the children's self-report being at a lower level than the parental report. In children younger than six years, parents rated the HRQoL of their children impaired in the subscales of physical functioning (stomach problems, motor functioning) and the domain of emotional functioning. Specific types of maltreatment were not significantly connected with HRQoL, neither were gender, age or nationality of the maltreated child. However, a low socioeconomic status went together with a low self-reported HRQoL.
Conclusion: Impairment of maltreated children's quality of life is not only an issue in the period of maltreatment. In the sample studied, the maltreated children's HRQoL was impaired two to four years after the intervention of the CPT. A child's HRQoL seems especially endangered if the consequences of child maltreatment combine with the permanent stress of a low socioeconomic status. Parents perceived their children's HRQoL more positive than the children themselves did. Possibly, the parents' blurred view on their children's quality of life is based upon a general difficulty to perceive their children's needs. In research and practice it is, therefore, essential to evaluate maltreated children's self-reported HRQoL independent of their parents' view.

CL42

Anesthesiologic care of infants in the Wallis region

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Introduction: Our Hospital in Sion is a reference Center for the Wallis region, which has a population of 270000 inhabitants, increasing to around 450000 during the tourist season. It has a neonatology Unit able to manage premature infants aged 32 weeks and above. The pupose of this abstract is to describe our anesthesiological approach to the management of infants defined as <52 weeks postconception in a non-University hospital, as well as the related structural considerations.

Obstetrical and neonatal activities: In 2008 there were 1'600 births in our Hospital. Of these 86 were premature births at less than 37 weeks, 30 were premature at less than 34 weeks, and 32 were patients returning from a University Center (total of 157 patients). Among these 157 infants, 35 had a total of 307 days of CPAP, of which 3 had pulmonary bronchodyplasia (PBD) and 1 was intubated. Normally in our hospital an infant who needs to be intubated is transfered to a University Neonatalogy Unit, if an early extubation with CPAP is not possible. Anesthesia for infants of less than 52 weeks (post conception) carries a number of risks and requires a particular expertise.
Patients: From 2005 to 2009 our department carried out 174 anesthesia on infants of which 40 had a caudal epidural anesthesia alone (with no sedation or general anesthesia) with 0.5% bupivacaine and 1% lidocaine in order to obtain an injection volume of 1 ml/kg. Of these 40 infants 17 had been premature births, and only 1 showed no signs of associated morbidity. Thirteen of the 17 had had a Respiratory Distress Syndrome (RDS), and 2 had PBD.
Discussion: This technique is particularly well suited for infants having been weaned off of CPAP or who are in the process. To our knowledge, there are no studies which have evaluated the benefits of a purely locoregional anesthesic approach to these patients at risk. With healthy infants, the benefits of locoregional anesthsia (LRA) vs general anesthesia (GA) have not been evaluated either.
Conclusion: Providing this type of anesthetic care in a Center which regularly manages non intubated infants of more than 32 weeks, not only allows us to relieve overloaded University Centers, but at the same time allows parents to remain close to their children, facilitating visiting, etc.

Pediatric research

Prenatal animal contact and Gene expression of innate immunity receptors at birth are associated with the development of Atopic Dermatitis

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Background: Previous cross-sectional studies have suggested that prenatal farm exposures might protect against allergic disease and increase the expression of receptors of the innate immune system. However, epidemiological evidence supporting the association with atopic dermatitis remains inconsistent.
Objective: The aim of our work was to study the association between prenatal farm-related exposures and the development of atopic dermatitis in the first two years of life in a prospective study. To analyse the role of the innate immune system, we further analysed the association between the expression of innate immune genes at birth, reflecting both genetic and prenatal environmental influences, and atopic dermatitis.
Methods: 1063 children who participated in a birth cohort study from rural areas were included in this study (PASTURE/EFRAIM). Doctor diagnosis of atopic dermatitis was reported by the parents from 1 to 2 years of age by questionnaire. Gene expression of Toll-like receptors (TLRs) and CD14 were assessed in cord blood leucocytes of these children by quantitative PCR.
Results: The maternal contact with farm animals and cats during pregnancy had a significantly protective effect on the development of atopic dermatitis in the first two years of life. The risk of atopic dermatitis was reduced by more than half among children with mothers having contact to 3 or more farm animal species during pregnancy compared to children with mothers without contact (adjusted OR and 95%CI: 0.43, 0.19 to 0.97). Elevated expression of TLR5 and TLR9 in cord blood leukocytes was associated with decreased doctor's diagnosis of atopic dermatitis in the first two years of life. The same tendency was observed with expression of TLR1, 2, 4, 6, 7, 8 and CD14 in cord blood.
Conclusion: Maternal contact to farm animals and cats during pregnancy and a higher expression of the receptors of the innate immune system at birth have a protective effect on the development of atopic dermatitis in the 2 first years of life.

Allergic rhinitis as predictor for school age wheezing

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Background: Rhinitis in older children and adults has been shown to be a risk factor for adolescent and adult onset asthma. These findings suggest an interaction between the upper and lower airways. Whether rhinitis is associated with childhood onset asthma is unknown. The objective of the study was, therefore, to investigate whether rhinitis in early childhood is an independent risk factor for childhood onset wheezing in the German Multicentre Allergy Study (MAS) birth cohort.
Methods: The MAS followed 1314 healthy children from birth to 13 years of age. The children were followed and specific immunoglobulin E levels were measured at yearly intervals. Airway hyperresponsiveness was assessed at 7 years.
Results: Allergic rhinitis until the age of 5 years was a risk factor for subsequent wheezing onset with an adjusted RR of 3.79 ($p = <0.001$). This association was not attributable to the type of sensitization, the severity of sensitization or atopic dermatitis during the first 2 years of life. The population attributable risk fraction for allergic rhinitis on the incidence of wheezing was 41.5% (95% CI: 20.0–61.3). Non-allergic rhinitis until the age of 5 years was not significantly associated with wheezing onset in childhood (adjusted RR 0.77, $p = 0.678$). Neither allergic (adjusted RR = 1.37, $p = 0.503$) nor non-allergic rhinitis (adjusted RR = 1.16, $p = 0.656$) until the age of 2 years was associated with wheezing onset thereafter.
Conclusions: The first manifestation of allergic rhinitis occurs in preschool children where it is a risk factor for subsequent wheezing onset. Rhinitis until the age of two, however, does not influence the development of wheezing in childhood. Preschool children with rhinitis might thus benefit from early assessment of allergic sensitization to identify the children at high risk of developing wheezing.

Low levels of varicella-specific antibodies in treated HIV-infected children results from failure to reactivate anti-VZV memory responses, rather than lower initial responses or accelerated antibody loss

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Background and aims: Varicella usually induces lifelong immunity. In immunosuppressed patients, severe and/or recurrent disease has been reported. The aim of this study was to compare VZV antibody titers and avidity index (AI) between HIV+ children and adults, and healthy children.
Patients and methods: We analyzed yearly blood samples from 97 vertically infected HIV+ children (541 samples), 78 HIV+ adults (440 samples) collected between 1997 and 2008, and an age-matched group of 97 healthy children. VZV IgG antibody titers and AI were measured with an ELISA. Evolution of VZV antibody titers across time was examined using mixed linear models.
Results: VZV IgG antibody titers were lower in HIV+ children than adults all along the study ($P <0.001$), and did not decline faster than in adults: it even slightly increased over time ($P = 0.01$). 20% of VZV-positive children failed to maintain anti-VZV titers above protection threshold, compared to 2.6% of adults (OR 17.74, $P <0.001$; IC 95%: 8.10–153.92). High HIV viral load and absence of HAART were associated with the failure to maintain VZV antibodies ($P = 0.001$ and $P = 0.037$, respectively). VZV IgG antibody titers were lower in HIV+ children than in healthy children ($P <0.001$). Antibody titers increased with age in healthy children ($P = 0.004$), but not in HIV+ children. The mean anti-VZV antibodies AI was lower in HIV+ than in healthy children ($P <0.001$). AI increased in HIV+ children with evidence of VZV reactivation ($P = 0.014$), but not in those without reactivation. Unexpectedly, AI decreased with time in 15 HIV+ children: their anti-VZV titers also decreased ($P = 0.037$), suggesting that they had failed to reactivate anti-VZV memory responses. A significant correlation between anti-VZV titers and AI was present in HIV+ children ($P = 0.001$), but not in healthy children.

Conclusion: This study confirms that HIV+ children have weaker antibody responses to VZV than HIV+ adults, or healthy children. The waning of anti-VZV antibodies which occurs in a significant proportion of HIV+ children does not result from an accelerated antibody loss, neither by the induction of lower initial responses, but from the failure to differentiate and/or reactivate anti-VZV memory responses sufficiently efficiently to maintain anti-VZV antibodies.

The influence of farming on lung function in school-age children – the GABRIEL Advanced Surveys

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Background: In contrast to its protective effect on atopy and asthma in children, the influence of farming on lung function at school age is yet unknown.
Methods: The GABRIEL Advanced Surveys are cross-sectional surveys in alpine areas of Germany, Austria and Switzerland as well as in Poland. In Phase III, lung function was measured by trained field workers using a mobile device (EasyOne, ndd, Switzerland) for spirometry including bronchodilation with a maximum of 400 µg of a short-acting beta agonist (Salbutamol) in a nested stratified disproportionate subsample in Bavaria only. This consisted of N = 895 children 7–12 years of age in 3 disease categories, i.e. atopic or non-atopic asthmatic (n = 282), atopic non-asthmatic (n = 278), and non-atopic non-asthmatic (n = 274) children in 3 exposure strata:
i) farm children, i.e. children living on a farm run by the family;
ii) exposed non-farm children, i.e. children not living on a farm but regularly exposed to stables, barns or cow's milk produced on a farm; and iii) non-exposed non-farm children as controls. We used weighted multivariable regression analysis to account for the stratified design and to assess a potential effect of farming on the measured parameters after adjusting for sex, age, and objectively measured body weight and body length.
Results: Based on current standards, acceptable spirometry results before and after bronchodilation were achieved in 711 and 652 children, respectively, with equal distribution among strata. Lower values for forced expiratory volume during the 1st second (FEV_1), its ratio over the forced expiratory volume (FEV_1/FVC) and midexpiratory flow (FEF_{25-75}) could be shown for asthma and wheeze variables derived 2 years earlier by questionnaire data in Phases 1 and 2. Among children with asthma or wheeze during the past 12 months, those children growing up on a farm run by the family had higher values for FEV_1 with 0.24 (0.03;0.44) L and FVC with 0.21 (0.06;0.37) L compared to controls.
Conclusions: In addition to the protective effect on atopy and asthma in general, farming may also have a positive influence on asthma severity measured by lung function at school age.

Restoration and maintenance of naive CD31+ and CD31-CD45RA+RO-CD4+ T-cell compartments after pediatric allogeneic hematopoietic stem-cell transplantation

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Aim: To explore in detail the reconstitution of 2 different populations of naive CD4+T-cells by analyzing CD31+ (PECAM+) on CD45RA+ RO-CD4+T-cells after pediatric allogeneic hematopoietic stem cell transplantation (HSCT). CD31+ discriminates naive CD4+ T-cells with high TREC (T-cell receptor excision circles) bearing T-cells representing recent thymic emigrants (RTEs) and naive CD4+T-cells with a higher replicative history, down-regulated CD31 and low/absent TREC content.
Patients and methods: A longitudinal retrospective analysis of children (n = 59) with malignant/non-malignant diseases up to 11.6 years after HSCT. CD31+ and CD31- naive CD4+ T-cells were measured regularly and compared to age-specific pediatric CD31+ and CD31-percentile curves generated by the analysis of 70 healthy children (age 0-16 ys).
Results: A triphasic pattern of reemerging CD31+ and CD31-CD45RA+RO-CD4+ was identified: a lag-phase, a phase of steep increase, and a maintenance-phase. For naive CD31+CD45RA+RO-T-cells, P1, P10 and P50 age-specific percentiles were reached at a median of +349, +487 and +1132 days after HSCT. For naive CD31-CD45RA+RO-T-cells, P1, P10 and P50 age-specific percentiles were reached at a median of + 293, +537 and +1639 days after HSCT. Any patient did not reach the P90 percentile for both naive CD31+ and CD31-CD45RA+RO-T-cells during the 11.6-year follow-up. The analysis of the maintenance-phase revealed that CD31+CD45RA+RO-CD4+ T-cells did not stabilize along the age-specific normal CD31+ percentiles, but continued fluctuating between the P10 and P90. During the first 4 years after HSCT, the ratio between CD31+ and CD31-CD45RA+RO-CD4+ T-cells showed a considerable inter- and intra-individual variability. Four years post HSCT, this CD31+/CD31- ratio stabilized finally at a ratio of 4:1.
Discussion: In children, age-specific P1 percentiles of CD31+ RTEs are reached about 1 year post HSCT underlining the importance of the reactivated thymus. Age-specific P1 percentiles of CD31-CD4+ T-cells are reached shortly thereafter indicating extrathymic expansion of naive CD4+ T-cells. Long-term analysis reveals that CD31+ lymphocytes remain the major fraction of naive CD45RA+RO-CD4+ T-cells up to 11 years after HSCT while absolute CD31+ and CD31- naive CD4+ T-cell counts continue fluctuating within the normal ranges of healthy children.

High Arginine-Vasopressin/Copeptin levels in umbilical cord blood after vaginal delivery and birth acidosis

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Background: The pituitary-secreted nonapeptide Arginine-Vasopressin (AVP) is unstable and therefore unsuited for diagnostic use but its secretion can be gauged by measuring copeptin, the C-terminal portion of the AVP precursor (CT-proAVP). We measured copeptin in infants' umbilical cord blood and at 3 days of age in order to identify normative values and perinatal factors influencing copeptin concentrations.
Methods: Paired arterial/venous umbilical cord samples were obtained from 117 infants and umbilical venous-only from additional 46 infants. In 102 infants, blood was also obtained at 3 days of life. Copeptin levels were determined using the CT-proAVP-Luminescence-immunoassay (Brahms, Hennigsdorf, Germany).
Results: Exceedingly high copeptin concentrations were observed after vaginal birth in umbilical cord venous (median [5-95% range]: 793 [6-4836] pmol/L) and arterial plasma [1610 [85-5000] pmol/L). Paired arterial and venous copeptin concentrations were closely related but were consistently higher in arterial than in venous samples ($p < 0.001$). Significantly lower copeptin concentrations were measured in umbilical venous blood of infants born by elective (5.2 [2.8–194] pmol/L) or secondary caesarean section (9.1 [3.1–1100 pmol/L). In addition, copeptin concentrations in umbilical venous and arterial blood correlated inversely with birth acidosis (pH, $r = -0.578$ and -0.639, both $p < 0.0001$). Copeptin concentrations measured at 3 days of life (13.5 [5.5-56.6] pmol/L) did neither correlate with copeptin concentrations at birth nor with delivery mode. Incremental postnatal body weight loss was related with increased copeptin concentrations at day 3 ($r = 0.412$, $p < 0.01$) and inversely correlated with copeptin concentrations at birth in umbilical venous and artery plasma ($r = –0.342$ and $–0,353$, both $p < 0.01$).
Conclusion: Vaginal birth is associated with a huge release of AVP/Copeptin. Umbilical cord copeptin concentrations exceed all values observed so far, including those in critically ill adult patients with myocardial infarction, shock, or brain injury.

The impact of adipose tissue drainage on glucose homeostasis

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Visceral obesity has been associated with insulin resistance, however the molecular mechanisms relating visceral fat accumulation and hepatic insulin resistance (portal theory) are still not well known. The portal theory implicates that fat tissue drained to the portal vein directly expose the liver to free fatty acids and cytokines and thereby inducing insulin resistance whereas in the case of systemically drained fat tissue these factors bypass the liver. We applied herein a novel adipose tissue transplantation approach to investigate a potential effect of fat pad localisation and in particular of venous drainage (caval versus portal) on glucose metabolism. Moreover, we hypothesized that IL-6 is a major initiator of hepatic insulin resistance associated with visceral fat accumulation. To this end, epididymal fat pads of C57Bl6J donor mice were transplanted either to the mesenterium (portal venous drainage) or the peritoneum (systemic venous drainage) of littermates. Sham-operated mice were used as control. Only mice receiving the portal drained fat transplant developed impaired glucose tolerance and hepatic insulin resistance. Moreover, mRNA expression of IL-6 was increased in portal transplanted fat pads compared to caval transplanted pads and portal vein plasma levels of IL-6 were elevated in mice with portal drained transplants. Intriguingly, mice receiving portal drained transplants from IL-6 knockout mice showed normal glucose tolerance and normal insulin signaling. Our results reveal an important role of fat tissue drainage respectively its localization on glucose homeostasis. Moreover, a causative role for portal IL-6 in the development of hepatic insulin resistance is demonstrated.

Analysis of the cell surface proteome for the identification of candidate diagnostic and therapeutic targets in drug resistant childhood acute lymphoblastic leukemia (ALL)

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In childhood acute lymphoblastic leukemia, persistence of significant levels of leukemic blasts after 6 months of treatment identifies a group of patients with very high risk of relapse (VHR-ALL). Prognostic markers are not available to identify this subgroup at diagnosis. Surface proteins that are preferentially expressed on refractory leukemia cells could serve as important diagnostic markers of high risk disease and promising candidate targets for therapeutic intervention. Here we present an extensive analysis of the cell surface glycoproteome of ALL cells from 8 VHR-ALL patients and from a corresponding set of ALL patients with good clinical outcome. Given the very limited amount of primary diagnostic material available for research, we have amplified primary human ALL cells in our established xenotransplantation mouse model. This allowed us for the first time to generate normally rare human leukemic cells in numbers sufficient for proteomic studies. We have optimized and extended the mass spectrometry-based Cell Surface Capturing (CSC) technology with complementary enrichment strategies, to increase the protein sequence coverage and the number of identified cell surface proteins. The immunophenotype analysis of leukemia associated surface markers by flow cytometry at diagnosis was recapitulated in our proteomic dataset in all cases. In addition several proteins – among them members of vanin (VNN) protein family – were detected that specifically mark a subgroup of VHR-ALL. Flow cytometry data of VNN-2 from xenografted samples correlated with the semiquantitative estimation of protein levels by the CSC technology. In an independent cohort of 29 ALL samples, we did not detect VNN-2 expression on ALL cells from standard risk patients, while we detected VNN-2 expression in 17% of high risk or relapsed patients. Since vanin family proteins have been proposed to mediate interactions between hematopoietic cells and their microenvironment, our findings also provide the basis to evaluate the functional role of vanins in ALL. Our data provide an unprecedented view at the cell surface landscape of the most refractory leukemia cases and identify subsets of cell surface proteins that could be used for diagnosis or therapeutic intervention in this deadly disease.

Identification and molecular characterization of human neuroblastoma tumour-initiating cells

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Neuroblastoma (NB), as many other solid tumors, displays a cellular heterogeneity within the tumor. There is increasing evidence that at the top of this observed tumor cell hierarchy, there is a sub-population of tumor-initiating cells (TICs), responsible for initiation and maintenance of the tumor. Candidates TICs have been isolated in a variety of adult solid tumors, representing a powerful potential therapeutic target. However, for some cancer types, including neuroblastoma (NB) and other childhood solid tumors, this population has not yet been identified nor characterized. Actually the identification and targeting of tumor initiating cells to definitively eradicate the disease represent an essential challenge for oncologists and researchers. NB is the most common extracranial childhood solid tumour originates from neural crest-derived malignant sympathoadrenal cells. We have identified cells within primary NB tissues and cell lines that express markers of neural crest stem cells and their derivatives, leading us to postulate the existence of TICs in NB tumour that recapitulate the properties of sympathetic precursor cells. In this study, we proposed a novel approach to identify and characterize NB TICs by prospectively identifying their self-renewal properties. From a very aggressive stage 4 NB sample, we selected self-renewing putative TICs by their sphere-forming capacity and analyzed their gene expression profiles by time-course micro-array analysis. Supervised and unsupervised analyses provided a list of sphere markers genes involved in embryogenesis and nervous system development (*CD133*, *EDNRA/B*, *NOTCH1/3*, *GPR177*…), and drug resistance (*MDR1*, *ABCA1*). Then to determine whether the sup-populations selected in spheres correspond to tumor-initiating cells, their tumorigenic potential was assayed by *in vivo* tumor growth analyses using subcutaneous and orthotopic (adrenal glands) implantations of tumor cells into nude mice. Tumors derived from the sphere cells were significantly more frequent and were detected earlier compared to whole tumor cells. However, a more detailed study of the potential NB tumorigenic-initiating cells revealed a phenotypic heterogeneity in the sphere sub-populations based on the expression of CD133 and MDR1 sphere associated markers. Thus, a further analysis of $CD133^+$ and $MDR1^+$ sub-populations characterized by the identified NB-TICs-specific markers by combined functional assays is now required.

The role of the mTor pathway for the development of the mouse thymic epithelium and function

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The thymus is the primary lymphoid organ responsible for the formation and maturation of naïve T-cells. These essential processes are controlled by a stromal microenvironment that is largely composed of thymic epithelial cells (TEC). TEC are responsible for the attraction, maturation, selection and export of T-cells that need to be tolerant to self-peptides but reactive to foreign antigens. The evolutionary conserved mammalian target of Rapamycin (mTOR) controls cellular differentiation and growth. mTOR activity is inhibited by Rapamycin, an immunosuppressant drug broadly used in clinical transplantation to inhibit T-cell activation. As Rapamycin is not tissue specific and targets mTOR also in other cells and tissues relevant for the regular continued formation and function of the immune system, we investigated the role of mTOR in TEC. For this purpose, we generated mice that specifically lack mTOR activity secondary to the absence of the mTOR specific regulator Raptor. The targeted loss of Raptor expression in TECs results in severe changes of the thymic microenvironment, profound thymic hypoplasia and peripheral lymphopenia. These observed changes demonstrate that the unique inhibition of mTOR in TECs impacts on the thymic capacity to support regular thymopoiesis. Studies are presently under way to define the molecular mechanisms operational for this lack of normal TEC differentiation and function. Taken together, Rapamycin not only acts as an immunosuppressive drug on T-cells but also disturbs TEC biology and thus affects the thymus-dependent maintenance of the peripheral T-cell compartment. This additional site of action for Rapamycin has relevant clinical implications which will be discussed.

The numbers refer to the pages of this supplement.