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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 woman, gravida 4, who was referred at 26 weeks of gestation for anhydramnios. The donor twin presented with anhydramnios, normal amniotic fluid index and normal Doppler velocimetry. Selective endoscopic laser ablation of connecting placental vessels was performed at 27 weeks of gestation, but amnioreduction was done. At 27 1/7 weeks of gestation a cesarean section was performed for acute or chronic inter-twin anastomoses leading to TTTS. In up to 5% an isolated twin anemia-polythemia sequence (TAPS) occurs, 15% of monochorionic twin pregnancies present a twin-to-twin transfusion syndrome (TOTS). 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.

Discussion: Almost all monochorionic twins share a single placenta with inter-twin anastomoses leading to TTTS. In up to 5% an isolated twin anemia-polythemia sequence (TAPS) occurs, 15% of monochorionic twin pregnancies present a twin-to-twin transfusion syndrome (TOTS). 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 TTTTS 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.

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 asphyxic 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 < 10 and/or BE < -4 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 27/infants below average in the CG vs 96 (56–122) with 1/infants below average in the NCG. Disabling CP was found in 1/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 clear that the worse the neurodevelopmental outcome would have been, if the CG had not been cooled. However, we observe far less severe asphyxial encephalopathy (proven 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 assess the benefit and to define the best clinical implementation of therapeutic hypothermia in asphyctic neonates.

W002 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-polythemia sequence (TAPS), with severe anemia in the donor and polythemia in the acceptor twin. This condition is characteristically associated with the twin oliga-polyhydramnios sequence (TOPS). Twin-to-twin transfusion syndrome (TTTS) often leads to 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 literature review.

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 ablation could be completed 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 placemic 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 day 5. The donor twin presented with severe anemia and hematocrit of 0.25.

His birthweight 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: Most cases of TTTS are caused by an imbalance in blood flow between the twin vessels, leading to an over- or underperfusion of the twin. In some cases, the imbalance is so severe that it results in a complete separation of the vessels. In such cases, the affected twin may develop severe anemia, while the other twin may develop polythemia. This condition is known as twin anemia-polythemia sequence (TAPS) or twin-to-twin transfusion syndrome (TTTS), depending on the severity of the anastomoses. Treatment options include amnioreduction to reduce the amount of blood flow to the affected twin, laser ablation of the anastomoses, and in some cases, fetal surgery to correct the anastomoses. However, the prognosis remains poor, with high rates of perinatal and neonatal mortality.
no other abnormalities and laryngoscopy simply showed mild laryngomalacia. Chest X-ray was normal and cerebral MRI excluded no other abnormalities and laryngoscopy simply showed mild laryngomalacia. Due to wall of the nasopharynx or even the superior aspect of the soft palate, examination of the regurgitated mass confirmed the supposed anaesthesia by mepivacaine 15th day of life but then could be discharged home without any respiratory distress.

Conclusion: Hairy polyps are infrequent benign tumours of the respiratory distress. 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.

Severe postnatal dehydration based on a Netherton Syndrome

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History: We report a male, preterm (36 1/7 wkgl) with a severe dehydration, hyponatraemia of 18 mmol/l and generalized scaly erythroderma. After correction of the hyponatraemia, the stabilization of the hydration was only possible with a high humidity (60–80%) in the incubator. At the age of 5 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 immunodeficiency (SCID) type one syndrome we made the diagnosis of the Netherton Syndrome by biopsy (Deficiency of LEKTI epidermal by immunohistochemistry) and the clinical manifestation.

Introduction: Netherton Syndrom is a rare autosomal recessive genodermatis characterised by ichthyosis, hair abnormality (trichorrhexis invaginata) and atopic manifestations. The ichthyosis is mostly present at birth with combined 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 Netherton Syndrom in mind whenever a severe dehydration, hyponatraemia is accompanied by congenital ichthyosiform erythroderma.

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 genodermatis 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 virus. The mother had a known genodermatis 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 neonatologist 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 exantheme of the newborn. Anticonvulsant therapy with phenobarbion 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 phenobarbion serum levels. A cranial ultrasound showed multiple echogenic lesions in the right frontal lobe. Cranial MRI detected right hemispheric multifocal gray and white matter lesion as well as cerebellar lesions resembling ischaemic 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 rash 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 subtle features of an apoptotic process.

Ophthalmological control at the age of 3 weeks was normal.

Conclusion: Incontinentia pigmenti is a rare neurocutaneous disorder which should be included in the differential diagnosis in newborns presenting with neonatal seizures, encephalopathy and vesicular rash.

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 Engström 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 (5601-Adult/Infant PNEUVIEW Michigan Instruments Inc) simulating the breathing of a newborn lung (compliance 1 ml/cmH2O and resistance 5 cmH2O/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 cmH2O, Positive End Expiratory Pressure (PEEP) from 5 to 8 cm H2O 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 six ventilators with an IT of 0.25s and 0.35s. However, Babylog was only able to deliver 90% of the 30 cmH2O PIP with an IT of 0.25s.

Conclusions: Recent ventilators are able to deliver desired volumes and pressures with short IT <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?
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). From conventional to HFV offers great practical and economic advantages. With an increase of the mean airway pressure (5 to 25 cmH2O), ventilator capability is decreased by 50% of Leoni Plus performance about 50% of Sensormedics capabilities, while Babylog reached only 15 to 10%. Sensormedics and Babylog were able to keep, given an unchanged amplitude, a constant tidal volume of 2 ml. 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 cmH2O with increasing amplitudes (at constant respiratory rate and tidal volume). The sensitivity of the SensorMedics decreased by 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 cmH2O, both Leonie and SensorMedics were able to keep, given an unchanged amplitude, a constant tidal volume of 2 ml.

Conclusions: In HFV, Leonie Plus performance is about 50% of Sensormedics, while Babylog doesn’t seem powerful enough with increasing settings. Being aware of such limitations, Leonie 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.

Fetal echogenic bowel: clinically relevant?
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Case 1: An 8-month old infant hospitalized for vomiting and abdominal distension. Abdominal ultrasonography showed a motility defect, 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 surgical correction and a temporary enterostomy. An echogenic bowel was present in prenatal ultrasounds, but abdominal X-ray and ultrasonography at birth were normal and genetic work-up for cystic fibrosis was negative. Interim medical history was unremarkable and weight gain was normal. 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 cmH2O with increasing amplitudes (at constant respiratory rate and tidal volume). The sensitivity of the SensorMedics decreased by 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 cmH2O, both Leonie and SensorMedics were able to keep, given an unchanged amplitude, a constant tidal volume of 2 ml.

Conclusions: In HFV, Leonie Plus performance is about 50% of Sensormedics, while Babylog doesn’t seem powerful enough with increasing settings. Being aware of such limitations, Leonie 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.

Automated infant auditory screening using the ALGO® 

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Objective: To compare 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 3 weeks and 41 weeks of gestational age. The test is performed within the first 48 hours of life. If the result is abnormal, the exam was repeated and if it is still abnormal, the child was referred to an ENT for audiological assessment. Results: During 6 months (08.2009–02.2010), 48 newborns at risk were tested for AABR. 62 tests were performed. 11 were abnormal (2) or failed (9) at the first test (23%). At the second test only 2 of 10 failed (20%). 1 of the 11 didn’t have a second test but had normal TEOAE. Of the 2, 17 newborns who had both AABR and TEOAE tests. In our small number of tested newborns AABR allowed to diagnose normal hearing in four newborns with abnormal TEOAE (false positive). The mean time of AABR screening is about 17 minutes, while TEOAE is considerably longer than the mean time of TEOAE (about 5 minutes).

Posters
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 neonates in addition to TEOAE to provide a better screening and to exclude a retrocochlear pathology.

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 as a complication of 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 macroscopic (diabetic fetoopathy) 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 and 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 mmol/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 started and stopped-calciemia 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.

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.

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, post-traumatic subarachnoid hemorrhage, peripheral subarachnoidal effusion, 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: peripheral neuropathy, peripheral facial palsy, Guillain-Barre syndrome, brachial plexopathy, posterior tibial nerve neuropathy, femoral neuropathy, ulnar neuropathy and mononeuritis multiplex. Persistent 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.


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 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, pancerbellar 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/hypsarrhythmia and the prenatal-onset microcephaly, are atypical. As long as the genetic etiology remains elusive, it will remain difficult to know on whom to focus treatment of PEHO syndrome and its variant form constitute a single disorder or not.

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

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 cases are 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 DOB1*0602. CSF hypocretin-1 level was 129 g/ml. IVlg 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. IVlg therapy for NC may be effective.

**P018**

**Infant poisoning, when should we think about it?**

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An eleven month old girl was brought to the emergency department for rapidly evolving neurological symptoms. She had first difficulty staying on her legs and sitting, and dysmetria when reaching for her bottle. Then she slept deeply, seeming to gaze in space. She didn’t have any systemic symptom and there was no history of tonicoclonical movements. After excluding meningocencephalitis, 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?

**PO19**

**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 post synaptic). Generic diagnosis of a CMS is often possible on the basis of myasthenic symptoms and findings on electrophysiologic 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 raspsyn mutation. The boy presented at birth with severe weakness and hypotonia, absent sucking, macrocephaly and mild dysmorphic features. Because of respiratory insufficiency he required ventilation for 8 days. Initial investigations including cranial magnetic resonance imaging, electron microscopic examination, creatin kinase and metabolic screening were normal. There were no signs for myotonic dystrophy or myasthenia in the mother. The clinical condition improved spontaneously, but general weakness and feeding problems persisted. At 5 months of age, a viral infection led to transient respiratory insufficiency. After excluding meningoencephalitis, atypical seizure, systemic symptom and there was no history of tonicoclonical movements. After excluding meningocencephalitis, 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?

**PO20**

**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 trigger this syndrome. 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 a myasthenic syncope, fatigue and poor speech. Her neurological status revealed horizontal and vertical bilateral nystagmus, oculo-motor skew deviation, dysarthria, general hypotonia, and cerebellar ataxia. Complete workup was conducted in both children including a CSF 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 and 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 should be made presumptively after exclusion of other diagnoses and confirmed by brain MRI seen as 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?**


We present the case of a 10% 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 headache. On the clinical exam residual left hemiplegia and hypotalamic lesions from birth was noted on the left trunk. MRI showed aspeciﬁc lesions in the cortico-subcortical left grey matter and moderate hydrocephalus. Blood tests excluded an infectious, inflammatory, thrombotic 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 hyperT A? She was transferred 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 hypersignalaization with aspecific 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 biopsy was performed. The histology revealed an increased cellular invasion with very mild inflammation and without signs of malignancy. The immuno- histochemistry revealed positive markers of the cells for HMB45 et Melan A. These results 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 these reason, 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 patient: 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 hypotonia, 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 month 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 abnormalities (leukodystrophy) and typical ventricular 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 findings 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 clinical 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 counseling of the family. The possibility of copper histidine treatment has to be considered and discussed with parents, but there should be an individual decision.

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 important that otorhinolaryngologists and pediatricians are aware of the effect of AOM on balance, the management should be discussed interdisciplinary.

Acute otitis media related ataxia
A. Carrard, B. Goeggel Simonetti, S. Grunt, M. Caversaccio, A. Duppenthaler, I. Steiner
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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 with present or ataxia

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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.

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. On the following days, his general condition deteriorated 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 painful mobilization. The both feet were discretely swollen and painful 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-anticoagins and anti nuclear antibodies were negative and 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 was 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 child was also administered starting on the 10th day of fever. This case is interesting in two respects. Firstly, it is a streptococcal infection suggested to the house staff an atypical Kawasaki syndrome. The child was PSRA using the diagnostic criteria of Ayoub and colleagues. The patient was initially treated with antibiotics, antiinflammatories 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.

Food allergy: Evaluation of the quality of life in Swiss children
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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 analyzed in term of emotional, 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 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 low and equal to 0.25, in group 2 the score was 2.03 and 1.77 in group 3. Food anxiety total score was 1.90, 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 1.89 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.
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) in case of 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 adolescents require two infusions at different sites and hence a longer infusion time.

Conclusions: The successful administration of IVIG in the paediatric population is safe, efficacious and considerably improves the quality of life of the patients and their families.

Incomplete Kawasaki Disease – Incomplete guidelines?

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Introduction: Kawasaki disease (KD) is an acute self-limiting vasculitis. Children aged 6 months 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 diarrhea. Gastroenteritis accompanied by a mild bilateral conjunctival injection and a macule 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. Echocardiography should be performed if fever persists for at least 7 days without other explanation.

Conclusion: St. Gennaro 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.

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 calprotectin. 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 constipation. Appropriate treatment with a gluten free diet solves the problem in most cases.

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 erythrocyte precursors 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, perportal fibrosis and canalicul 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/m², 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 declining, haemolysis remains mild and the boy is followed as inpatient with a good clinical condition.

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.

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 forcible 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

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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)
combination with hemorrhagic colitis, which our patient did not show. In
contrast, Ibuprofen is independently associated with GIB due to
secondary to an increased intra-abdominal pressure due to incomplete
opening of the cricopharyngeal sphincter occurring during vomiting or
cough. Rarer causes include eosinophilic or Barrett’s esophagitis, HIV
developmental delay or other predisposing health conditions such as
depressed 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 bowel 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 ileocecal 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
necrosis and perforation, volvulus, fistula formation, peritonitis and
postpyloric location of the magnets. However, severe or even lethal
one magnet is ingested, early extraction is indicated. This may either
and parents’ awareness of possible ingestion may be absent. Ingestion
psychiatric diseases. The initial clinical symptoms are rather unspecific
predisposing health conditions such as developmental delay or
aged 1–3 years. Another risk group are older children in context with
majority of magnet ingestions occurs in children
10 days. Adaptation to normal diet was easily attained. Full recovery
resection and end-to-end anastomosis. Antibiotic treatment with
necrosis and perforation, there was a massive intramural haematoma and local
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Pericarditis 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 extracardiac involvement in 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 hyposonorous 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 normal, 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.

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 intramuscular compartment causes capillary 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 the 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 femoral cannulation in a critically ill 15-year-old status post-cardiac catheterization was performed on post-operative day 4 by a left femoral canulation to exclude aorto-pulmonary collaterals. After 8 days of heavy sedation, the child presented predominantly right leg induration and symptoms of nervous injury with bilateral paresis. 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 prepared for 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 contracture. Awareness and early diagnosis is essential and can be made by the directed clinical and radiological examination. A compartment pressure >40 mm Hg for >6 hours is an indication to prompt fascitomy and can avoid devastating complications.

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

L. Vaujois, M.-H. Decray, V. Finci, S. Fokstuen, P. Externmann, Y. Aggoun, M. Baghetti, C. Tissot, Cecile Tissot Hôpital des Enfants de Genève

Introduction: Heterotaxy syndrome is characterized by abnormal left-right axis formation resulting in a complex variety of splenic abnormalities (asplenia/polysplenia), gastrointestinal malrotation as well as complex and severe heart defects. A twin pregnancypremium in case of dizygotic twins. Genetic counseling was proposed to the couple and L. Vaujois, M.-H. Decray, V. Finci, S. Fokstuen, P. Externmann, Y. Aggoun, M. Baghetti, C. Tissot, Cecile Tissot Hôpital des Enfants de Genève

Introduction: In conditions with a wide range of differential diagnoses characteristic 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 over a year, and feeding disorders were reported. Abdominal distension and vomiting developed, and the parents reported intense crying of the baby, especially after drinking. A gastrointestinal work up of failure to thrive ensued. In the case presented aprominent precordial impulse was impressive both visually and by palpation. ECG abnormalities (asplenia/polysplenia), gastrointestinal malrotation as well as complex and severe heart defects. A twin pregnancy premium in case of dizygotic twins. Genetic counseling was proposed to the couple and L. Vaujois, M.-H. Decray, V. Finci, S. Fokstuen, P. Externmann, Y. Aggoun, M. Baghetti, C. Tissot, Cecile Tissot Hôpital des Enfants de Genève

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Central cyanosis in childhood, think about pulmonary arteriovenous malformations

L. Vaujois, C. Tissot, M. Beghetti, Y. Aggoun, Cécile Tissot
Hôpital des Enfants de Genève

Introduction: Central cyanosis is rare in childhood and should make pediatricians think about a pulmonary arteriovenous malformation (PAMV) when the heart is normal. AVMs are abnormal fistulous connections between pulmonary arteries and veins, without intervening capillaries. PAMVs result in direct right-to-left shunt, causing hypoxemia and dyspnea on exertion. Patients may present life-threatening complications such as stroke, transient cerebral abscesses, hemoptysis or spontaneous hemotherax. Early diagnosis is essential because these complications can be prevented by PAMV embolectomy and antibiotic prophylaxis.

Case report: We present the case of a 9 years 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 (SaO₂) of 84% and digital clubbing. Cardiac auscultation was remarkable for a low pitched systolic-diastolic murmur on the left-sided side. 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 dilation. A bubble test showed rapid filling of the left cardiac cavities with contrast after 3 cardiac cycles, suggestive of a PAMV. Three-dimensional reconstructions from a multi-slice CT scan showed an aneurysmal saccular PAMV 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 vein. Transcatheter embolectomy with a 2 mm coil plug was performed allowing for an increase in the SaO₂ to 98%. One month later, the girl had no murmur on clinical exam and a SaO₂ of 96% on room air.

Conclusion: PAMVs 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 choice of treatment is transcatheter embolization of the PAMV. Early diagnosis is important to prevent the life-threatening complications of this malformation.

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

L. Vaujois, C. Tissot, M. Beghetti, Y. Aggoun, Cécile Tissot
Hôpital des Enfants de Genève

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 weighing 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 distal from the atri-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 MVSD 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 was confirmed by 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.
These patients showed IVIG resistance. They finally responded to needing treatment in an intensive care unit. These cases are reported treatment with high dose of anti-inflammatory drugs and repeated IVIG describing other cases of cardiogenic shock post-Kawasaki disease. to have elevated inflammatory markers with important cardiac immunoglobulins and high dose aspirin. The echocardiogram dysfunction. These patient’s illness are often mistaken for toxic or treated with fluid replacement, dobutamine, one dose of intravenous patient was diagnosed with Kawasaki disease shock syndrome and risk of more severe coronary artery disease development. The cardiac dysfunction in a patient also with partial KD diagnostic criteria. make and should always be considered when there is shock with ventricular dysfunction with an ejection fraction of 48%, a pericardial amoxicillin/clavulanate. The day after hospitalization and 5 days after with a diagnosis of cervical adenitis and treated with intravenous blood chemistry. A neck ultrasound was also performed showing elevated CRP (>200), a leukocytosis with a left shift, and a normal malformation accounts for 5–10% of all congenital cardiovascular causes include delayed recognition of aortic coarctation. This 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 treated 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.

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 in both necks. 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 chills, 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 (0.46 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’ resistance to 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.

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

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Aims: To compare the taste of equivalent doses of pulverized amldipine and lercanidipine, two calcium channel blockers, among children with kidney disease.

Methods: Each child received a test dose of 1 mg of amldipine 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 amldipine 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 amldipine (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 crucial available tablets and administer the medications 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 amldipine.

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). Of importance, about 1/3 of the initial prehypertensive or hypertension children become normotensive at the end of the consultation (29.9% vs. 36.1%, p < 0.0001). 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. Dosing IVIG response to avoid overestimation of hypertensive individuals. Nevertheless, hypertension should be confirmed with ambulatory 24-h blood pressure or home blood pressure measurements.
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 (130/70 mm Hg), altered consciousness, and aggressive behaviour. Laboratory findings included hypernatremia (130 mmol/l), hypokalemia (2.7 mmol/l) and metabolic acidosis requiring massive fluid and sodium supplementation. Plasma creatinine level was normal, and 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 hypernatremia/hypokalemia, 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 chemistyr 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 renal Fanconi syndrome. The long-term remission after omission of cyclohexylamine suggests a causal relationship as reported once in renal Fanconi syndrome. The long-term remission after omission of cyclohexylamine suggests a causal relationship as reported once in renal Fanconi syndrome. Thus, after 8 episodes of recurrent renal Fanconi syndrome following ingestion of cyclamate, dietary advice was given to omit all potential sources of the artificial sweetener cyclamate.

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.

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 subheadings: hypospadias and urination, ultrasonography (US), urinary tract/abnormalities, urinary bladder/urethra/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 were performed with normal results, secondary to marked differences in the characteristics of the studied population and also to the striking absence of any specific indications to urological 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 benefits of postnatal uro-radiologic 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 this population. For all these reasons, no clear conclusions regarding the need for postnatal uro-radiological studies in newborns with hypospadias can be drawn at the present time.

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 therapy for 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 intense 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 ureteropexy 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 our case, these cases are most 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 endovascular contrast is the keystone to diagnosis. Nevertheless, this case demonstrates that the full extent of the injury could only be revealed by pyeloscopy.

Goodpasture’s disease presenting with acute renal failure

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A 15-year-old boy was admitted for vomiting, diarrhoea, fatigue, crampy abdominal pain and oliguria. A renal failure was diagnosed (creatinine 2523 µmol/l, urea 55,1 mmol/l) with severe regenerative anemia (80 g/l), metabolic acidosis, hyperkalemia, elevated inflammatory markers and normal platelet count. A nephrotic proteinuria was noticed (350 µmol/l). Patient’s creatinine was normal 4 months before. 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 hospital’s 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 parent’s 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.

Long-term consequences of preterm birth

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Introduction: Prematurity or small for gestational age birth are frequently characterized by short-term, next-day-long 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 hypertrophic 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

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 usage 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 evoked 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.

ANCA positive vasculitides 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 m²). Additional symptoms: Arthralgia, recurrent epistaxis, petechiae. Vasculitis associated findings: Leucocytosis, anemia, CRP (350 g/mol) and C-ANCA-titer: 1:1280. Renal biopsy: Extraglomeruläre proliferative and necrotizing GN.

Treatment: Nine sessions of plasmaexange (PEX) within 13 days. Induction therapy with methylprednisolone (M-PDN) i.v. (3 doses of 500 mg/m²/BS each), thereafter continued with prednisolone (PND) orally (1 mg/kg/d); cyclophosphamide (CPy) i.v. (3 doses, initially 500 mg/m²/BS, increased to 1000 mg/kg/m² every 4 weeks), Follow up after 3 months: GFR: 62 ml/min/1.73 m², proteinuria: 1000 g/mol, C-ANCA-titer: 1:10; blood pressure: 135/90 mm Hg. Current treatment: Daily PND (tapering, orally), CyP 1000 mg/kg/m² every 4 weeks (in total 6 doses). Thereafter a switch to Azathoprine (AZA) is planned. GIRL: Diagnosis at the age of 13 years. Initially diagnosis of a parvovirus-infection (pos. IgM-titer for parvovirus) with fatigue, gonarthrosis, anemia. Symptoms progressed within 8 weeks and renal function decreased (GFR 35 ml/min/1.72 m²). ANCA-titer (1:640). Renal biopsy: Extraglomeruläre proliferative GN with fibrosis and crescents. Treatment: 160 days of induction therapy with M-PDN i.v (3 doses of 500 mg/m²/BS each), thereafter PND p.o 1mg/kg/d and CyP 2.5 mg/kg/d p.o during 12 weeks. Follow up after 3 months: GFR 60 ml/min/1.73 m², ANCA neg. Switch from CyP to AZA 1mg/kg/d p.o and tapering of PND. Follow up after 2 years: Recurrence of arthralgia and manifestation of cutaneous lesions: Switch from AZA to MTX (15 mg/m² weekly). Follow-up after 6 years: in remission with a GFR of 65 ml/min/1.73 m², mild proteinuria and borderline ANCA-titer (1:3). Normal blood pressure. Current treatment: Treatment with PND 2.5 mg every second day and MTX 10 mg/week p.o.

Conclusions: The differential diagnosis of a multi-organ disease should include the diagnosis of ANCA pos. vasculitis. Early and adequate treatment with immunosuppressiva and plasmaphexange may prevent development of rapid progressive glomerulonephritis, preserving glomerular renal function.
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 catecholamines and steroid profile. Kidney size was normal on ultrasound and renal artery stenosis was ruled out by angiographic magnetic resonance imaging; however, the venous 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 swelling of the 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.

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 intraocular pressure. Ultrasound biomicroscopy showed a central posterior stromal defect connecting the anterior chamber with an intracorneal neo-chamber, as well as iridocorneal adhesions on both sides. Taken together these findings were consistent 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 thickening. Cornea transplantation is planned in the near future.

Discussion: Peters anomaly is a rare form of anterior segment dysgenesis in which abnormal slaving 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 B3GALT1 gene. We are currently searching for PAX6 gene mutations in that family.

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 is myotonic dystrophy. CF-phenotypes seems worthwile to be considered, especially in unexplained severe clinical manifestation of CF in young children.

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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 worthwhile to be considered, especially in unexplained severe clinical manifestation of CF in young children.

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, hypoplastic cardiomyopathy), and variable cognitive defects. 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 dorsolimb

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 to 5000 lifeborn per year and an overall mortality rate of 40–60%. It has the power to interrupt normal and mainly cardiac and pulmonary 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 with the Zurich Neuromotor Assessment. Intellectual performance was examined with the German version of the Wechsler Intelligence Scale 3rd edition (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 deficits (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 75, range 50–98; 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.

Cloudy corneas at birth: a case of bilateral Peters anomaly

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Background: Cloudy corneas 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 amblyopia. We present such a case.
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) use and 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 and text search and review 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 years (range 0.1–18); median duration of hospitalisation 4 days (range 1–35); 37% (74 patients) were admitted; 41 (10%), 5% respectively, of these, 101 (91%), 63 (76%), and 2 (20%) received AB respectively. CRP values in the 166 patients underlying AB were >30 mg/l in 79 (47%), >50 mg/l in 72% (32 (20%) and >120 mg/l in 32 (20%) patients. A microbial organism was identified in 86 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 1–35), 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 confined restriction of antibiotic use are needed.

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 aged 0.1–18 year with patients with haemato-oncological, surgical, and other diseases. Mean age at CVC insertion was 1 months (Interquartile range 0–51 months). Twenty BSI occurred in 17 CVC in 14 patients (9%). 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, >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.
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 terms of the number of visits to the pediatric emergency department (ED) and estimated its costs.

Methods: All outpatient 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 potential patients with local H1N1 infection. 100% had H1N1 PCR test performed: 6 were positive (20% of 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 7 in-hospital patients, 2 had H1N1 PCR positive result (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, 800 and 3’093 SFs, 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 anaemia
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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 VSSA refractory to immunosuppressive treatment underwent an haploidentical HSCT without engraftment and a rescue double cord blood (UCB) transplant because of persistent aplasia. VSSA had developed 17 months earlier and at the time of transplant,transfusion 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 engraftment 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 triple therapy (voriconazole, posaconazole, amphotericin 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 gastrointestinal tract. The patient died shortly of multorgan 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 toplustifiable 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 S. enteritidis (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 suspicion of underlying rheumatoid arthritis. 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 further 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.
Posters

**P071**

**Pediatric A/H1N1 infection in Hôpital Neuchâtelos:**

*epidemiological study using database report*

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A/H1N1 virus have infected 1–15 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 situation. Student's t test was used for statistical analysis. From May 4th 2009 until Jan. 5th 2010, results from s40 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 S ± 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 < 0.00003).

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), immunosuppressive illness and age (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 antiepileptic 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 and 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 contributed to the development of 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 an oral antibiotic therapy with Co-trimoxazole was introduced for patients with another type of pulmonary TB, but initially, for those patients without identifiable disease. In conclusion, it is essential to underline the importance of K. kingae 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 hospital. 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.

**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 cocccobacillus is difficult to identify with the usual techniques and requires enhanced culture media, prolonged incubation or the use of PCR. Osteomyelitis, a clinical entity that relates mainly to bone tumors 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. We also report here a second case of 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 amoxicillin-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 hospital.

**P074**

**Visceral leishmaniasis and hemophagocytic syndrome**

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A 11 months old infant from Portugal, free of family history, consults for apathy, weight loss, tachycardia, tachypnea, petechia, pallor without icterus and hepatosplenomegaly. Seven months earlier, while being in Portugal, she presented a persistent anemic 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, PT 41 sec.), hypotension (124 mmHg/l), elevated CRP (139 mg/l), high ferritin (34.775 mg/l), thrombocytopenia (13 G/l), impaired coagulation (INR 1.4, PT 41 sec.). Investigations demonstrated an inflammatory process (sed rate 107 mm/h, C-reactive protein 86 mg/l), normal liver function test (LFT), discrete leucopenia, retropitoneal and paravertebral cystic masses, multiple mesothelial thickening and a left iliac fossa fluid collection. 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 Pyrazinamide) was started with close follow-up of LFT. Over a few days, he developed decreased level of consciousness, 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 HH syndrome 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.

**P075**

**Visceral leishmaniasis and hemophagocytic syndrome**

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A 11 months old infant from Portugal, free of family history, consults for apathy, weight loss, tachycardia, tachypnea, petechia, pallor without icterus and hepatosplenomegaly. Seven months earlier, while being in Portugal, she presented a persistent anemic 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, PT 41 sec.), hypotension (124 mmHg/l), elevated CRP (139 mg/l), high ferritin (34.775 mg/l), 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 given during the course of the disease. Dexamethasone (10 mg/m²) 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. It 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 presenting fever and laboratory diagnostic criteria include cytopenia, hypertransamidemia, 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 primary cause. In children with 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.

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 diagnostic 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 controversy 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 Bernal® 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 antibiotic therapy 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 is clear 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.

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 cobalamin (B12 vitamin) 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 neuro-motor 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 abnormality. The gastroenterologist 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 retardation of acquired type and psychomotor regression. 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 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 lamidazoles (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 clinical symptoms in 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.
This case report illustrates 1) the need for a detailed endocrine and ophthalmologic monitoring of hyperthyroidism after slow dose reduction of carbimazole after 2 years. Laboratory investigations revealed a severe Vitamin B12 deficiency, centrilobular hypothyroidism, low TSH-receptor antibodies, and complete suppression TSH values. Autoimmune hyperthyroidism was diagnosed (236 nmol/L, N 60–160) and T3 (6.9 nmol/L, N 1.1–2.8), and completely normalized on the basis of elevated TSH-receptor antibodies. Thyroid suppressive therapy with carbimazole subsided initially with propranolol normalized partial amelioration of symptoms. During hospitalization, he was fed by nasogastric tube and quickly resumed growth height and weight. The oesophagus for an unknown period of time. Vitamin B12 deficiency can be 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.

Pay attention to attention deficit - and the growth curve

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A 14 year old girl was presented with progressive muscular hypotonia, delay of motor development and failure to thrive. She was hardly able to sit or hold his head and only succeeded to lift the arms a few cm from the surface. Her speech comprehension seemed normal and she spoke one word ("Mama") with a 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. Vitamin B12 was administered intravenously. The further course was very favourable. The boy could eat porridge, increasing amount of food and regaining weight and height. In 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.

Neuronal calcium channels 1A 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 Spino-cerebellar Ataxia type 6 (SCA6, late-onset and progressive).

A 9-year-old girl was seen for hypotonia, ataxia and recurrent hemiplegic attacks. In vitro expression studies of the identified mutation are underway, aiming at understanding its functional consequences and finding an efficient treatment.
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 (136/6.7 mmol/L) and C-peptide (700/840 pmol/L) levels during a supervised 72-h fast. Thus, in addition to undetectable sulfonylurea levels, factitious hyperinsulinemic hypoglycaemia 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 its’ smaller glucose stores. Therefore, auðer ond diagnostic criteria for insulin-secreting tumours may not be valid in children.

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 abruptio. In the first days of life he demonstrated a 15% weight loss (302 mosmol/l) and low urine osmolality (96 mosmol/l) corrected by intravenous caloric supply to escape catabolism, and ammonia 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 its’ smaller glucose stores. Therefore, auðer ond diagnostic criteria for insulin-secreting tumours may not be valid in children.
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 closure, delayed ear development and slightly retarded. Thyroid function testing confirmed extremely high T4T (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 (26.0 pmol/l), anti-gut antibodies (anti-gut peroxidase (TPO) antibodies) and 4.72 nmol/l (N 30-90) and thyroid 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. 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.

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 cholesterol metabolism. GA II may present with nonketotic hypoglycemia, developmental delay, muscular weakness and hypotonia. It can be complicated by leucodystrophy. We report on a child with a metabolic crisis due to GA II presenting with coma and severe leucodystrophy.

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 unaffacted grey matter. MR spectroscopy showed an increase in lactate. Urine analyses revealed an increased excretion of glutaric acid, 3-OH-gluutaric acid and fatty acid metabolites, parallel changes in the chain fatty acids, thus – together with the cerebral neuroimaging – pointing towards the diagnosis of GA II. On a protein-restricted diet with an adapted amino acid formula, vitamin B2 supplements, carnitine and maltodextrine, the boy recovered fully to the level of motor function present with nonketotic hypoglycemia, developmental delay, muscular weakness and hypotonia. It can be complicated by leucodystrophy.

Case study: pitfalls in evaluating and treating bone disease in a female adolescent with anorexia nervosa
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Introduction: Adolescents with anorexia nervosa (AN) are at high risk of osteopenic bone disease. 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 amenorrhea 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 OPG 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 primarily renal 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 underapplying adult diagnostic criteria; finally she was about to be over-treated (notably with a highly controversial intervention) by uncritical thyrotoxicosis. Evaluation and treatment of pediatric bone disease including DXA and BP therapy requires involvement of the specialist.

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.

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 8.9 g 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); T3: 21.0 pmol/l (range: 2.4–6.4 pmol/l); T4: >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. Serous conditions are rare and no lethal case after monogenesis 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.

Results: The mean BMI was 25.2 ± 3.7 kg/m² and BMI z-score was 2.7 ± 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% that had none. We observed that 69% admitted 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 11h/day in front of television or computer and 17% spent more than 3 h/day. We found that the patients eating quickly ate more (86 vs. 25, p = .008). Those who did not play outside nibbled more (62 vs. 25, 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 play outside in front of television or computer nibbling 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.

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 health 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 (23 ± 3 to 15.3 ± 3 years old, body weight 21.5 ± 4.2 kg/m², height 144 ± 7.5 cm) 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 ± 3.7 kg/m² and BMI z-score was 2.7 ± 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% that had none. We observed that 69% admitted 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 11 h/day in front of television or computer and 17% spent more than 3 h/day. We found that the patients eating quickly ate more (86 vs. 25, p = .008). Those who did not play outside nibbled more (62 vs. 25, 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).

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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. 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%), ascites (81%), genito-urinary (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 trauma. Abnormal ultrasounds, but not abnormal liver function 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.
**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 grade 3 reaction, antivenom was administered. While the edema significantly decreased, the livid discoloration of the arm subsided. 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, direct the patient to the hospital for at least 24 hours. There is no evidence in the literature that antihistamines, steroids or epinephrine are of benefit for grade 2 reactions (local edema of the limb, moderate systemic reactions like hypotonia, vomiting and/or diarrhea). No further systemic 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.

**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, diarrhea, coughing, and coughing 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 nasogastric 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 I-II. The patient was progressively repleted and was able to be discharged from the emergency room 5 days later. Microscopic analysis of sodium chloride 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 chloride poisoning leading to encephalopathy, failure, and death. The lethal dose of sodium chloride is 10 to 15 grams. Our patient ingested 2.24 g. Caustic gastroesophageal lesions in children are very common with a large range of lesions, ranging from minor burns to severe necrosis. Complete structure, 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.

**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 generalised edema of the face and extremities with extensive desquamation, A skin biopsy 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 dyspnea, hypoxemic desaturation, respiratory acidosis (pH 7.26, PaCO2 45.5 mmHg, PaO2 63 mmHg), hypoalbuminemia (19 g/l), and eosinophilia (1.3 G/l). Thus, differential diagnosis was extended to immunodeficiency syndromes incl. NS. Immunohistochemistry 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 septicaemia 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 gestational weeks. Intravenous nutrition consisted of eight erythrocyte transfusions. Directly postnatal his haemoglobin was stable. Immunoglobulins (IVIG) were given prophylactically once. Photopherapy was recommended. In the age of 124 months his blood group became stable, and for the first time his own blood group 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 newborn haemolysis is less or even absent in comparison to anaemia caused by Rhesus- or ABO-incompatibility. The cause is the quasialplastic 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 anti-Kell alloimmune anaemia of the fetus and newborn haemolysis is less or even absent in comparison to anaemia caused by Rhesus- or ABO-incompatibility. The cause is the quasialplastic 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. **Pathophysiology:** In anti-Kell alloimmune anaemia of the fetus and newborn haemolysis is less or even absent in comparison to anaemia caused by Rhesus- or ABO-incompatibility. The cause is the quasialplastic 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. **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.

**Allergic 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 of Kell alloimmune anaemia. **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. The baby did not show any clinical symptoms and was discharged symptom-free 5 days later. 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 myeloid 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.

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

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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, hypersplenoglyceridemia (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 a massive macrophage infiltration 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 HCT 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 can be primary but severe disease be 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.

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


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 anemia (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 Gammain) and cyclophosphamide (CA) were started. A week later he developed a serum sickness syndrome that responded to corticosteroid treatment. 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. In this case, patient’s allograft was functioning well. 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.
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 correlate 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 paediatric 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 composed 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 is no evident antibody deficiency against 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.

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. However, 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 pulmonaryopathy 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 of these families have important implications for the management of cardiovascular functions in patients with CF and require further exploration so that cardiovascular health can be maintained.

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 result in tension pleurothorax. Early starting ventilating as pleurothorax with cardiac 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 weight loss. He presents with minor respiratory distress and tachypnoea. Thoracic 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 after the child was ultrasonicated 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 CF are at increased risk for pneumococcal pneumonia. Preventive strategies are crucial and include silos with good ventilation systems. The child should have an ultrasound control and eventually a diagnostic puncture. In the situation of a major effusion, an immediate diagnostic and therapeutic drainage must be performed and the child carefully observed.

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

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Background: Compared to developing countries, community acquired pneumonia is 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 antibiotic 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 parental 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 direct Coombs test positive, 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 uraemic syndrome (P-HUS) was made. After two pneumothoraces, 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 <150 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+H) 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.
Discrepancy between clinical and radiological presentation of pneumonia in a 6-year old boy

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Padiatrie, Kantonsspital Freiburg, HFR

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 hypoxemia and on percussion marked hypoesthesia of the entire left hemithorax. No wheezing, no retractions and no nasal flaring.

Diagnosis: 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.

Neonates born to syphilis positive mothers: management and outcome

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1Department of 1 Paediatrics and 2 Dermatology Triemli Hospital Zurich; 3Department of Dermatology University Hospital Zurich

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 syphils 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.
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 hypoxic-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.

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 ± 2.9 weeks, birth weight 1795 ± 456 g) were followed longitudinally by lung function testing. Five of the 14 subjects had been traqueotomized in early childhood.

Results: Patient characteristics in 2008: 3/14 had persistent upper airway obstruction (2 from subglottic stenosis, 1 due to vocal cord paralysis). 7/14 were smokers and/or atopic. 6/14 had current respiratory complaints (exercise intolerance, chronic cough, or asthma).

Lung function:

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>14.9 (3.6)</td>
<td>18.4 (3.2)</td>
<td>38.1 (3.2)</td>
</tr>
<tr>
<td>TLC (%predicted)</td>
<td>94.6 (9.5)</td>
<td>95.9 (12.5)</td>
<td>113.2 (19.0)</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>23.7 (4.9)</td>
<td>26.1 (7.3)</td>
<td>39.4 (8.7)</td>
</tr>
<tr>
<td>FEV1/Vc (%)</td>
<td>73.6 (12.8)</td>
<td>72.2 (13.3)</td>
<td>69.7 (10.9)</td>
</tr>
</tbody>
</table>

Conclusion: 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.
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 than 1 year old 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 <88%), 92%, fractionated meals and rhinopharyngeal 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 were included, group 1 and 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 median respiratory rate, the mean SpO2 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.

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 (FEV1), FEV1/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 (FEV1) did not change significantly over time (p > 0.05). However, the FEV1/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. FEO2 remained stable and FEV1/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.

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

Methods: Six children with PBO, ages 6 to 15 years, were treated with inhaled corticosteroids (ICS), and macrolides and/or IVIG.

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.

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

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

Methods: Six children with PBO, ages 6 to 15 years, were treated with inhaled corticosteroids (ICS), and macrolides and/or IVIG.
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 advises 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 90 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 in 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 videothoracoscopic 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 third month, and the patient was discharged. After 8 days of unsuccessful attempts, a videothoracoscopic 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 pneumothorax, successfully drained by a chest tube. Five months later a new pneumothorax occurred contralaterally, 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. Postoperative mechanical pleural abrasion. 3 months later, a third partial left pneumothorax happened, successfully controlled by a chest tube. Physical examination suggested Marfan syndrome, no skin anomalies were found. Family history was negative for any known relevant predisposing disease. Alpha 1-antitrypsin levels were normal. Echocardiography revealed mitral valve prolapse, Furthermore supporting the Marfan syndrome hypothesis. FN1 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 spontaneous 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 positive 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 in Leicestershire, UK. Spirometry performed at 7, 10 and 15 years of age, adjusted for age, sex, cancer diagnosis, cancer therapy and time since diagnosis. Prevalence of asthma and intake of analgesics in the past two years were assessed by questionnaire in 2008 in young adults (≥16 years) diagnosed with cancer between 1976 and 2003 (Swiss Childhood Cancer Survivor Study).

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 AMJRCCM 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 in the last 12 months".

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 Leicestershire 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).

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.

Funding: Asthma UK 07/048; SNF 3200B-122341
Liver transplantation for inborn errors of metabolism in children: the Geneva experience

Hôpitaux Universitaires de Genève

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 transplantation, and special diets 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 (0.5–15) in contrast to 5.5 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.

Parents: Mothers' performance score improved from a mean of 72.2±15.4 pre-LT to 86.7±11.2 post-LT. P = 0.022 at 24 months post LT. Protective factors for normal DQ at transplant (66.7% vs 50% for older age group) were reported previously.4 patients were not evaluated pre-LT. 19 mothers were employed (67%) and 32% were housewives. Among patients transplanted in the older age group (p = 0.02). Parent-child relationship was measured as normal in 59% of families assessed more frequently in P2 (P <0.001, <0.001, 0.001, 0.013 and 0.013 respectively). Protective factors such as gender, age at OLT or diagnosis did not explain these differences. Among P2 patients, pre- and post-LT titers for D, T and HAV were up-to-date for DTAP (70% versus 43%, P = 0.023) and MMR (74% versus 44%, P = 0.032). HBV, HAV, SPn and VZV vaccines (P = 0.000, 0.011, <0.001 and 0.009 respectively). Confounding factors such as gender, age at OLT or diagnosis did not explain these differences.

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.

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

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Celiac Disease (CD) is an autoimmune condition that can cause several manifestations largely under diagnosed. 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 Department 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 and known CD with poor GFD. 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.

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were read by two independent observers (IO). Using binary scores, an excellent concordance between IO was found with an inter-class correlation coefficient of Cohen of 0.93 (0.84–1.00). The sensitivity of CD-LFIA test compared to that of ELISA assays was 94.1% (71.3–99.9) and 88.2% (77.0–94.8%). For each IO response, 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 (94.8–100.0). The specificity of 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 demands more expertise for all the 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 98.1% (94.8–100.0), the CD-LFIA test is highly suitable to rule out CD in screening HID...
sensitivity equal to these ELISA. Within an interval of 7 to 10 days, the Borrelia ViSE test demonstrates rapid increase of titer 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 hosts.

**2007–2009 experience in canton: Valais**

ViSE 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 (IgM for Borrelia) were not conclusive and diagnosis of Lyme borreliosis could not certainly be established. In approximately ¾ of our cases, the ViSE test was positive. Initial negative ViSE test can’t exclude a definitive diagnostic, consequently ultrasonographic examination should be performed to exclude and to follow the activity of Borrelia in the host.

**In conclusion,** ViSE 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 can be used as a follow-up marker, reflecting the treatment response. Nevertheless, complementary studies should be done in the future to confirm these data.

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

_Pierre-Alex Crisinel_
_Département de l’Enfant et de l’Adolescent, Hôpitaux Universitaires de Genève_

**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 compare 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 University Children Hospital of Geneva. METHODS Children presenting with a febrile respiratory tract infection or a febrile illness 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 bronchiolitis or asthma. When compared with H1N1 negative patients, H1N1 positive patients were older (median: 3.1 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 (41% vs 25%, p = 0.04). The vs 41% were more cases of bronchospasms 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 febrile presentation 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/wheezeing episodes among H1N1 negative patients.

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**Altered Surfactant Protein Metabolism due to NK2 homeobox 1 (NK2X2-I) Mutations cause Interstitial Lung Disease in “Brain-Lung-Thyroid Syndrome”**

_G. Szinnai_, A. Clement, L. Guillot, M. Castanet, R. Epaud, F. Jaubert, François Cachat

**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...
A 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-Scales of Infant Development was the most frequent 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.

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 making 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.

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, gyneacological age (age-age at menarche), academic track (student/apprentice) and age. Results: 12.4% (95% CI: 11.0–14.1) 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: 1.72; 95% CI: 1.39–2.15), to feel in poor health (AOR: 1.49; 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 body image 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.

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 2.6 ± 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 (66%) 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/parent’s separation: 37 (29); Medication/disease: 7 (5); Other: 10 (8). Presence of, N(%): Systolic hypertension: 14 (11); Dyslipidemia: 10 (8); Hyperfondrosis: 37 (29); Genu valgum: 44 (34); Anacrophagia 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 hyperfondrosis (–0.40 ± 0.6 vs. –.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 early present early signs of complications. They usually complain about their weight excess. We demonstrated that 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.
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 face was pale but cardio-pulmonary 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. In combination 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 a hemorrhage consistent with episodic 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 later.

Discussion: Familiarity with choking 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 choking 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 of institutions of strangulation activities should rise the attention of pediatricians and other health care providers. Addressing the topic with potentially concerned adolescents may be a life saving strategy.

Conclusions: It is extremely important to recognize the choking game as a potentially dangerous activity among adolescents. Health care providers should look for signs of strangulation activities and integrate basic factual information about the dangers of the choking game in their prevention activities.

Are adolescents aware of adverse consequences of their illegal psychoactive substance use? M. Gaille, P.A. Michaud, R.E. Bélanger

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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), 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 risk ratios: RRR [95%CI]).

Results: In bivariate analysis, groups differed significantly (p <0.05) on daily, NPCC: 36.7%, CPC: 16.5%, NCC: 18.8%, 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 (1.90 [1.22–2.53]). 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.

Fatal attraction: smoking among adolescents with chronic pulmonary conditions R.E. Bélanger, C. Akre, A.E. Ambresin, P.A. Michaud, J.C. Suris Research Group on Adolescent Health, Institute of Social and Preventive Medicine, University of Lausanne

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 (SMASH02). 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 not respiratory problems (NPCC, n = 459); and healthy controls (no chronic condition: NNCC, 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, NPCC: 36.7%, CPC: 16.5%, NCC: 18.8%, 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 (1.90 [1.22–2.53]). No differences were found on having consulted in the last year regarding tobacco.

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Overweight affects approximately 25 000 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 programs, 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 programs 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 fulfill criteria for group therapy. Other 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/m² (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 multifunctional 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.

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

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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 the age-specific incidence rate of childhood HUS and possible association of Shiga-toxin associated HUS (Stx-HUS) with risk factors in Switzerland. Ecological analysis revealed strong association with indicators of livestock farming intensity and recent studies have revealed an association between indicators of livestock density (cattle / cultivated area, P = 0.013).

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.

Conclusions: Our study emphasizes the importance of a careful evaluation of social resources, not only during hospitalisation, but also already during pregnancy and afterwards. 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.

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 neurodevelopmental 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 and 25 with iNO and other treatments. 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
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 of 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 CXCR4-induced 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 phosphorylation 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 cytometry.

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 confirmed 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 that probably through regulation of the phosphorylation of the CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 receptor. Interfering with the phosphorylation of serine 339 may therefore constitute a novel strategy to therapeutically block of CXCR4 receptor.
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 bronchopneumopathy (PBD) and 1 was intubated. Normally in our hospital an infant who needs to be intubated is transferred to a University Neonatology 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 anesthesias 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 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 respiratory distress. To our knowledge, there are no studies which have evaluated the benefits of a purely locoregional anesthetic approach to these patients at risk. With healthy infants, the benefits of locoregional anesthesia (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.

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/EPRAIR). 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 leucocytes 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 our study was 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


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 = 276), 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 (FEV1), its ratio over the forced expiratory volume (FEV1/FVC) and midexpiratory flow (FEF25–75) 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 FEV1, 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.

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, Henningsdorf, Germany).

Results: Exceedingly high copeptin concentrations were observed after vaginal birth in umbilical cord venous (median [5-95% range]: 793 [6-8368] 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).

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 exposes 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, epidymal fat pads of C57Bl6J donor mice were transplanted either to the mesenterium (portal venous drainage) or the peritoneum (systemic venous drainage) of littermates. Seminca blasts after 6 months of treatment could identify a group receiving the portal drained fat transplanted 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 its 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 can identify groups 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 outcome. Due to the 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 cell numbers (cell numbers) 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 database 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 tumors 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 are sub-populations 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 or 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, EDNRB, 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 assessed 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 T-cells. These two 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 tumor-specific, 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 Raport. The target loss of Raport expression in TEC 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 TEC impacts on the thymic capacity to support regular thymopoiesis and T-cell generation and function. 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.
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