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SwissDRG and pediatric clinics: Conclusions one year after the launch

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Introduction: In 2012, Switzerland launched SwissDRG, a nationwide new reimbursement system for all inpatient hospitals, which classifies patients into Diagnosis Related Groups (DRG). Patients are assigned to a certain DRG using patient-related variables (e.g. diagnoses, procedures, age, ventilation requirement etc). Cost weights (CW) of the DRGs intend to reflect the mean expenditure for patients classified in the same DRG. In pediatric clinics, costs are driven by substantially higher caring efforts, specific infrastructural and other needs, like rooming-in of parents.

Methods: Cost-benefit calculations based on hospital accounting data and SwissDRG tariffs allow defining a minimal base rate needed for full reimbursement of all hospitalization-related costs. The same accounting data can be used to identify special groups of patients with a high discrepancy between expenditure and compensation.

Results: Pediatric inpatients show a high variability both in terms of their DRG classification and the length of hospitalization, even within individual DRGs and often outside the minimal or maximal threshold (outliers). At UKBB, 254 upper outliers in 126 different DRGs caused a financial deficit of 4.1 Mio. CHF. 36% of inpatients were lower outliers leading to a mean financial deduction of 41%. Certain procedures (e.g. VEPTR implantation) resulted in an extremely inappropriate cost weighting of the DRGs. Mathematical simulations showed that the introduction of SwissDRG version 2.0 will lead to revenue reductions of 3–6% in 2013.

Conclusion: SwissDRG in its current status only partially maps special requirements and high expenditures needed for the inpatient care of children. Until sufficient corrective measures are put in place (e.g. adapted outlier handling, auxiliary payments for expensive medications, procedures, and implants), higher baserates are needed to compensate for the increased costs of pediatric patients. Such rates should be calculated using a benchmark process amongst pediatric clinics as long as the SwissDRG system inadequately pictures the situation of pediatric patients treated in a children's hospital.

Accuracy of infrared ear and contact forehead thermometers in a private pediatric practice

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Background and objective: The aim of this study was to compare infrared tympanic and infrared contact forehead thermometers with the traditional rectal digital thermometer.

Methods: 254 children (117 boys and 137 girls) 1 to 24 months of age consulting a private pediatric practice because of fever were prospectively recruited. Body temperature was measured using the 3 different devices.

Results: Median and IQR for rectal, tympanic and forehead thermometers were 37.6 (37.1–38.4), 37.5 (37.0–38.1) and 37.5 (37.1–37.9)°C, respectively. The tympanic and the forehead measurements were 0.1°C [–0.1, 0.4, p <0.01] and 0.15°C (–0.3 to –0.7; p <0.05) lower than the rectal measurements, respectively. Limits of agreement in the Bland-Altman plots, were –0.73 to +1.04°C for the tympanic and –1.18 to +1.64°C for the forehead thermometer. While specificity and positive predictive values for detecting fever above 38°C was good, sensitivity was low and negative predictive values were acceptable, both using the tympanic or the forehead thermometers. Moreover, forehead measurements are susceptible to the use of a radiant warmer.

Conclusions: Both the tympanic and forehead devices detect lower temperatures than digital rectal measurements. Limits of agreement were particularly wide for the forehead thermometer and considerable for the tympanic thermometer. Thus, a reliable and valid alternative of the more invasive rectal temperature measurement is still lacking. In the absence of valid alternatives, owing to easy to use and little degree of discomfort, tympanic thermometers can still be used with some reserve. Forehead thermometers should not be used in the pediatric practice.

Training Pediatricians in Oral Health: A Team-Based Learning Project

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Introduction: Dental caries are a common problem in Switzerland. In Geneva, 30% of children in pre-school and 54% of children in primary school have caries. A child’s first contact with the healthcare system is the pediatrician. These visits are an ideal opportunity to inform families about the causes of caries, the possible preventive measures, to identify families at risk, and to refer patients to a pediatric dentist. The FMH has identified these competencies as an essential element of training. We set out to teach pediatric interns these competencies by creating a workshop using real pediatric patients and Team-Based Learning.

Methods: Team-Based Learning (TBL) is an instructional method based on constructivist learning theory that was originally developed by Dr. Larry Michaelsen in the 1990s. The key components of TBL involve: 1) individual advanced student preparation, 2) individual and group readiness assurance tests (IRAT/GRAT) with immediate feedback, and 3) in-class group application exercises. The advantages of this method are that TBL is learner-centered, the instructor acts as a guide, the learner is exposed to inconsistencies between their baseline knowledge and the information that is presented, and that the group experience solidifies the learner’s understanding and allows for focused reflection.

Results: Thirty pediatricians participated in the workshop. Performance on the IRAT was measured on average at 66% (95% CI 58%, 74%). Performance on the GRAT improved to 69% (95% CI 56%, 80%). The assessment of the group application exercise involving the clinical vignettes was 76% (95% CI 69, 83%). The Team-Performance Scale revealed that the pediatricians were highly satisfied with the workshop and the team collaboration. Team ratings were variable with a mean score of 76 (SD 6) out of 108.

Conclusion: Training pediatricians to become competent in oral health is an essential part of postgraduate training. Using the TBL is an active method of knowledge acquisition and application. This model will be useful to improve future training in oral health.
Food for neuroprotection: Assessment of lactoferrin after hypoxic-ischemic injury in the neonatal rat brain

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Background: Animal models of preterm brain injury can be achieved by Hypoxia-ischemia (HI). Lactoferrin (Lf) is an iron-binding glycoprotein with anti-oxidant, anti-inflammatory and anti-infectious activities. In rodents, after oral administration, Lf is rapidly transferred in the brain. Aim: The aim of this work was to assess the neuroprotective effect of Lf supplementation trough lactation after P3 HI brain injury by using high field multimodal magnetic resonance imaging (MRI).

Methods: At birth, rat pups were divided in 3 groups: The dams of the HI-Lf group (n = 6) received Lf-enriched food, HI-Lso received a diet isocaloric to the Lf (n = 6) and a Sham group (n = 3). At P3 pups from HI-Lf and HI-Lso groups underwent HI injury. At P25, Multimodal MRI with conventional T2W images, H-MRSpectroscopy and Diffusin imaging (DWI, DTI) were performed. A Mann-Whitney test was used to compare values between the different groups.

Results: When compared to HI-Lso group, the number of rats injured (51% vs. 61%), the percentage of injured cortex at P3 (49 ± 3.6% vs. 15.0 ± 7.1%, P = 0.02) as well as the percentage of cortical loss at P25 (4.6 ± 4.8% vs. 16.7 ± 11.9%, P = 0.09) were reduced in the HI-Lf group. At P25, using H-MRS, brain metabolites of HI-Lf rats is almost normalized with [Glu+Gln] only remaining decreased whereas the Iso-HI group showed also decreased levels of [Asp] and [totalNAA]. With DTI, white matter integrity was tested and Fractional Anisotropy values tend to be higher in the HI-Lf group than in the HI-Lso group and were comparable to Sham.

Conclusion: This study shows a potential neuroprotection from maternal nutritional supplementation with Lf after HI in the developing brain of progeny.

Diagnostic characteristics of MR-proANP und CT-proET-1 plasma levels in very preterm infants with patent ductus arteriosus

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Background: Echocardiographic diagnosis of haemodynamically relevant patent ductus arteriosus (PDA) in very preterm infants is crucial, although the predictive value is limited by the physicians’ skills and the short time window of investigation. Further, it may not be available at the time of treatment decision making. Biomarkers may improve the diagnostic performance. The objective of this study was to examine baseline characteristics of mid-regional pro-atrial natriuretic peptide (MR-proANP) and C-terminal pro-endothelin-1 (CT-proET-1) in very preterm infants in parallel to echocardiography.

Methods: Plasma levels of MR-proANP and CT-proET-1 on 1st and 6th day of life (DOL) were correlated to results of simultaneously performed echocardiography in 54 very preterm infants born before 32 weeks of gestational age (GA). Non-parametric descriptive statistics were used.

Results: MR-proANP was significantly elevated in very preterm infants with PDA (n = 32; median GA 28 3/7; 95%CI: 27 4/7-29 3/7 weeks) compared to those without PDA controls (n = 22; 28 4/7; 28 4/7-30 3/7 weeks) on DOL 2: median 1609 (95%CI 1355-1872) vs. 919 (820-1473) pmol/L (p = 0.024). CT-proET-1 showed a similar significant elevation on DOL 2: 385 (338-504) vs. 278 (226-314) pmol/L (p = 0.01). 7 children underwent surgical closure of PDA after unsuccessful treatment with indomethacine. On DOL 6 these children had significantly higher MR-proANP levels (median 993 (95%CI: 770–1454) pmol/L) compared to children with no need of indomethacine (n = 30; 309 (302-436) pmol/L; p < 0.001). Indomethacin treated children had fewer perioperative lesions and better heart functions (p = 0.005).

Conclusions: MR-proANP and CT-proET-1 may play a supportive role in diagnostic and treatment surveillance of PDA in very preterm infants.

White matter repair and functional recovery after intra-arterial delivery of human NPC in rodent neonatal hypoxia-ischemia

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Introduction: White matter damages in the immature brain are a hallmark of neonatal hypoxia-ischemia (HI) and cerebral palsy (CP), and the most common cause for persisting sensory-motor, cognitive and learning deficits in the developing child. Many preclinical studies have evaluated the effects of stem cell transplantation (SCT) on endogenous repair mechanisms such as neurogenesis or immunomodulation, however the specific impact of SCT on myelination in the developing brain has not been adequately characterized. Using a neonatal rat HI model, we investigated the effect of human neural progenitor cell (NPC) transplantation on myelination and functional recovery.

Methods: Male Wistar rats underwent left common carotid artery ligation followed by hypoxia on post-natal day 7 (P7). On P10, cyclosporine immunosuppressed neonates were intra-arterially injected with NPC expressing a luciferase-eGFP reporter system or saline control. In vivo bioluminescence images (BLI) were obtained 1,2,3,4,7 and 10 days post-injection. Results were compared by using the elevated plus maze (EPM) and novel object recognition (NOR) at P40.

Results: BLI demonstrated homing of NPC to the stripped hemisphere and myelination further proceeded to their localization to the corpus callosum and cortex at 3, 10 and 30 days after treatment. LFB and immunohistochemistry and myelination was monitored using luxol fast blue (LFB) and myelin basic protein (MBP) stained sections and quantified. NPC transplantation resulted in early NPC homing to the injured brain and maintenance for up to a month upon treatment. Behavioral performance suggests cell-treated animals had reduced levels of anxiety and improved working memory compared to saline-treated animals. Although stem cell therapy is already accepted as a promising therapeutic approach for children with HI injuries that can lead to devastating life-persisting conditions, here we suggest that one potential mechanism of action is the functional repair of white matter tracts.

Neonatal cerebral MRI in relation to neurodevelopmental outcome at one year of age in infants operated for congenital heart disease

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Background: Cerebral injury may occur in infants undergoing bypass surgery for congenital heart disease (CHD). No information is available on the association between periprocedural lesions and neurodevelopmental outcome. The objective of this study was to determine the correlation between periprocedural cerebral injuries detected on cerebral MRI (dMRI) and neurodevelopmental outcome at one year of age in infants who underwent full-flow neonatal bypass surgery for severe CHD.

Methods: Between 12/2009 and 01/2012, we included 30 neonates born at a median of 39 2/7 weeks (range 36 5/7–41 6/7) with severe CHD (dTGA n = 22, univentricular heart defect n = 7, interrupted aortic arch n = 1). Thirty infants underwent cMRI before and 28 after the first surgery. Median age at 1st cMRI was 6 (range 1–12) days, age at 2nd cMRI was 26 (range 13–52) days. At the age of 12 months (11–16), 26 children were tested with the Bayley Scales of Infant Development III.

Results: Median cognitive composite score was 103 (range 60–125), language composite score was (LCS) 91 (65–132) and motor composite score was (MCS) 90 (46–130). Outcome was significantly poorer than the norm for the LCS (p = 0.005) and the MCS (p < 0.001). Preoperative white matter injury or cerebral stroke occurred in 7 of 30
patients (23%), with isolated WMI in four, isolated stroke in one, and 5 S thrombosis but no other lesion. We could not find any significant correlation between pre- or postoperative cerebral lesions (WMI or stroke) and any neurodevelopmental outcome variable. Conclusion: Neonates with severe CHD showed predominantly a WMI pattern on cMRI before and after full-flow bypass surgery. Lesions were mostly small. One-year outcome was poorer in the language areas. However, the long-term development linearity hypothesis seemed to hold true. Therefore, more follow-up studies are needed in this group of infants in order to reinforce the findings presented. In fact, these results should be considered as a starting point for further research because they are based on a limited number of patients and more data are needed to confirm the findings.

The neuronal correlates of mirror illusion in children with hemiparesis: a pilot study using transcranial magnetic stimulation

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Introduction: Mirror therapy (MT) provides the visual illusion of a normal moving paretic limb by using the mirror reflection of the non-paretic arm and is used in rehabilitation medicine to improve hand motor function. However, little is known about the neuronal correlates underlying the effect of MT in patients with hemiparesis despite promising clinical results.

Methods: Children and adolescents with congenital or acquired hemiparesis during childhood and age-matched healthy subjects participated in this study. The excitability of the corticomotor tract of the hemisphere projecting to the affected (non-dominant) hand was obtained during two different conditions using single-pulse transcranial magnetic stimulation (TMS) of the primary motor cortex (M1). Each condition (1x without mirror/1x with mirror) consisted of a unimanual and a bimanual motor task. While moving their hands the participants either looked at both hands directly (non-mirror condition) or at the mirror illusion of their unaffected (dominant) hand (mirror condition). Motor evoked potentials (MEPs) were recorded from the M. flexor digitorum superficialis (FDS) of the affected (non-dominant) hand.

Results: Preliminary results of 5 subjects with hemiparesis (1 girl, 4 boys; 11–20 years) and 4 healthy participants (1 girl, 3 boys; 11–17 years) showed a significant increase during the mirror condition of MEPs in the FDS of the affected (non-dominant) hand in the bimanual task (p = 0.034) but not in the unimanual task.

Conclusions: Motor-evoked cortical excitability was more pronounced during bimanual training. This preliminary finding provides neurophysiological evidence supporting the application of MT in children and adolescents with hemiparesis.

Longitudinal Neurodevelopmental Evolution in Children with Severe Non-progressive Encephalopathy

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Aim: The aim of this study was to evaluate the longitudinal neurodevelopmental evolution in children with severe non-progressive encephalopathy.

Methods: Between 1984 and 2005, 17 patients diagnosed with severe non-progressive encephalopathy under the care of the Institute Provvidা Madre underwent neurodevelopmental evaluation on an annual basis for at least 5 consecutive years using the Munich Functional Developmental Diagnostics test. The severity of each patient’s encephalopathy was assessed using the Capacity Profile (CAP). Longitudinal development trends were assessed by means of linear regression analysis, while the degree of discontinuity of the development trajectories was quantified using the Mean Absolute Deviation from Perfect Linear Development (MADPLD).

Results: We found that patients with severe non-progressive encephalopathy showed, on average, a linear maturation of 1.5 to 2.5 months per year, irrespective of the neurodevelopmental area considered. Nevertheless, we also discovered that the development trajectories could be quite variable. Indeed, no significant correlation between pre- or postoperative cerebral lesions (WMI or stroke) and any neurodevelopmental outcome variable.

Conclusion: The main findings of this study are important for physicians to form prognoses, counsel effectively and appropriately target therapeutic interventions. In this perspective, there is a strong need to collect longitudinal follow-up data on this group of infants in order to reinforce the findings presented. In fact, these results should be considered as a starting point for further research because they are based on a limited number of patients and more data are needed to confirm the findings.

A Survey of monogenic diabetes forms in Switzerland

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Introduction: Monogenic diabetes (MD) are due to single gene defects affecting beta-cell development or function, thereby disturbing insulin secretion. They result in neonatal diabetes or in diabetes, usually first diagnosed in young adults and also referred to as maturity onset diabetes of the young (MODY). MD affects 2–5% of all diabetic patients. In Switzerland, this represents an estimated population of 10’000 to 25’000 patients, most of which are diagnosed and treated as type 1 or type 2 diabetes. Nonetheless, recognizing MD is important for patients, since the diagnosis will determine treatment modalities and allow for a more precise estimate of the risk for long-term complications. We have performed a survey to assess the number of suspected and diagnosed cases in Switzerland. We now also offer genetic analysis for all genes implicated in known monogenic diabetes forms.

Methods: A questionnaire was sent to all members of the Swiss Society of Endocrinology and Diabetology to determine the number of diagnosed or suspected cases of monogenic diabetes in Switzerland as well as to gather information on clinical parameters and current treatment. Genetic analysis of monogenic diabetes is performed by HaloPlex technology allowing sequencing of amplified target DNA.

Results: So far, 29 families with monogenic diabetes were reported. The diagnosis was genetically proven in 52% of the suspected cases. Mutations in the glucokinase (GCK) gene was found in most cases, followed by mutations in HNF1β. The distribution was similar in adult and pediatric patients.

Conclusion: We are currently working on gathering information about monogenic diabetes forms in Switzerland and offer genetic diagnosis for all known monogenic diabetes genes. First results indicate that mutations in GCK are most frequently found in suspected cases.

Effect of Statin Treatment on Inflammatory and Prothrombotic States in Obese Adolescent

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Introduction: Increased inflammatory cytokines, C-reactive protein (CRP) and prothrombotic parameters have been identified as potential markers of cardiovascular risks in obesity already in adolescence. We investigate whether statins can reverse these inflammatory and prothrombotic states in children.

Methods: We conducted a randomized controlled double-blind study with 28 obese adolescents aged 12–16 years at the Children’s University Hospital of Geneva. They were allocated to either receive placebo (P) or Atorvastatin (A) for 4 months. Monocyte Chemoattractant Protein 1 (MCP-1), Interleukin-6 (IL-6), Interferon-γ-inducible Protein (IP-10), Interleukin-10 (IL-10), Interleukin-1 Receptor antagonist (IL-1Ra) and CRP were measured. Hypercoagulability was evaluated by prothrombin time, activated partial thromboplastin time and endogenous thrombin potential (ETP).

Results: After 4 months median MCP-1 increased in P (137.3 to 169.8 pg/ml) while it decreased in A (172.2 to 141.6 pg/ml). ETP also increased in P (366.2 to 379.2 mAU) and decreased in A (397.1 to 384.9 mAU).
Lab-score: a safe way to reduce antibiotic treatments in children with fever without source?

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Background & Aims: Detecting serious bacterial infections (SBI) in children with fever without source (FWS) is a diagnostic challenge. The recently described Lab-score, based on the combined determination of Procalcitonin (PCT), C-Reactive Protein (CRP) and urine dipstick result, is an accepted rule to avoid overtreatment to assess the usefulness of the Lab-score in decreasing antibiotics prescription in children with FWS.

Methods: Randomized controlled trial in children 7 days to 3 years old presenting to a tertiary care center with FWS, randomly allocated into 2 groups: the Lab-score group and the control group (following standard guidelines for SBI detection: white blood cell count, band count and CRP ≥40 mg/L). Antibiotic prescription rates and diagnostic properties were compared.

Results: 234 children were included. No statistically significant difference concerning antibiotic prescription rates was observed: 40.7% (46 of 113) in the Lab-score group, 41.3% (50 if 121) in the control group (p = 1.000). However, if the Lab-score had been strictly followed, only 29.2% of children (33 of 113) in the Lab-score group would have been treated with safety regarding SBI detection and 6 patients (5.3%) suffering from febrile urinary tract infections would have been misdiagnosed. Lab-score showed the following diagnostic characteristics: sensitivity 78.7% (95% CI: 69.4–89.9%), specificity 88.0% (95% CI: 83.2–92.8%), positive predictive value 69.1% (95% CI: 58.1–80.1%), negative predictive value 92.8% (95% CI: 88.8–96.7%). Positive and negative likelihood ratios for a Lab-score ≥3 or <3: were 6.84 and 0.23 respectively.

Conclusion: No difference was observed regarding antibiotic treatment rates when using the Lab-score, due to lack of rigorous adherence to guidelines especially in younger children. However, if the Lab-score had been strictly followed, a safe reduction of 28.5% antibiotic treatments would have been observed. Medical education needs to be reinforced in order to observe rather than treat low-risk Lab-score well-appearing children with FWS.

Rate of hospitalisation of paediatric patients with acute gastroenteritis prior and after the introduction of ondansetron at the emergency room

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Introduction: Acute gastroenteritis (AGE) is a common reason for infants and children to require emergency treatment and hospitalisation. Several recent studies showed a reduction of the rate of hospitalisations after the introduction of antiemetic treatment with ondansetron at the emergency room. The aim of our study was to compare the rate of hospitalisations of a period prior and after the introduction of ondansetron at the paediatric emergency room of our hospital.

Method: The charts of 323 patients seen for AGE between January and May 2011 (prior) and of 451 during the same period in 2012 (after) were reviewed.

Results: The overall rate of hospitalization was 3.4% in 2011 and 6.8% in 2012. However, the two cohorts differed significantly: In 2012 patients were more numerous, younger (median age 29 and 22 months, respectively, p < 0.001) and more severely dehydrated (mean z-score for weight age 0.1 and −0.1, respectively, p < 0.05). We therefore analysed a subgroup of children ≥36 months of age (141 and 161 patients) with comparable mean z-scores for weight age (0.25 and 0.27, p = ns). The rate was the same: their hospitalisation rate was 3.5% and 2.5% respectively (p = ns) despite antiemetic treatment with ondansetron in 15 (10.6%) and 44 (24.5%) (p < 0.05) patients, respectively.

Conclusion: In contrast to the conclusion of a recent Cochrane review about the reducing effect of antiemetics on the hospitalisation rate in children with AGE, in regions with already low hospitalisation rate, such as ours, the use of ondansetron had no impact on this parameter.
Method: This prospective clinical study included 234 adolescents aged between 11 and 18 years (mean 13.1 ± 1.7), who had at least 5 months of treatment at the Pediatric Obesity Care Program of the Geneva University Hospitals. Patients and their parents choose between the Contrepoids group therapy (n = 74, 32%) or the individual therapy (n = 160, 68%), depending of their availability and motivation. In both arms, we used an integrative approach including cognitive behavioral techniques and motivational interviewing. In group therapy, patients and their parents attended psycho-educational sessions in separate groups, 1x/week during 5 months. Adolescents also had physical activity sessions 1x/week. Then, patients came every 3 months for individual pediatric follow-up. In individual therapy, adolescents and their parents, when available, had structured individual consultations every 1-3 months with a trained pediatrician. The change in BMI z-score was calculated between the start and the last recorded visit.

Results: The mean follow-up time was identical in both arms (Group: 20.2 ± 8.5; Individual: 19.2 ± 11.3 months; range 5 months to 4 years). The BMI z-score decreased significantly and similarly in both therapies (Group: –0.24 ± 0.5 vs Individual: –0.20 ± 0.5). Despite identical characteristics at baseline, changes were greater in boys (girls: –0.13 ± 0.34 vs boys: –0.30 ± 0.57, p = 0.008) and in the younger group compared to older adolescents (12–14 yrs: –0.25 ± 0.39, p <.001; 14–18 yrs: –0.23 ± 0.67, p = 0.065).

Conclusion: There was no difference in BMI z-score changes between the group and individual behavioral therapy, and the magnitude of decrease was similar to international published data. Structured individual therapy with a trained pediatrician is a promising approach to treat a large population of obese adolescents in Switzerland.

PIRSM-Ado: cluster randomised trial of a brief primary care intervention addressing excessive substance use in young people

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Introduction: Most young people see a primary care physician at least once a year. These consultations provide an opportunity to discuss substance use. The aim of this study was to assess the effectiveness of a brief intervention delivered by primary care doctors to reduce binge drinking and/or excessive cannabis use in young people.

Methods: This was a cluster randomised trial involving 32 family doctors (paediatricians or general internists) in the French-speaking part of Switzerland. The doctors were randomised to receive training in delivering the brief intervention or to provide usual care (control condition). Young patients between 15 and 24 years consulting these doctors for any motive were invited to participate. Before the consultation they completed a confidential questionnaire about their health and substance use. During the consultation all patients were first offered usual care for the reason for which they had come. Depending on the random assignment of their doctor, they were exposed to the brief intervention in addition to usual care. Patients were followed-up by phone 3, 6 and 12 months after the consultation. Main outcomes were excessive alcohol (≥1 binge drinking episode) and/or excessive cannabis use in the past 30 days.

Results: 594 young people (48% male) were included in the trial between January 2009 and November 2010, 45% of which presented excessive substance use at baseline. Follow-up rates at 3, 6 and 12 months were 87%, 80% and 73%. Overall there was a 30% reduction in the proportion of excessive substance users at follow-up among those who were excessive users at baseline but no statistically significant differences between the intervention and the control group.

Conclusions: Though excessive substance use decreased in the year following a consultation with a primary care doctor, this reduction did not seem to be related to exposure to the brief intervention.

Fetal rhabdomyolysis in a child with LPIN1 mutation

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Introduction: Autosomal recessive mutations in the LPIN1 gene encoding for the nuclear Inositol-1,4,5-triphosphate 5′-kinase IP5K1 lead to a severe hypokalemia, carnitine palmityltransferase II deficiency and Fanconi-Bickel renal tubulopathy. Despite maximal efforts, the girl died. Laboratory tests revealed hyperkalemia (8.3 mmol/l) and elevated CK (12’163 U/L) consistent with rhabdomyolysis. A legal autopsy was performed with results still pending. Two recent publications (Michot C et al, Hum Mutat 2010; Zeharia A et al, Am J Genet Genet 2008) prompted analysis of the LPIN1 gene revealing a homozygous deletion (c.2295-866_2410del) in the girl and a heterozygous trait in both parents and the healthy brother.

Conclusion: Rhabdomyolysis is rare in children. Main causes include viral myositis, trauma, drug reactions and metabolic diseases. Severe hypokalemia, carnitine palmityltransferase II deficiency and FAO defects. Mutations in LPIN1 cause severe, often recurrent and fatal rhabdomyolysis with onset before the age of 5 years. Episodes are precipitated by febrile illness or fasting. It is thought that the acute-phase response induced by inflammation could change the lipid and lipoprotein metabolism and thereby trigger episodes of rhabdomyolysis.

Risk factors and practical criteria to avoid extensive crying in newborns

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Introduction: All newborns have crying phases in their first 3 months as an expression of their adaption to extra-uterine life. Symptoms are normally well interpreted by parents and also self limited. Some 10% of otherwise healthy newborns present with extensive crying. Parents are severely concerned and extremely disturbed. The consequence is a change in binding pattern, severe sleep deprivation and eventually harm to the child. Since 5 years we run an interdisciplinary short stay inpatient and ambulatory care program at the Triemli hospital in Zurich in order to unburden and support families with extensive crying infants (TII).

Methods: We analyzed the data sheets of parents and children who were participating in the years 2008–2010 in the Triemli program for extensive crying babies (TIKSS) and sent also questionnaires to the parents. We analyzed risk factors including age of parents, number of child, socio-economic status, educational status of the mother, pattern of birth and psychosocial stress factors. Parents were asked also for the immediate and prolonged impact of the intervention.

Results: We found 3 major risk factors: 1) Missing familial and social network both for families with migration and highly educated background leading to a «golden cage of the nuclear family». Most parents suffered from lack of support and understanding of the their educational problems. 2) Primiparas in their third decade, who «planned» their child and wanted to just perfectly organize their «project». 3) Mothers, who had a lack of sleep in the third trimester of pregnancy or who had an unplanned C- section. All of these factors resulted in a disturbed binding pattern and often in an misunderstoodness of the needs of the newborn baby.

Conclusion Having this outcome, we developed a semi-structured questionnaire and risk stratification sheet for parents and children at risk. We propose that midwives, nurses and pediatrics should be sensitized to these risk factors. Families at risk should be easily detected by using semistructured questionnaires and referred to specialised ambulatory centers in order to avoid unnecessary suffering for the parents and dangerous situations for the infants.
Parental heart rate variability during pediatric consultation
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Introduction: Research regarding communication between pediatricians and parents in pediatric consultation has mainly focused on parental satisfaction. However, there is paucity in research regarding parental stress levels during pediatric consultation. Therefore, the aim of our study was to measure parental heart rate variability related as a measure of stress levels during pediatric consultation.

Methods: Video recordings with simultaneous monitoring and recording of parental heart rate were obtained from 38 pediatric consultations in the ambulatory or hospital setting of the department of pediatrics (HFR, Fribourg, Switzerland). Pulse variation was measured every 5 seconds and heart rate variability (increase or decrease were analyzed) in relation to various sections of the consultation.

Results: Heart rate significantly decreased at the end of the consultation compared to the beginning of the consultation (p = 0.0567). In addition, heart rate significantly decreased at the beginning of clinical examination (p = 0.0476) compared to psychosocial history taking. During the discussion of laboratory findings and diagnosis, heart rate was significantly elevated compared to the discussion of the prognosis (p = 0.0505).

Conclusion: We conclude that pediatric consultation has a significant impact on parental stress levels shown by parental heart variability. In general, it can be shown that stress levels significantly decrease at the end of the consultation compared to the beginning of the consultation. In addition, stress levels decrease at the beginning of clinical examination and during psychosocial history taking and discussion of laboratory findings and diagnosis. Therefore, our findings highlight the importance of a thorough consultation which include a comprehensive clinical examination with special care taken regarding psychosocial issues and information given regarding the diagnosis.

Obesity-related complications in children and adolescents attending a specialized pediatric obesity center
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Introduction: The burden of childhood obesity is considerable worldwide, as it is associated with several co-morbidities, such as dyslipidemia, hypertension, insulin resistance, glucose intolerance type 2 diabetes (T2DM), orthopedic and psychosocial problems. We aimed to determine the prevalence of these complications in a population of overweight and obese children and adolescents consulting in a specialized obesity center.

Methods: This is a cohort study including 782 new patients (1.7-179 yrs, mean 11.1 ± 3.0) attending the Pediatric Obesity Care Center of the Geneva University Hospitals between January 2008 and August 2012. We assessed personal and family medical histories, physical examination, systemic blood pressure, biochemical screening tests for thyroid, glucose, liver and lipids disturbances.

Results: 90% of children suffered from at least one complication. Conditions related to quality of life were the most frequent (79.4%), followed by orthopedic pathologies (54%), metabolic (45%) and cardiovascular anomalies (31%). Except for psychosocial complaints, all complications were BMI-related. Family history of dyslipidemia tends to correlate with the child's lipid disturbances (r = 0.115, p = 0.053), and ischemic events or T2DM were correlated with the total number of cardiovascular risk factors present in the child (r = 0.074, p = 0.046; r = 0.09, p = 0.038, respectively).

Conclusion: The majority of obese children suffer from physical and psychosocial complications that must be actively screened. A positive family history for cardiovascular diseases or T2DM should be warning signals to perform further complementary tests. Furthermore, quality of life related-complaints should not be underestimated as they were extremely frequent whatever the degree of weight excess. Psychological intervention on selected situations.

Sudden cardiac death in a pediatric population
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Background: Sudden cardiac arrest (SCA) is a uncommon, but tragic event in childhood and there are no data available, defining the annual incidence of SCA in childhood. As many studies suggest, the outcome of pediatric cardiological resuscitation in children is bad, compared with survival rates in adults.

Objectives: The aim of this study was, to determine the epidemiology and underlying causes of sudden cardiac death in childhood for a defined area and to evaluate outcomes and survival rates of out-of-hospital and in-hospital resuscitation as well.

Methods: Retrospective review of patient charts in a 5-years period starting in 2005 and ending in 2010. The two centers of University children's hospital Bern and University children's hospital Lausanne drain a stable area with a population of 450254 children under 16 years of age (Bundesamt für Statistik 2011).

Results: 21 patients with sudden cardiac death were included in the analysis, accounting for an incidence of 0.93/100000 childhood years. 16 patients had SCA in presence of a wide range of underlying cardiac disease. 5 patients were diagnosed with primary electrical disease. Mean age at event was 8.2 years. Overall mortality was 67%, whereas mortality in children with known cardiac disease was 81%. 8 patients (38%) survived out of hospital cardiological resuscitation, 2 died shortly after, 6 patients (29%) were discharged from the hospital. In 4 patients, the diagnosis of the underlying heart disease or primary electrical disease was made after sudden cardiac arrest.

Conclusion: Sudden cardiac arrest in childhood is a rare event with a high overall mortality. But surprisingly, 38% of patients survived out-of-hospital cardiological resuscitation where in other studies none or few children were discharged from hospital after SCA. Because of the limitations of our study, this might be an overestimation of the real situation.
Dysfunctional Voiding and Incontinence Scoring System: the Basle Experience

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Introduction: Functional voiding problems in children are common. There are only few studies which describe symptom scoring systems, but until today there is not yet a generally accepted method of standard evaluation. Akbal et al. published in 2005 a symptom scoring system including psychological aspects. The aim of our study is to evaluate a modified symptom scoring system including patients’ history and to assess the symptom course during functional voiding and the clinical course of our patients using this scoring system

Material and methods: Patients group included all children who presented with DV and/or urinary incontinence at our specialized outpatient clinic within a period of 24 months. Patients’ symptoms were listed and scored using our modified scoring system. The form contained questions concerning day- and night time wetting, voiding disorders as pain, urge, straining as well as bowel movement and quality of life. According to the experience of Akbal, a score of >8.5 was suggestive for the presence of relevant voiding abnormalities. To compare the calculated score with the clinical course and the outcome, we also included complete patients history as well as the results of voiding protocols, renal ultrasound and urodynamic studies. Additionally, type and duration of therapy were recorded as well as time interval from first consultation to complete resolution of clinical symptoms.

Results: Our study includes a total of 89 patients (58 boys, 31 girls) with an average age of 9.2 years (range 4–20 years), 62 patients showed a score ≥8.5. The median time for symptom resolution in this group was 20.5 months. 27/89 patients had a score <8.5 with a symptom resolution of 14.4 months. Patients with a score >8.5 showed a lower average voiding volume than those in the other group. A current ongoing study aims at meticulous evaluation of more detailed data in order to validate a more differentiated cut off point.

Conclusion: A differentiated scoring system to assess DV and urinary incontinence is a useful tool to evaluate children who present with DV. Our scoring system might enable us to record severity of the disease, to determine the necessity of additional examinations and to predict patients’ clinical course as well as duration of treatment. A more detailed evaluation including statistical analysis of recorded data will help us to define the cut off point more accurately.

Herpes simplex virus – The “bad player” in chemotherapeutically associated mucositis?

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Introduction: The painful ulceration of mucous membranes lining the gastrointestinal tract is called mucositis. Oral mucositis (OM) is a common chemo- and radiotherapy adverse effect in oncologic pediatric patients. Herpes simplex virus (HSV) infection can cause a severe clinical course. Following a nearly fatal HSV positive mucositis in a lymphoma patient, all subsequent patients received a local HSV-PCR of OM for detection positive patient (PCR+) even who might profit from an antiviral therapy. We report on the prevalence PCR +, and the correlation between HSV seropositivity/ negativity (IgG+/ IgG-) and the frequency of OM in our cohort.

<table>
<thead>
<tr>
<th>HSV IgG (n = 50)</th>
<th>Patients with chemotherapy</th>
<th>Chemotherapeutic associated OM</th>
<th>HSV-PCR positive OM</th>
<th>HSV-PCR negative OM</th>
<th>Total OM episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>11</td>
<td>7 (68%)</td>
<td>6</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>negative</td>
<td>39</td>
<td>30 (30%)</td>
<td>11 (30%)</td>
<td>0</td>
<td>14</td>
</tr>
</tbody>
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Methods and results: We performed a retrospective study of 50 pediatric patients with various oncological diseases to evaluate the prevalence of HSV IgG+/IgG- in patients with and without chemotherapy and to illustrate the correlation to HSV-PCR positive OM.

Conclusion: The rate of IgG+ (19%) in the chemotherapy group was as expected. The relative risk of OM in IgG+ is 2.34. All IgG+ receiving chemotherapy (apart from one who received interferon alpha only) developed OM and PCR+ reactivation in OM episodes, and none of the IgG-. OM episodes were 3 times more frequent in IgG+ than in IgG- patients. Patients under chemotherapy and initial HSV IgG positivity have an increased risk for and a substantially increased risk of multiple mucositis episodes. In IgG+ patients more than every second mucositis will show HSV reactivation – these patients should be investigated for reactivation in every mucositis episode.

Fertility preservation in pediatric cancer patients: the multidisciplinary experience in Geneva and Lausanne

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Introduction: Almost 80% of the 200 children diagnosed each year with cancer in Switzerland will be long-term survivors. Due to cancer treatment, 23% of them will suffer from gonadal insufficiency. Different fertility preservation options (FPO) are available for pubertal patients (embryo/oocytes and sperm cryopreservation (CP)). Only recently experimental options can be offered to prepubertal patients such as ovarian/testicular tissue CP. Once the patient is ready to conceive, two possibilities are available: auto-transplantation of the cryopreserved tissue (already performed in women/not reported for men) or perhaps in the future (not yet feasible today) in vitro maturation of primordial follicles/ spermatids followed by in vitro fertilization.

Method: To offer FPO to prepubertal patients, a multidisciplinary team was formed in CHUV and HUG in 2010, including specialists in pediatric oncology, endocrinology, gynecology, surgery, reproductive medicine, ethics and law. The indication for FPO was discussed for every newly diagnosed oncological female patient with potentially gonadotoxic treatment. When indicated, FPO was proposed to the girl and her family.

Results: To date, FPO was indicated for 21 patients and was realized in 18 of them (aged 5 months-17 years) in the context of a study protocol. FPO was refused by one teenager herself and by her parents. Two patients were prepubertal at diagnosis and further patients were referred for another surgery for all patients but one. No complications were reported. The patients’ diagnoses: high risk neuroblastoma (stem cell transplantation (SCT)) (6), high risk acute leukemia (SCT) (4), high risk osteosarcoma (3), relapse of Hodgkin lymphoma (3), metastatic medulloblastoma (1), familial lymphohistiocytosis (SCT) (1). The study protocol to offer FPO to boys is under elaboration.

Conclusions: Fertility preservation techniques are nowadays also proposed to prepubertal pediatric cancer patients. As the methods of fertility restoration are experimental, accurate information should be provided to patients and their parents. A multidisciplinary approach and the follow-up using a patient registry are indispensable.

Gastroesophageal reflux in young children operated for esophageal atresia: prospective follow-up at a single center

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Introduction: Gastroesophageal reflux (GER) is frequent after repair of esophageal atresia (EA). The aim of our study was to evaluate prospectively the management and evolution of GER in children treated for EA. The methods of fertility restoration at an early age should be provided to patients and their parents. A multidisciplinary approach and the follow-up using a patient registry are indispensable.

Results: Thirty-seven patients (23 males; median age 3.8 years, range 1.6–6.6) were included. PPI (n = 32) or H2RA (n = 4) were introduced in 18 of them (aged 5 months-17 years) in the context of a study protocol. PPI was refused by one teenager herself and by her parents. Two patients were prepubertal at diagnosis and further patients were referred for another surgery for all patients but one. No complications were reported. The patients’ diagnoses: high risk neuroblastoma (stem cell transplantation (SCT)) (6), high risk acute leukemia (SCT) (4), high risk osteosarcoma (3), relapse of Hodgkin lymphoma (3), metastatic medulloblastoma (1), familial lymphohistiocytosis (SCT) (1). The study protocol to offer FPO to boys is under elaboration.

Conclusions: Fertility preservation techniques are nowadays also proposed to prepubertal pediatric cancer patients. As the methods of fertility restoration are experimental, accurate information should be provided to patients and their parents. A multidisciplinary approach and the follow-up using a patient registry are indispensable.
LeCompte Maneuver for Airway Compression
Management in Late-presenting Absent Pulmonary Valve Syndrome
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Introduction: Patients with absent pulmonary valve syndrome (APVS) often present early with airway compression, from diffuse aneurysmal dilatation of the pulmonary artery branches. Repair usually includes pulmonary artery reduction plasty to relieve proximal obstruction of the mainstem bronchus. The LeCompte maneuver has been proposed to address this issue, although there is limited data available. This study reviews our recent experience in managing APVS syndrome in later presenting children, and surgical techniques used for managing airway compression.

Methods: This study is a retrospective chart review of all patients who underwent repair of tetralogy of Fallot and APVS from 2000 to 2012 at our institution. Patients with clinical evidence of airway compression underwent systematic pre- and post-operative bronchoscopy. The primary endpoints were post-operative bronchoscopy and clinical evidence of persistent airway compression, and need for reinterventions or reoperations on the pulmonary arteries.

Results: 19 patients were included during the study period. The mean age at repair was 4.3 ± 3.0 years (range, 10 months – 11 years). 6 patients had associated anomalies: 3 with discontinuous left pulmonary artery from major aorto-pulmonary collaterals (MAPCA), 1 with a MAPCA to the LPA, 1 with a right aortic arch, total anomalous pulmonary venous return and infradiaphragmatic MAPCA to the right lung, and 1 patient with 22q11 microdeletion. There were no perioperative deaths. 6 patients with respiratory symptoms had preoperative bronchoscopy, which showed airway compression in 7 patients and managed by pulmonary artery reduction plasty in 4 patients, and LeCompte maneuver in 3 patients. In the first group, 2 patients had no postoperative airway compression, 1 patient had improved compression, and 1 patient had unchanged compression. In patients managed with a LeCompte maneuver, 2 patients had no or trivial airway compression and had improved compression (P = 0.1). There were 6 late reinterventions or reoperations on the RV-PA conduit (2/4 in the PA plasty group, 1/3 in the LeCompte group, P = 1.0).

Conclusion: In patients with APVS and airway compression, either pulmonary artery reduction plasty or the LeCompte maneuver can relieve proximal airway compression, without a significantly different risk of pulmonary artery reintervention between techniques.

Necrotizing Fasciitis: a 4-year review of cases of a single-institution
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Aim: Necrotizing fascitis (NF) is a rare but devastating disease, which progresses very quickly. It requires early diagnosis, expedite surgical debridement and targeted antibiotherapy. To assess quality of our management, we reviewed the outcome of our patients.

Methods: Retrospective review of pediatric cases of the department of Pediatrics of the University Hospital of Geneva, between November 2008 and January 2013, identified from our surgical database.

Results: Seven patients were admitted for NF: 3 boys and 4 girls, with an average age of 7.09 ± 5.19 years. 4/7 patients had NF as a complication of chickenpox, 2/7 due to other skin lesions and 1/7 without any skin lesion. 5/7 patients had NF caused by Group A Streptococcus pyogenes, as single or mixed flora. All patients were treated with beta-lactam antibiotics and Clindamycine as soon as NF was suspected. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score was calculated in the 4 children who had all the required data: 3/4 had a score >6: "should raise the suspicion of necrotizing fasciitis" at the time of admission. Two to 14 surgeries (median 4) were required to remove infected tissues and obtain skin closure. Median time from admission was 3.5 days (range 0–3%), with a median fasciectomy of 3% (range 1.5–15%). In 6/7 children negative pressure wound therapy was used for a median of 6 days (range 5–15 days). 3/7 patients underwent 6–9 sessions of hyperbaric oxygen therapy, at 24-hour intervals. 5/7 patients presented complications directly related to the infection: 3 had septis shock, 2 coagulation perturbations and 1 agranulocytosis. Intensive care stay for a median of 6.5 ± 5.3 days was necessary for 6/7 patients, and 5/7 patients required intubation for 5.2 ± 12 days. Median hospital stay was 16 days (range 10–43 days). There was no mortality in this series.

Conclusion: Clinical course of NF patients is severe. Quick management of all patients resulted in no mortality and minimal skin loss. The LRINEC score may help for early identification of NF cases, yet, the diagnosis of NF must be ruled out in all cases of rapidly progressing and painful cellulitis associated with high inflammatory parameters.

Similar lung function in infants with cystic fibrosis diagnosed by newborn screening compared to healthy controls shortly after birth
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Background: In children with cystic fibrosis (CF) small airway disease occurs early in life. Introduction of CF in the newborn screening (NS) enables early diagnosis. Since recent lung function data in CF infants at the age of 3 months have been shown to be abnormal we examined whether lung function is already abnormal shortly after birth in infants with CF-diagnosed by NS.

Methods: We performed multiple-breath washout (MBW) using 4% sulfur hexafluoride and tidal breathing measurement during non-REM sleep in 23 infants with CF, aged median (range) 6.5 (3.9 – 12.6) weeks, and compared it to a previously reported equipment and tracer-gas specific normative data population of 292 healthy infants, aged median 5.1 (3.6 – 8.7) weeks (Fuchs et al., EJU 2011). We compared LCI and functional residual capacity (FRC) of MBW and the following tidal breathing parameters: tidal volume, respiratory rate, minute ventilation, mean and peak tidal inspiratory and expiratory flow and the ratio of time to peak tidal expiratory flow and expiratory time.

Results: Compared with controls, and after adjustment for body weight and age, LCI was higher in infants with CF (95% difference (95% CI): 0.37 (–0.10 to 0.83) z-scores, p = 0.12), as was FRC (mean difference (95% CI): 0.36 (–0.09 to 0.82) z-scores, p = 0.12). No difference was found for any of the tidal breathing parameters between CF and controls. Only one (4%) infant with CF had elevated LCI (>1.96 z-scores), while none of the CF infants showed elevated FRC (>1.96 z-scores).

Conclusions: CF infants shortly after birth showed normal LCI values and thereby no sign of ventilation inhomogeneity. Since also FRC and tidal breathing parameters were in a normal range, this seems to reflect the still undamaged state of small airways. This highlights the importance of early therapy to maintain normal lung function as long as possible.

Ara h2 is a marker allergen for a more severe form of Peanut allergy
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Background: After cow’s milk and hen’s egg, peanut allergy ranks in the third place in Switzerland in children at the age of above 36 months. Allergy to peanuts usually implies a dangerous form of allergy and is taught to persist lifelong. In this study the aim was to evaluate whether a correlation between severity of symptoms and the peanut allergen component based diagnostic exist.

Method: 17 children were followed from 5.19 years (16 months–15 y; 9 m. & 8 f.) referred to an allergy work-up were included. Diagnosis of peanut allergy was based on the history, clinical symptoms, skin test with native peanut, and serological tests (tIgE; rAra h1, rAra h2, and rAra h3 [ImmunoCAP, Phadia]). 14/17 children (82%) had systemic reactions (urticaria [7], angioedema [5], bronchospasm [5], vomiting [4]; shock [0]), and 3 had acute worsening of atopic dermatitis without systemic symptoms.

Results: 12/17 (70%) of the children were atopic based on the sensitization pattern to common inhalant allergens and clinical symptoms (allergic rhinitis [3], asthma [5]; other food allergies [5], atopic dermatitis [7]). Skin test to native peanut was positive in 11/17 (65%) patients. Total IgE was available from 12/17 (%) patients with a mean level of 982 kU/l (145–4151). Of the peanut allergen components rAra h2 was elevated in 16/17 (94%) patients with a mean of 45.5 kU/l (0.99–100 kU/l), rAra h1 in 10 (59%) with a mean of 21.0 kU/l (<0.35–100), and rAra h3 in 7 (41%) with a mean of 13.0 kU/l (<0.35–100 kU/l).

Conclusion: rAra h2 seems to be the most promising marker for detecting severe forms of peanut allergy, particularly with a cut of level of greater than 10.0 kU/l.
Factors modifying the breastfeeding effect on the frequency of respiratory symptoms in infancy

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Introduction: We have recently shown that tobacco smoking and air pollution during pregnancy increase the risk for respiratory symptoms in the first year of life. The aim of this study is to assess whether or not breastfeeding modifies these harmful effects.

Method: A prospective birth cohort study of 380 children provided the weekly information about the breastfeeding status, and incidence and severity of respiratory symptoms during the first year of the life. A generalized additive mixed model (GAMM) with quasi Poisson distribution was used to assess a potential impact of breastfeeding duration and exclusiveness on the development of respiratory symptoms in infancy.

Results: The multivariable longitudinal analysis showed that age modified the protective breastfeeding effect on the respiratory morbidity (p value for interaction <0.05). There was no interaction effect between breastfeeding and maternal smoking during the pregnancy. The effect of NO2-air pollution levels during pregnancy on respiratory symptoms in the offspring was significantly modified by the breastfeeding status (p for interaction <0.05). Additionally, we observed the age-dependent effect of maternal smoking during pregnancy on the frequency of respiratory symptoms in infancy (p value for interaction <0.001).

Conclusion: Breastfeeding protects children against respiratory symptoms during the first year of life, but the effect is modified by age. The effect of air pollution during pregnancy is modified by the breastfeeding status.

Pulmonary complications after liver transplantation in children: the Swiss national center experience

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1Pediatric pulmonology; 2Pediatric surgery; 3Pediatric gastro-enterology, Department of pediatrics

Introduction: Liver transplantation (LT) has become the treatment of end-stage hepatic failure. No recent data are available on pulmonary complication in children after LT, even if advances in patient selection, surgery or immuno-suppression, have improved the outcome, and pulmonary complications which are a main cause of morbidity and mortality. As Geneva is the Swiss national center for adult and pediatric LT, we aimed to study pulmonary complications post-LT in a four pediatric cohort, in order to identify pre- and peri-operative risk factors.

Methods: We retrospectively included all children (below 16 years) requiring LT from January 2000 to December 2011 at the Geneva University Hospital. We recorded patient's characteristics (age, sex, origin, and weight), pre-operative data (past medical history, liver disease and related complication, cardio-pulmonary evaluation, MELD score), donor characteristics (age, sex, blood group, CMV- and EBV-mismatch, living or deceased donor, graft weight), operative data (emergency level, surgical procedures and duration, ischemia duration), post-operative management (length of stay in hospital and in intensive care unit, mechanical ventilation, chest drain), and outcome.

Results: Seventy-nine children (50.6% girls) underwent eighty-two liver transplantations (mean ± sd age: 3.4 ± 4.6 years). Liver diseases were biliary atresia (n = 32), other cholestasis (n = 16), fulminant hepatic failure (n = 6), metabolic disorder (n = 14), neoplasia (n = 3), other cirrhosis (n = 7) and graft rejection (n = 4). To date, data from 37 liver transplantations were recorded. Pre-operative assessment showed portal hypertension (n = 22), hepato-pulmonary syndrome (n = 1), hepatic encephalopathy (n = 9), ascites (n = 24) renal failure (n = 4) and no pulmonary hypertension. Early post-operative (<1 month) lung assessment showed pulmonary edema (n = 16), pleural effusion (n = 22) requiring chest tube for 5 patients, atelectasia (n = 14), pulmonary infection (n = 3), but no pulmonary hemorrhage, pneumonitis or pulmonary atheromatous paralysis. No delayed (1 to 3 month) pulmonary complication occurred. In long term (>3 months) pulmonary follow-up, pneumonia (n = 3), extrinsic alveolitis (n = 1), central and obstructive apnea (n = 1) were observed. Four patients died, but not lung-related.

Conclusion: The incidence of pulmonary complications after LT and their associated mortality seem to decrease compared with older published cohorts. The further analysis of potential risk factors will help to better understand and prevent such complications.

Anaphylaxis in children-data from Zurich

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Introduction: Anaphylaxis is a severe, potentially life-threatening systemic hypersensitivity reaction. Over the last years the number of allergic disorders in the paediatric population is increasing and so does the incidence of anaphylaxis. Therefore the diagnostics of anaphylaxis can help to improve the medical care of these patients. The aim of this study was to analyse the symptom profile, to identify patients at risk and to evaluate the actual treatment of anaphylaxis from the pediatric data we collected at the University children’s hospital Zurich.

Methods: All children and adolescents with the diagnosis of anaphylaxis referred to the allergo-ky unit of the University children’s hospital Zurich from 2007 to 2012 were registered prospectively. For the data evaluation we used a password-controlled online-questionnaire of the anaphylaxis registry of German speaking countries (www.anaphylaxie.net) under the leadership of Prof. M. Worm, Allergy-Center Charité, Berlin. Only severe systemic allergic reactions with concomitant pulmonary and/or cardiovascular symptoms were accepted. Data included demographic data, personal and family atopy histo-ry, clinical features, place of occurrence, eliciting allergen, diagnostic tests, aggravating or triggering factors, the emergency treatment including the administering person, hospitalization and performance of prophylaxis before and after the event.

Results: In children and adolescents the most frequently affected organ systems in anaphylaxis are the skin and the respiratory tract. The most frequent elicitors responsible for anaphylaxis were food allergens, followed by hymenoptera sting and drugs. Medical treatment included antihistamines and corticosteroids in the majority of the cases, meanwhile adrenaline was not often used. The definitive analysis of our results will follow.

Conclusion: Even if cutaneous symptoms were one of the most frequent symptoms they can be absent in anaphylaxis. Food is the most underlying cause of anaphylaxis in childhood. The rare use of adrenaline in the emergency treatment of anaphylaxis and the high incidence of repetitive reactions, show the need for further education of physicians, patients and their relatives.

Symptom-guided, two-step diagnostic algorithm for children with acute viral respiratory tract infections

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Background: Acute viral respiratory tract infection is one of the leading causes for child consultation in paediatrician in developed countries. In clinical practice specific viruses are often not identified due to the lack of sensitive tests. During the last Influenza season we studied the effect of adding molecular testing to antigen test-negative specimens of selected patients , following a symptom-guided, two-step diagnostic algorithm.

Methods: From January 12 to April 22, 2012 the nasopharyngeal aspirates of children presenting with symptoms of acute viral respiratory tract infection were systematically tested for the presence of Respiratory Syncytial Virus (RSV) and Influenza virus A/B antigens. Antigen test-negative specimens were submitted for molecular testing on the basis of clinical judgement, i. e. specimens from children in respiratory distress, requiring intensive care or mechanical ventilation and specimens from children with a predisposing medical condition.

Results: A total of 125 specimens from 121 children (male:female = 1:2.5; median age = 2.6 years) were tested. Of these, 50 (40%) were antigen test-positive (RSV, 40; Influenza virus, 10). Molecular testing of 41 (32.8%) antigen test-negative specimens revealed additional 12 RSV and 2 Influenza virus infections, respectively. In 7 (5.6%) specimens multiple viral agents were detected. Antigen test-negative specimens were submitted for molecular testing on the basis of clinical judgement, i. e. specimens from children in respiratory distress, requiring intensive care or mechanical ventilation and specimens from children with a predisposing medical condition.

Discussion: In our study RSV (41.6%) and Influenza virus (9.6%) were the two dominant viral pathogens that led to clinical consultations. Symptom-guided molecular testing revealed additional 12 (29.2%) RSV and 2 (4.8%) Influenza virus infections, respectively, that were missed by direct antigen testing alone. These results suggest that direct antigen testing is inaccurate and inapt to guide modern patient management. Since evidence-based clinical decision making depends on timely and accurate laboratory test results direct antigen testing should be replaced by molecular tests when feasible. This holds particularly true when caring for severely ill patients.
Pertussis immunization in the maternity ward

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Introduction: Pertussis incidence has increased in recent years, resulting in an increase of infant hospitalizations and complications, including death. Recently the Swiss vaccination plan has been modified to reduce the risk of infant contamination. We fear that these changes may not be easy to implement and could even meet resistances. Trying to immunize as many mothers as possible, the maternity hospital of Aigle launched a campaign to offer to all non immune parents a dTPa booster as soon as possible after the birth of the newborn.

Methods: All new parents in our maternity (about 1000 births per year) are questioned about their pertussis immunity (i.e. PCR-proven pertussis or vaccination against pertussis less than 5 years (mothers) or 10 years (fathers) ago). We offer pertussis vaccination to non immune parents at the first medical examination of the newborn, and again during their stay in the maternity ward. Since October 2012, the following items are documented: the proportion of already immunized mothers, the acceptance of the vaccination, whether repeated incentives improve vaccination acceptance and how the newer recommendations are followed.

Results: Through two weekly immunization sessions of one hour, 36 mothers were vaccinated in October, 50 in November and 33 in December, out of respectively 60, 81 and 80 births. More comprehensive and prospectively collected data will be presented.

Conclusion: In view of our encouraging preliminary results, a prospective data collection is being undertaken, including the assessment of the proposition / acceptance of immunization during pregnancy, hoping that in the future more and more women will be immune at admission. A questionnaire will be distributed to all mothers to assess their general knowledge about pertussis and their acceptance of the new recommendations. We would enjoy more hospitals joining our programme.
Sub-aponeurotic fluid collections in young infants
Légeret C.¹, Adank E.¹, Malär R.¹

Introduction: Skull masses are common in newborns, mostly due to haematomas or edema associated to minor delivery trauma and appearing within the first days of life. As differential diagnosis traumatic lesions, congenital malformations, vascular malformations or other tumours may occur. Scalp swellings appearing after the neonatal period are unusual. Sub-aponeurotic fluid collections (SFC) are poorly described in the literature and poorly recognized as the condition is rare.

Case presentation: We present the case of a boy who presented at the age of 7 weeks with a large new swelling of the scalp. He was born via secondary Caesarean Section at term. His adaptation and the following weeks passed uneventful. The swelling was fluctuating, painless and without skin reddening, occurring after using a new ring pillow. Otherwise he was healthy, well-thriven and neurological appropriate. The cranial sonography was normal, except a collection of clear liquid outside the skull without signs of an underlying fracture. The first interpretation was a resolving haematoma, previously not apparent- due to birth trauma. As the swelling was increasing and getting firmer a MRI was performed which showed a sub-aponeurotic fluid collection without cerebrospinal fluid, without blood, normal intracranial findings and no extra-intracranial connections or malformations.

Discussion: Sub-aponeurotic fluid collections are rarely recognized lesions and the etiology remains largely uncertain. In all cases reported in the literature the fluid was proven to be cerebrospinal fluid (CSF). Since major bone fractures were absent, microtrauma related to traumatic labor, vacuum extraction or the use of fetal scalp electrodes were used as cerebrospinal fluid leakage and result in the delayed fluid collection. In all patients, where CSF was aspirated, the lesion refilled immediately. Conservative management is the treatment of choice, since the swelling disappeared spontaneously in all patients within 2–6 months. As history and clinical presentation of sub-aponeurotic fluid collections is distinct, invasive and potentially risky procedures could be avoided, if the diagnosis became more known.

Take home message: Sub-aponeurotic fluid collection is a differential diagnosis in young infants with scalp swelling with a distinct history and clinic. The treatment of choice is conservative management.

Dermatitis vernalis juvenilis aurium Burckhardt: an outbreak report and systematic review of the literature
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Background and objectives: Dermatitis vernalis juvenilis aurium Burckhardt (English: juvenile spring eruption of the helices of the ears; German: Frühjahrslichtdermatose der Ohren, Frühjahrsperniosis der Ohren; French: dermatite printanière des oreilles, pernio printanière des oreilles, herpes des alpinistes) is a distinctive suninduced condition appearing on the light-exposed skin of the ears, typically in boys and young men in early spring. Our aim was to determine clinical features and outcome of dermatitis vernalis Burckhardt.

Methods: We report a new outbreak in Swiss-Italian children.

Swiss-Italian outbreak: At least 14 pediatric cases (12 boys and 2 girls ranging in age from 3 to 11 years) of dermatitis vernalis Burckhardt were observed in the canton of Ticino in the period between 1st and 20th April 2011. The duration of the eruption ranged from 5 to 16 days.

Review of the literature: Five further outbreaks in children involved a total of 203 cases (boys, 72%), and three outbreaks in young adults involved 223 male subjects. A further 54 sporadic cases were found: 41 among children (boys, 97%) and 13 among young adult males. The typical presentation included itching and diffuse erythema of both ears starting in the evening after exposure to bright sunlight during cold weather, followed within 24–48 hours by papules or blisters. The subjects recovered spontaneously within 1–2 weeks. In New Zealand, among 162 school-aged boys, 20 developed the condition.

Conclusions: Dermatitis vernalis Burckhardt is a self-limiting and easily recognizable variant of polymorphous eruption, Overwintering appear on sunny and cold spring days. Pediatricians might rapidly develop the skills necessary to appreciate this condition, which is not addressed in most textbooks.

Activity-Related Energy Expenditure Decrease during Lower Limb Cast Immobilization in Adolescents
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Introduction: Physical activity (PA) is fundamental for children and adolescents’ normal health and development, whereas physical inactivity is recognized as a risk factor for the development of several diseases. A decrease of PA is frequently associated with a sedentary lifestyle, but may also results from immobilization. This study aimed to quantify the decrease of activity-related energy expenditure due to cast immobilization for lower limb fractures, and to assess if this decrease might constitute the starting point from which injured adolescents may become overweight.

Methods: We conducted a longitudinal matched case-control study of 34 adolescents with a first episode of lower limb fracture and a control group of 34 healthy cases. Physical activity was assessed during cast immobilization by accelerometer and data were expressed in total counts per minute and in minutes per day. The decrease of activity-related energy expenditure was calculated using the regression equation predicting energy expenditure from activity counts developed by Puyau et al.

Results: Activity-related energy expenditure in adolescents with lower limb fractures was estimated to be 16.0% lower than healthy controls. When converted in kcal per week, the difference in activity-related energy expenditure amounted to 125 kcal/day, which corresponds to 5.2 hours of slow walking.

Conclusion: A significant reduction of activity-related energy expenditure in adolescents with lower limb fractures may lead to a significantly positive energy balance, most of which is probably stored as fat, as there is usually no compensatory reduction of energy intake. An increase of walking seems unrealistic in this situation and patients should be advised to reduce their energy intake during the immobilization period.

Dermatitis vernalis juvenilis aurium Burckhardt: a distinctive sun-induced condition appearing on the light-exposed skin of the ears, typically in boys and young men in early spring.

Clinical evolution of children and adolescents attending a specialized childhood obesity center
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Introduction: Multidisciplinary group therapies for obese children and adolescents are effective but very difficult to implement. There is a crucial need to evaluate simpler management programs that target the obese child and his family. This study aimed to determine changes in body mass indexes (BMI) after single family obesity sessions with a physician in a specialized obesity center for child and adolescent.

Method: This cohort study included 283 patients (3.3 to 17.1 years, mean 10.7 ± 2.9) attending the Pediatric Obesity Care Program of the University Hospitals of Geneva. Anthropometric were assessed in consultations. We used an integrative approach in consultation to help the child and his family to make changes, which included cognitive behavioral techniques (psycho-education, behavioral awareness, behaviors changes by small objectives and stimulus control) and motivational interviewing.

Results: Mean follow-up duration was 11.4 ± 9.8 months. The decrease in BMI z-score (mean: −0.18 ± 0.40; p < .001) was significant and was dependant of age and BMI at baseline (better in youngest and higher BMI) and the total number of visits (p = .025). Additional psychological intervention was associated with reduced BMI z-score in children aged 8 to 11 years (p = .048).

Conclusion: Ambulatory single family obesity sessions during a year induce a significant reduction in BMI z-score, especially in the younger children and severely obese patients. This study emphasizes the need for the physicians to provide a follow up in obese children as soon as possible and confirms the beneficial effect of a psychological intervention on selected situations.
Does patient or parent satisfaction with nitrous oxide/oxygen procedural analgesia change with reiteration of the treatment?
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Introduction: Premixed equimolar mixture of 50% Nitrous Oxide/Oxygen (EMONO) delivered by inhalation is a widely accepted technique to control brief procedural pain. In 2004 this method was introduced at the pediatric clinic of the Cantons Hospital of Fribourg and until 2011 a questionnaire asking for satisfaction and pain levels was completed by the nurse after each EMONO application. The aim of this study was to analyze patient, parent and staff satisfaction and pain levels in patients with only one or with repeated EMONO applications.

Method: Retrospective analysis of 532 questionnaires including 11 questions asked to patients aged 2–191 months and/or their parents between January 2004 and December 2011. Group 1 (only one treatment) included 293 (164 boys), and group 2 239 (160 boys) questionnaires from patients with 2 to 26 treatments.

Results: There was no statistically significant difference for pain scores (0–10 and visual analogue scale: no/slight pain 62.6% and 66.4%, moderate pain 76% and 4.6%, severe and excruciating pain 5.7% and 8% for groups 1 and 2, respectively, \( \chi^2 = ns \)), for parent satisfaction (satisfied and very satisfied 85.1% and 86.5%, unsatisfied and very unsatisfied 5.4% and 3.4%, \( \chi^2 = ns \)) between the two groups. There was however a significant difference between the 2 groups for the satisfaction of the specialized nursing staff giving the treatment (satisfied 77.4% and 92.3%, unsatisfied 11.9% and 6.4%, \( p <0.05 \)).

Conclusion: Patient perception of pain and parent satisfaction does not change with the reiteration of analgesia with EMONO, but specially trained nursing staff satisfaction seems to be higher with known that with new patients.

Does additional topical anesthesia improve the analgesic efficacy of inhaled nitrous oxide/Oxygen mixture?
Sabrina Faleyras, Monika Spannaus, Denise Herzog
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Introduction: Premixed equimolar mixture of 50% Nitrous Oxide/Oxygen (EMONO) delivered by inhalation is a widely accepted technique to control brief procedural pain. In 2004 this method was introduced at the pediatric clinic of the Cantons Hospital of Fribourg and until 2011 a questionnaire asking for satisfaction and pain levels was completed by the nurse after each EMONO application. The aim of this study was to assess pain scores and satisfaction levels in patients with or without additional topical lidocain/prilocain (EMLA®) anaesthesia (TA).

Method: Retrospective analysis of 532 questionnaires including 11 questions asked to the patients aged 2–191 months and/or their parents between January 2004 and December 2011. Group 1 (only one treatment) included 293 (164 boys), and group 2 239 (160 boys) questionnaires from patients with 2 to 26 treatments.

Results: There was no statistically significant difference for pain scores (0–10 and visual analogue scale: no/slight pain 62.6% and 66.4%, moderate pain 76% and 4.6%, severe and excruciating pain 5.7% and 8% for groups 1 and 2, respectively, \( \chi^2 = ns \)) between the two groups. There was however a significant difference between the 2 groups for the satisfaction of the specialized nursing staff giving the treatment (satisfied 77.4% and 92.3%, unsatisfied 11.9% and 6.4%, \( p <0.05 \)).

Conclusion: Patient perception of pain and parent satisfaction does not change with the reiteration of analgesia with EMONO, but specially trained nursing staff satisfaction seems to be higher with known that with new patients.

Do pre- or in-hospital delays prior to appendectomy have an impact on the outcome and the duration of the hospitalisation?
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Introduction: It is generally accepted that delays in diagnosis and treatment of acute appendicitis lead to higher rates of perforation and post-operative complications. We therefore asked the question whether pre-hospitalization and/or in-hospitalization delays prior to surgery could affect the outcome and duration of hospitalisation in the paediatric patients treated at the Cantons Hospital of Fribourg.

Method: retrospective study of 112 charts of patients with appendectomy between January 1st 2010 and June 30th 2012. After exclusion of 44 patients operated in Taferns or Riaz and 4 transferred to Bern or Lausanne, 68 patient charts were analysed.

Results: 29 girls and 37 boys had a median age of 140.8 (34.9–203.3) months and a median z-score for weight-age of 0.35 (–2.8–4.3), and no relevant co-morbidities. Median duration of symptoms before diagnosis was 2 (0.5–21) days, and median in-hospital delay was 402 (31-1390) minutes. Perforated appendicitis was present in 18 (27.3%) and no inflammation in 7 (10.6%). Pre-hospital delay was a predictor for the duration of hospitalisation (\( R^2 = 0.07, p = 0.04 \)) but not for complications. \( R^2 = 0.06, p = 0.14 \) was not a predictor, neither for complications nor for the duration of hospital stay (\( r = 0.02, p = 0.3, \) and \( r^2 = 0.02, p = 0.7 \)).

Conclusion: Only a delay in the diagnosis of acute appendicitis but not an in-hospital delay had an impact on complications and the duration of hospitalisation for acute appendicitis.

Transient benign hyperphosphatasemia of infancy and early childhood – a systematic review of the literature
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Background: Sometimes, a temporary increase in alkaline phosphatase level is found in healthy infants and toddlers without evidence of liver or bone disease. The condition is customarily termed transient benign hyperphosphatasemia of infancy and early childhood. Most textbooks do not refer to the condition.

Methods: We completed a systematic review of the literature using the principles underlying the UK Economic and Social Research Council guidance on the conduct of narrative synthesis and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.

Results: The 142 reports retrieved for analysis included 813 cases (male : female ratio = 1:1:1.0): 733 in subjects ≤18 years of age and 80 in subjects >18 years. The alkaline phosphatase ratio, calculated by dividing the measured level by the upper normal limit, was ≥5.0 in 57% and the duration of the elevation ≤4 months in 80% of the cases. Transient benign hyperphosphatasemia often followed a benign infection but available data fail to demonstrate a causal link. The prevalence of transient benign hyperphosphatasemia ranged 1.1–3.5% in infants 2 to 24 months of age. Alkaline phosphatase isoenzyme studies, performed in 516 subjects, were not useful to evaluate subjects with isolated elevation of the alkaline phosphatase test. Although there was a history of a recent infection in >60% of the cases, no clear cut causal link with the preceding infection could be identified.

Conclusions: Transient benign hyperphosphatasemia is likely the most common cause of hyperphosphatasemia among healthy infants and toddlers. Sometimes, it also occurs in older children and adults, indicating that the traditional term transient benign hyperphosphatasemia of infancy and early childhood might not be correct. The elevation in alkaline phosphatase persists for >4 months in >20% of the cases. Recognition of this benign condition is crucial to avoid unnecessary investigations.
Sant’e-scalade: an initiative promoting physical activity and healthy diet in children 6–12 years
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Background: Lack of exercise associated with excess calories intake explains the increased global prevalence of obesity, children being increasingly affected. Grassroots initiatives may be useful auxiliary preventive strategies. In the realm of the largest Swiss popular city running event (Course de l’Escalade, Geneva, >30,000 participants in 2012) we developed a program (Sant’e-scalade). Launched in 2004 in a former municipal initiative, this program was extended to public and private schools in 2005 enrolling teachers to run the program. It consists of weekly running training combined with teaching of basic dietary concepts. It takes place during eight weeks preceding the Escalade run. We here present participation statistics and results of surveys quantifying changes in knowledge in participating children.

Methods: Between 2006 and 2012 we documented the number of participating schools and recorded the number of participating children comparing these with the number of children of the same age participating to the race and official government statistics. In 2006 a questionnaire was distributed in one school before the race, just after and 6 months later. In addition all children who participated to the program in 2008 and ran the race filled out a survey just after.

Results: Participation increased from 145 children in 2006, to 758 in 2007, 1033 in 2008, 2398 in 2009, 3154 in 2010, 3154 in 2011 and 6–12 yrs participated. Knowledge about good dietary habits increased significantly and remained up to 6 months. The post-race survey showed good knowledge of healthy eating concepts. In general teachers were generally very positive.

Conclusion: The best interests were neither seen as a standard, which demands the maximally or best possible nor becomes apparent exclusively in situations where the child's security and integrity is at stake. Rather it was seen as a tool to adequately distribute responsibility and competence in different areas to strive for an optimum concerning the child. Based on our data we subsequently present a comprehensive method of how to implement the best interests in clinical practice.

Estimation of dehydration using bioelectric impedance in children with gastroenteritis
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Purpose: The estimation of the degree of dehydration is essential for the correct management of acute gastroenteritis. According to the clinical score of the American Academy of Pediatrics (AAP), patients are classified into three subgroups: mild dehydration (3–5% of body weight reduction), moderate dehydration (6–9%), and severe dehydration (>10%). The aim of the present study was to compare the clinical score of the AAP with the measurement of the body water content with a bioimpedance device.

Methods and Materials: Children aged between 0.5 and 10 years with acute gastroenteritis were included in the study. Prior to fluid resuscitation, the clinical score of the AAP and the bioimpedance measurement (BCM-Monitor, FMC) were assessed.

Results: 26 children aged between 0.6 and 9.2 years (median 3.1 years, 14 females) were included. According to the clinical score of the AAP, 14 children had mild, 12 moderate or severe dehydration. The bioimpedance measurement was not possible in one child. The median relative dehydration measured with the bioimpedance device was –3.3% of body weight (interquartile range –9.8–0.3%) for children with mild dehydration, –5.3% (interquartile range 2 – 13%) for children with moderate/severe dehydration. The dehydration calculated by the device did not correlate with the clinical score. The group of children with mild dehydration had significantly lower impedance values at 50 kHz compared to the group of children with moderate/severe dehydration (p = 0.003). A cut-off set by 810 Ω is able to discriminate mild to moderate/severe dehydration with a sensitivity of 92% and a specificity of 86% (p = 0.0002).

Conclusion: The results of this exploratory study demonstrate that the relative dehydration calculated by the device does not correlate with the validated clinical score. However, the absolute resistance measured at a frequency of 50 kHz is able to discriminate the degree of dehydration and estimating the possible degree of dehydration for the assessment of dehydration. Future larger studies are needed to assess the clinical usefulness of these devices in clinical practice.

Infected urachal cyst: an uncommon cause of abdominal pain
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Introduction: Urachal cyst (UC) is one of the malformations due to an incomplete closure of the allantoid canal. We report a case of UC presenting with abdominal pain and a palpable mass.

Case report: A previously healthy 3 y.o. girl was investigated for abdominal pain, swelling and redness of the umbilical with a palpable underlying mass. An abdominal ultrasound showed a cyst with heterogeneous content. MRI confirmed its location in the Retzius space and was interpreted as an infected UC with a fibrous process to the bladder but no fistula. Co-amoxicilline IV was started and a secondary surgical ablation planned but emergency resection was performed 3 days later because of worsening symptoms and signs of peritonitis. An 8x10 cm intact abscessed cyst was removed. Histopathology confirmed the diagnosis and excluded any malignancy. MSSA was identified on the culture. Favorable evolution occurred after surgery and antibiotic treatment. Patient was discharged 10 days later.

Discussion: Discovery of an UC, unless fortuitous, is usually made at any age when infection or enlargement occurs. Typical symptoms include abdominal pain, redness and swelling around the umbilic or urinary symptoms. Infected UC can progress to peritonitis. MRI is the gold standard for identifying structure and location, as well as associated fistuluses. Although rare in children, urachal adenocarcinoma or rhabdomyosarcoma have to be ruled out by histopathology.

Conclusion: Remnants of the urachal canal should be part of the differential diagnosis in patients with abdominal pain especially if peri-umbilical inflammation is present. UC, unless infected, can spontaneously regress in the newborn. After 6 months, any UC has to be surgically removed (with prior IV antibiotic treatment if infected).

Pelvic cyst in a teenager, a medical and surgical challenge
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Introduction: Ovarian cystadenofibromas (CAF) are benign tumors originating from the ovarian epithelium and underlying connective tissue of the ovary generally appearing in the fourth and fifth decade and difficult to diagnose pre-operatively. We found less than ten described cases in children.

Case report: A 13 y.o. girl was admitted for lower right quadrant (LRQ), supra-pubic abdominal pain, vomiting, but no diarrhea or fever. She did not have any current gynecological complaints. The physical exam showed pain in the LRQ, right side and pelvis, with guarding in the LRQ and no palpable mass. Initial blood and urine workup was...
normal, with a negative pregnancy test. Extensive radiological workup comprising MRI, showed a 9 cm cystic lesion of unknown origin with ovariectomy was performed. Final diagnosis was CAF of the right ovary.

Discussion: Ovarian torsion and CAF are both a challenge for radiological diagnosis. Although ovarian torsions secondary to a malignant neoplasm is rare in children (~2%), surgeons tend to opt for ovariectomy in 80–90% of cases. Malignant transformation from a CAF being extremely rare a conservative line of treatment has been proposed.

Conclusion: Ovarian torsion can be a difficult diagnosis. Recent literature shows that the underlying cause is rarely dangerous in children. CAF however may mimic a malignant tumor. The conjunction of these two situations is a rare and challenging event.

Familial hypertrophic pyloric stenosis
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Introduction: Infantile hypertrophic pyloric stenosis (IHPS) is a disease that occurs mainly in male newborns in the first 3–8 weeks of life. Typical symptoms include projectile vomiting and weight loss. Constant hunger, belching and discomfort are other possible signs. We report a case with very early symptoms and a family background.

Case report: A previously healthy 12-days-old newborn boy was admitted for projectile vomiting and weight loss. He was referred to a pediatric ward because of projectile vomiting lasting 24 hours associated with discomfort but no normal stools. Precocious postprandial vomiting occurred 10–20 times per day. A 5% weight loss was noted. Infections were ruled out. An initial ultrasound (US) showed a normal pyloric muscle (2 mm thickness). Symptoms persisted 3 days later and a second abdominal US showed hypertrophic pylorus (4 mm), confirmed by an upper GE series. Despite a pyloromyotomy (Fredet Ramstedt), vomiting persisted and a 3rd US done 4 days after the operation showed a permeable passage but a hypertrophic pyloric muscle (4.5 mm). Nine days after the operation, full enteral nutrition was achieved and US was normal. Familial history (mother and brother) was positive for this pathology.

Discussion: Early presentation of IHPS is rare. US diagnosis may then be difficult and, in case of doubt, exam should be repeated. The timing of surgery is challenging: operation done too soon carries the risk of post-operative hypertrophic progression with persistent vomiting, if done too late the risk of complications increases.

Conclusion: Vomiting in the neonatal period should evoke the diagnosis of hypertrophic pyloric stenosis. This illness should not be excluded even when the initial US shows a normal muscle size, especially when family history is positive. The timing of the intervention remains a difficult choice for the pediatric surgeon.

Prevalence, type, clinical presentation and management of pediatric foreign body ingestion in a Swiss cantons hospital
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Introduction: Accidental ingestion of a foreign body (FB) such as coins, small batteries, and jewelry occurs frequently in children, and generally causes little or no morbidity. Endoscopic or surgical intervention is considered when a FB causes obstruction, or when it is potentially caustic. The aim of our study was to assess for the prevalence and type of FBs ingested as well as for the resulting morbidity.

Method: Retrospective chart review of 80 patients consulting at the emergency room (ER) for accidental ingestion of a foreign body (FB) between January 1st 2011 and August 31st 2012.

Results: There was no difference between boys and girls (41 f, 39 m), p = 0.07), and delay between FB ingestion and consultation at the ER (1.13 hours (0.5–120) and 16 (0.5–192), p = ns), and an FB was found in 27 (33.8%) patients. An endoscopic intervention was required in 13/80 (16.3%), for 3 visible and 3 non visible oro-pharyngeal organic FBs, for oesophageal location of 3 coins and 1 food impaction, with 2 of them having residual mucosal lesions, and for 3 with no detectable FB. Totally 45 radiographies resulted in the localization of 24 FBs. (12 coins, 4 batteries, metallic objects and food).

Conclusion: Only the 2 patients with oesophageal mucosal lesions had sequelae, the remaining required uncomplicated or no FB extraction. The rate of interventional extraction was similar to that published by others, as well as the type of objects ingested.

Hypertensive urgency after methylphenidate (MPH) overdose in a 8-year old boy
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Introduction: Methylphenidate (MPH; Ritalin®) is commonly used as pharmacological treatment in children and adolescents diagnosed with attention deficit and hyperactivity disorder (ADHD). Known side effects include tachycardia, dizziness and elevated blood pressure as result of sympathetic nervous system activation. We report on a boy diagnosed with hypertensive urgency following MPH overdose.

Case report: An 8 year old boy on MPH therapy for ADHD presented with vomiting, periumbilical pain, temperature and hypertension 90 mm Hg but normal heart rate (65/min). Laboratory tests, i.e., renal function, electrolytes and blood gas were all normal. Urinalysis showed microhaematuria, but no proteinuria. Furthermore diagnostic tests showed normal findings incl. renal (Doppler) sonography, echocardiography and urinary catecholamines. The boy was admitted for cardiovascular monitoring and MPH (½-life: 2 hours).
was stopped. Blood pressure normalized gradually within 38 hours (111/82 mm Hg) without any antihypertensive therapy, and the boy recovered completely.

Conclusion: This case illustrates both the need for cardiovascular monitoring in children on methylphenidate and the potentially hazardous side effects of MPH dose escalation.

Incidence and treatment of developmental hip dysplasia in Mongolia: a prospective cohort study
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Background: In Mongolia, adequate early diagnosis and treatment of developmental hip dysplasia (DDH) have been unavailable and its incidence was unknown. We determined the incidence of ultrasonographic DDH in newborns and established adequate procedures for diagnosis and treatment of DDH at the largest maternity hospital in Ulaanbaatar/Mongolia.

Methodology/Principal Findings: For one year (Sept 2010 – Aug 2011) we assessed the hips of 8,356 newborns (median age: one day) by ultrasound. We used Graf's categories and found 14,873 Type 1 (89.0%), 1715 Type 2a (10.3%), 36 Type 2c (0.2%), 70 Type D (0.4%), 14 Type 3 (0.08%), and 4 Type 4 hips (0.02%). Children with Type 1 hips (normal) were discharged. Children with Type 2a hips (physiologically immature) received follow-up ultrasounds at monthly intervals. Children with Type 2c to 4 (DDH; deformed or misaligned hips) were treated with a Tubingen hip flexion splint and also followed up. The hip abnormalities resolved to mature hips in all children who were followed up. No severe complications from the treatment occurred.

Conclusion/Significance: The incidence of DDH in Mongolian newborns is comparable to that in Europe. Early ultrasound-based screening procedures for diagnosis and treatment of DDH at the largest maternity hospital in Mongolia/Gold, 2013; 143(Suppl 197) · www.smw.ch

Restless Legs Syndrome in association with mycoplasma pneumoniae infection
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Background: Restless legs syndrome (RLS) was first described in 1685 by Sir Thomas Willis. It is characterized by an uncomfortable sensation or unpleasant urge to move the legs or other affected body parts. Symptoms increase with inactivity and show a circadian enhancement in the evening or at night. RLS can be a primary disorder or can occur secondary to other conditions. The pathophysiology of RLS remains unknown, but dysfunctioning of the brain dopaminergic system is argued. We report the case of a 10-year old girl with RLS-like symptoms possibly associated with mycoplasma pneumoniae infection.

Case report: A 10-year-old girl presented with a 6 day history of rhinitis, cough, vomiting and fever and has been treated with amoxicillin/clavulanic acid for possible pneumonia. She was complaining of discomfort and pain in both legs and she had to move her legs and walk around constantly to get some relief. Physical neurological examination revealed no abnormalities. Laboratory examinations showed a CRP of 46 mg/l and normal white blood cell count. A urine toxicological screening was negative and EEG was normal. During hospitalization she needed supplementary oxygen supply and chest X-ray showed retrocardial infiltration. PCR for Mycoplasma pneumoniae from nasopharyngeal swab was positive. She was started on oral clarithromycin. Within a few days her RLS-like symptoms improved and she ended of hospitalization she only had a minimal discomfort of the legs in the evening.

Conclusion: Restless legs syndrome is primarily a disorder of adults, but also has been described in children. M.pneumoniae infection is known to cause extrapulmonary problems, for eg, neurologic, cardiac, hepatic, and hematopoetic diseases. Acute transverse myelitis, ADEM, and acute disseminated encephalitis are the most severe neurologic complications. But a few cases of children with M.pneumoniae infection and restless legs syndrome-like symptoms have also been described in the literature. Therefore we speculate that in our case the transient RLS might be causally related to the underlying infection with M. pneumoniae. Pediatricians should be aware of this possible association.

Whirlpool-associated Folliculitis: a case report
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Pseudomonas aeruginosa is a Gram-negative bacteria with a special predilection for warm and moist area. It can be found in soil, carpeting, sink, and tap water. Infections due to P. aeruginosa are not confined to the hospital inpatient care units and immunosuppressed patients. It may also be the culprit of less severe community-acquired infections that have to be recognized by the primary care pediatrician.

Case report: A 14-years old boy was brought to the emergency department for a pruritic maculo-papular rash that appeared 48h after the hot tub had been purchased 2 years prior to its installation. It was installed a few days prior to its first use. It was then used for 4 days in a row and the rash appeared 48h after the last immersion.

Discussion: Our patient presented a Whirlpool-associated folliculitis. P. aeruginosa is known to be a water organism. The organism is present in whirlpool water and lesions associated with outbreaks of dermatitis and folliculitis related to whirlpool exposure is in Northern America. At present, few cases are reported in the literature in Europe but our hypothesis is that the prevalence of outbreaks will increase as private whirlpool become more available, affordable and fashionable. Therefore it may become a public health problem in the future. The challenge for the physician will be to recognize the diagnosis and to understand the natural history of this infection. Indeed, although it is a P. aeruginosa infection, no treatment is required in the majority of cases and the folliculitis will resolve spontaneously within 4–10 days. Needless to say the patient should seek advice in order to decontaminate their hot tub.

Screening obese adolescents for Binge eating disorder: the ADO-BEDS auto-administered scale

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Introduction: Recognition of Binge eating disorder (BED) in obese adolescents is essential, as it is predictive of excessive weight gain and requires specific treatment. Clinicians often struggle to identify these disorders in children due to puberty changes. They may present differently than in adults. Recently researchers have proposed ten adapted criteria for measuring BED in children. The study consisted in two phases: translation and adaptation of the proposed criteria to a French population of adolescents and test validity of the questionnaire in detecting current BED as diagnosed by the psychologist. 62 obese and non obese adolescents aged 11 to 19 years completed the questionnaire and were then interviewed by a psychologist blinded to the results. Sensitivity analyses were conducted to determine the best cut-off score for ADO-BEDS.

Methods: The study consisted in two phases: translation and adaptation of the proposed criteria to a French population of adolescents and test validity of the questionnaire in detecting current BED as diagnosed by the psychologist. 62 obese and non obese adolescents aged 11 to 19 years completed the questionnaire and were then interviewed by a psychologist blinded to the results. Sensitivity analyses were conducted to determine the best cut-off score for ADO-BEDS.

Results: The auto questionnaire ADO-BEDS had a sensitivity of 88.9% and specificity of 71.7% for the identification of binge eating disorder in adolescents using only the first 7 criteria. Responses to questions evaluating the last three criteria, related to frequency of the episodes and compensatory behaviors, did not improve the diagnostic performance of ADO-BEDS.

Conclusions: The ADO-BEDS, a brief auto-administered scale measuring BED in adolescents can be a useful screening instrument as it quickly identified adolescents with BED within a general clinical consultation. Primary care physicians may use it to raise their index of suspicion of an eating disorder in order to propose adapted care for their obese patients.
Leg pain due to chronic recurrent multifocal osteomyelitis mimicking a osteosarcoma

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Case report: A 13 years old boy, otherwise in good health, complained of left leg pain, with soft tissue swelling and nocturnal pain, without any history of trauma. Clinical examination revealed redness, painful edema, from the left leg. There was no other skin lesion. Blood tests showed no inflammation. The initial X-ray showed subtle sclerosis on the mid shaft of the left tibia. Subsequent MRI showed bone marrow edema with peri osseous soft tissue involvement and contrast enhancement. A whole body Tc-Scintigraphy was performed which revealed a focal involvement. A bone biopsy revealed no evidence of malignant cells. A bacteriological research was negative. Clinical evolution with NSAID was good, with regression of pain and radiological lesion. 7 months later, the patient presented with left elbow pain. MRI showed involvement of bone marrow of the proximal ulna and Chronic Recurrent Multifocal Osteomyelitis (CRMO) was retained as diagnosis.

Discussion: CRMO is a rare disease (1 over 1,000,000) of unknown origin. It usually resolves itself, and most of affected children do not suffer any major lingering or long term disability. However, when the lesion is diaphyseal, it may be confused with Ewing sarcoma, Langerhans histiocytosis, or much less likely, osteogenic sarcoma. This case with a single lesion was disturbing because of a presentation simulating bone tumor.

What do we know about the profile and clinical pathways of young people seeking care in specialized adolescent medicine clinics: a systematic review

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Introduction: Adolescent medicine has been a growing field in recent years. National population surveys have provided a better understanding of the health needs of this age group. Pediatric associations recommend developmentally appropriate health services (youth-friendly services), which provide comprehensive care, information and guidance. The aim of our research was to gain an understanding of the clinical pathways of adolescents seeking care in a specialized adolescent medicine clinic. We sought to identify the presentation and outcomes of the young people attending such clinics.

Method: We conducted a systematic literature review over 10 years (2002–2012) using the following search engines: Pubmed, Embase, CINHAL, PsycINFO. The research question was addressed according to PICo search criteria (Population Intervention Comparison Outcome). The key words involved MeSH terms such as “adolescent health services”; “adolescent medicine”; “health status” and “mental health”. The age-range was 13–24 years, i.e. “young people” according to WHO definitions. Population-based studies or school surveys were excluded as well as those reporting about single, specific health problems such as anorexia, depression, cancer or asthma.

Results: The use of key words enabled us to identify 2044 articles eligible for inclusion in the review. 2020 were excluded based on their titles. The analysis of 24 remaining abstracts did not lead to the identification of a single study describing the profile and clinical pathway of young people seeking care in a specialized adolescent medicine clinic.

Conclusions: There is a gap in the literature in relation to the presentation and clinical outcomes of young people receiving care within an adolescent medicine clinic. This provides an argument in favor of the development of a study describing the profile and clinical pathways of patients seen within the adolescent and young adult program of the Department of Pediatrics at Geneva University Hospitals.

Severe skin and soft tissue complication during varicella disease

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Introduction: We present a case with severe skin and soft tissue inflammation during varicella infection which we assume to be associated with the use of nonsteroidal anti-inflammatory drugs.

Case: A 5 year old boy presented with a 4 day history of acute varicella infection. He was treated with topical calamine lotion and diclofenac. Three days later he developed severe soft tissue inflammation in the right inguinal area. He was admitted to the hospital for further investigations and therapy. Clinical examination showed a right groin a 10 x 10 cm painful skin area with induration, swelling, hyperemia and hyperthermia, expanding to the right lower abdomen and pubes. To treat a supposed bacterial superinfection we started an intravenous antibiotic treatment with high closed amoxicillin/clavulanic acid. After 36 hours of treatment the area of inflammation extended rapidly and progressively to a multple of the primary size. Moreover the boy still had high fever peaks. A sonographic ultrasound examination showed diffuse inflammation of the subcutaneous tissue but no abscess. Clindamycin was added to the primary intravenous antibiotic therapy. After another four days of treatment clinical symptoms were slightly regressive. Blood cultures remained negative. Clindamycin was then stopped and amoxicillin/clavulanic acid was continued orally for 10 days to ensure a treatment of bacterial superinfection.

Discussion: In literature the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with varicella zoster virus infection is reported to be associated with higher risk of severe skin and soft tissue complications as cellulitis, abscess, fascitis or necrosis. Regarding the pathogenesis there are different hypothesis discussed. Based on literature we assume that the severe soft tissue complication in this patient was associated with the use of diclofenac.

Conclusion: Severe skin and soft tissue infection are possible complications using NSAID in patients with acute varicella zoster infection. Therefore caution is recommended for the use of NSAID in this context.

Intracranial hypertension caused by craniosynostosis in a 5-year-old boy with non-ossifying bone lesions leading to the diagnosis of osteoglophonic dysplasia

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Background: Pseudotumor cerebri or idiopathic intracranial hypertension (ICH) is defined by elevated cerebrospinal fluid (CSF) pressure without pathological findings in neuroimaging or CSF examination. Chronic or acute present with headache and papilledema as the leading symptom of ICH and papilledema. Often comorbidities or medications are identified with unknown causative role. We report on an unusual case of a 5-year-old boy who presented with ICH which was finally found to be caused by craniosynostosis due to osteoglophonic dysplasia (OD).

Case: The boy first came to our attention at the age of 4 years because of delayed tooth eruption and broad alveolar ridges. Histological diagnosis of multiple giant cell granulomas of the jaw was made. The lesions were treated by repeated curettage and local injection of corticosteroids. In addition, daily subcutaneous injections of calcitonin were started. 18 months later he presented with severe headache. Idiopathic ICH was diagnosed based on bilateral papilledema and elevated CSF opening pressure. Further diagnostic workup did not reveal any pathology. Calcitonin treatment was assumed to be a possible cause and was stopped. Treatment with Acetazolamide showed not to resolve the headaches. One year later the boy complained of lower limb pain. Radiological work-up revealed gross multicellular metaphyseal non-ossifying lesions of the long bones. Because of these lesions OD was suspected. Manifestation of an already rare genetic disease is usually during early childhood with rhizomelic dwarfism, non-ossifying bone lesions, disturbed dentition and craniosynostosis, the later leading to severe complications. In our patient craniosynostosis was confirmed by CT-scan. He was then treated successfully with expansive cranioplasty. Genetic analysis revealed a heterozygous missense mutation in the fibroblast growth factor receptor (FGFR1) gene, known to be causative for OD.

Conclusions: It can be difficult to differentiate between coincidence and causality of factors in children with ICH. Secondary ICH has to be evaluated especially in patients with associated rare symptoms – in our case skeletal dysplasia. Craniosynostosis can cause ICH even beyond infancy. It can be missed when premature closure of all sutures does not lead to obvious head deformity.

Aggressiveness in adolescent girls: theoretical and clinical role of the mentalization model

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Introduction: There is a growing idea that a new phenomenon of aggressiveness in adolescent girls is emerging, but it is also though that girl’s aggressiveness has always existed. This article does not directly take position in this debate but gives light on a growing question. How does aggressiveness in adolescent girls emerge? The main aim of this study is to determine the risk factors in developing aggressiveness in girls during adolescence. The second aim is to determine the role of mentalization (as defined by Fonagy & al., 1999) in this problematic.

Methods: Two groups of girls between 13–17 years old are compared. The control group (n = 40) was recruited via announcements and had no major psychopathology. The clinical group (n = 30) was recruited at the Geneva prison for juvenile delinquents. They all had a diagnosis of behavioral disorder, mainly conduct disorder.

Results: The girls of the clinical group had a more vulnerable psycho-social background, less education and poorer capacities of mentalization. Furthermore, the quality of mentalization coupled with the quality of attachment and the non presence of abuse were together greater indicators of the amount of aggressiveness in these adolescent girls. The girls of the clinical group showed higher levels of aggressiveness than the control group. This study provides a preliminary overview of the relationship between mentalization and aggressiveness in adolescent girls.

Conclusions: The better the quality to mentalize, the better the quality of attachment and the absence of an ill-treating environment, the less observed, but taken together with other risk factors such as the presence of abuse, the variance explained is much higher. This study shows that increasing the capacity to mentalize could help diminish the aggressive traits in adolescent girls.

A workshop with simulated adolescent patients to teach clinical skills to 4th year medical students: Students and facilitators’ views

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Introduction: Complex adolescent health clinical situations require effective coordination between various health professionals and could provide opportunities to develop interprofessional training modules for nursing and medical students. This project consists in an experience of interprofessional collaboration using adolescent simulated patients to improve interviewing skills for nursing students built on a project initiated by the multidisciplinary adolescent health unit of the Department of Child and Adolescent health and Geneva university with 4th year medical students at the request of the Health School in Geneva.

Methods: Senior lecturers of Geneva’s Health school (dietician, midwife and nurse) reviewed the training material developed for 4th year medical students and filled an open questionnaire about their expectations and the appropriateness of training material for their students. A training in group facilitated with adolescent simulated patients was developed and tested on their needs. A new optional training session for 3rd year nursing students was tested: interactive lecture and 3 sessions of small group work (one simulated patient and a facilitator). Facilitators and nursing students’ feedback was collected.

Results: The 4 facilitators and 23 students considered training content (objectives and clinical situations) and format useful and adapted to their needs. Facilitators had never worked with simulated patients and saw this learning method as effective. Training of trainers sessions offered opportunities to overcome issues of professional boundaries as well as clinical and pedagogical skills building. Conclusions: This training module is adapted for nursing students and will be renewed in 2013. It could be integrated in the future developments of simulation programs of Geneva University and Health school in Geneva.
Training general practitioners to assess young people’s mental health needs: impact on general practitioner’s A.E. Ambresin
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Purpose: To investigate the short-term effectiveness of training general practitioners (GPs) in their detection of mental health needs in young people.

Methods: Forty general practices were randomised to an intervention (32 GPs) or a comparison group (56 GPs). Intervention GPs participated in a specially designed training program that emphasized health risk screening and risk-response using motivational interviewing. The comparison group GPs were offered brief standard talks on best practice in adolescent health. Consecutive 14 to 24 year olds (18 per practice) attending general practices were recruited. They completed a computer assisted telephone interview following the self-perception of having a mental health problem. GPs completed a questionnaire following each consultation in which they rated the young person’s mental health.

Results: GPs' identification of young people's mental health needs (OR: 0.87; CI: 0.77 to 0.99; p = 0.02) and their detection of mental health needs among young people (sensitivity: 0.37; 95%CI: 0.27 to 0.47; specificity: 0.56; 95%CI: 0.46 to 0.65 and 0.60; 95%CI: 0.50 to 0.70 respectively). Yet, GPs received training in screening and motivational interviewing or not. Seeing young people repeatedly when mental health distress is progressive with potassium normalization. Positive familial history -father as well as brother- was noted with the same impairment of the extremities.

Discussion: GPs' detection of mental health needs among young people. Yet, primary care physicians are well placed to respond to the enormous demand that mental distress represents. However, young people repeatedly when mental health distress is suspected and possibly the use of more accurate diagnostic tools could improve accuracy. Further research on other barriers to further intervention trials.

Lethal violence against children – Medico-legal study in the north of Portugal
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We conducted a retrospective study on cases of suspected fatal violence against children, whose autopsies took place at the Northern Delegation of the National Institute of Forensic Medicine and corresponding Medico-legal Offices, between January 2004 and December 2009.

The aim of this work was to explore the relevance of clinical records and autopsy reports in supporting legal decisions. In order to achieve this goal, detailed information regarding fatal violence against children in the northern region of Portugal was gathered (including violence in utero and in the perinatal and postnatal care periods, as well as life up to 18 years old), through the review of autopsy reports and court records.

Nineteen (n = 17) autopsy reports were analyzed. The corresponding court records were reviewed in loco in the criminal courts where those cases were trialed. Some of the cases will be individually presented.

A medico-legal etiology of crime (homicide and criminal abortion) was explicitly pointed out by the experts, in their reports, in 9 cases. Cases whose trials had already come to an end were all ruled as criminal acts, regardless of witness accounts that might exist. There was a full agreement between the medico-legal findings and the judicial decisions, which is indicative of the relevance of such procedure and also of the importance of all the available information (clinical and police records, as well as witness accounts) be provided to the expert, in order to support his diagnosis.

In some cases (n = 10) the offender was someone close to the victim and in 7 of such cases she was, in fact, the mother of the child (the fatal event taking place, for instance, in the course of a post-partum depression). This stresses out the need of also paying attention to social and family issues when observing the child in consultation. It all leads us to believe that, the more clinical records are provided and the more detailed the information in those records is, namely in suspected abuse cases, the stronger their probative value to the judge is.

Acute respiratory decompensation in a previously healthy 3-year old boy resulting in diagnosis of late-onset congenital central hypoventilation syndrome (LO-CCHS)
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Introduction: Congenital central hypoventilation syndrome (CCHS) is a rare disorder with impaired autonomic control of breathing. Its reported incidence is 1 in 200,000 live births, although this may be underestimated due to a broad spectrum in severity and clinical presentation.

Case report: A previously healthy 3-year old boy with normal development presented in our emergency department with acute upper airway infection and suspected asthma with silent chest. Due

Preventive treatment consists in daily kalium supplementation, low carbohydrates diet and medications such as a potassium-sparing diuretic in order to maintain normal to slightly high blood potassium values.

Conclusion: In case of acute muscle weakness or paralysis, clinicians should be aware of this rare disease. Low kalium suggests this diagnosis, especially when family history is positive, but needs to be confirmed with a genetic test. Treatment is symptomatic.

Familial periodic hypokalemic paralysis
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Introduction: Acute muscle weakness or paralysis without lack of sensibility can have many different etiologies, the most frequent being muscular, hysteric, and metabolic. A genetic disease, the periodic hypokalemic paralysis, can be however a very rare cause as well.

Case report: A 15-year-old Asian boy was hospitalized after skiing during several hours for a first paralysis attack. He initially presented a sudden weakness of his legs, forcing him to lay down with a following total paralysis of his arms and legs. Severe hypokalemia (1.8 mmol/l) was noted and IV potassium was administrated. Recovery happened progressively with potassium normalization. Positive familial history -father as well as brother- was noted with the same impairment of the extremities.

Conclusion: Hypokalemic periodic paralysis is a rare channelopathy characterized by periodic muscle weakness or paralysis as kalium drops, primarily due to a defect in a voltage-gated calcium channel. Attacks mainly start in adolescence and are triggered by strenuous exercise followed by rest, high carbohydrate meals, sudden changes in temperature, and even excitement, noise or flashing lights. This spans from local mild weakness to severe full body paralysis. Attacks may last for a few hours or persist for several days. Recovery is usually sudden and is due to release of potassium from swollen muscles.
to severe global respiratory insufficiency, the boy was intubated and remained on high levels of invasive ventilation for a total of 8 days, also requiring intermittent muscle relaxant. In addition, he was treated with iv and inhaled Salbutamol, iv steroids and iv antibiotics. Highly elevated bicarbonate levels (37 mmol/L) on admission indicated an underlying chronic disorder. After extubation severe muscular hypotonia and adynamia were evident therefore critical illness polyneuropathy/mypathy was suspected (CIPNM). A congenital myopathic syndrome was excluded with normal electrophysiological tests. In the recovery phase elevated pCO2 persisted with consistent sharp increases in pCO2 during sleep, indicating hypoventilation and necessitating nocturnal non-invasive ventilation. Hence, genetic analysis of the PHOX2B gene was performed, revealing an expansion mutation of 5 alanine expansions, consistent with late-onset congenital central hypoventilation syndrome. Although not confirmed by electrophysiological testing, CIPNM remained a plausible complicating factor in view of the quick recovery of the muscular hypotonia and adynamia.

Conclusion: Late onset CCHS should be considered as a differential diagnosis in patients developing nocturnal hypoventilation after an episode of acute illness.

Neonatal diabetes management in a very low birth weight premature infant

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Introduction: Transient and Permanent Neonatal Diabetes Mellitus (NDM), usually defined as diabetes diagnosed within the first 6 months of life, are rare conditions occurring in 1:100,000–260,000 live births, and resulting from impaired insulin secretion due to abnormal beta-cell development or function. Usually unrelated to autoimmunity, NDM is a monogenetic disorder and represents a complex challenge with regard to glycemic control.

Case report: We describe the case of a very low birth weight (VLBW) female neonate born at 28 weeks of gestation and with a birth weight of 1030 g. After an uneventful early adaptation, on day 12, capillary routine checks revealed repeated asymptomatic hyperglycemia between 15 and 20 mmol/L. Prematurity, low birth weight and size represent considerable management challenges. We successfully treated this neonate from the beginning and for 33 days by subcutaneous and thus less invasive insulin delivery, via an insulin pump at an initial rate of 0.55 UI/kg/hour. By treatment day 17, insulin had to be progressively reduced and could be finally stopped.

Discussion: To the best of our knowledge, this is the first report of successful management of NDM in a VLBW neonate with continuous subcutaneous administration of short lasting insulin. DNA sequencing did not detect mutations in the KCNJ11 gene encoding the Kir6.2 subunit of the pancreatic KATP channel involved in the regulation of insulin secretion; further genetic work-up is ongoing.

Gastric lactobezoar in a Zidovudin treated ELBW infant

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Introduction: Gastric lactobezoar (GLB), a pathological conglomeration of milk and mucus in the stomach causing gastric outlet obstruction is a rarely reported disorder.

Case report: We report of the repeated appearance of a GLB at day 11 and day 23 in an extremely low birth weight (ELBW) male neonate born at 27 3/7 weeks of gestation with a birth weight of 730 g. He was fed with artificial milk, under Zidovudin (AZT) treatment and had a history of pulmonary hemorrhage. Plain X-rays for abdominal distension without significant residues and abdominal ultrasonography allowed diagnosis based on typical radiological features.

Repeated gastric lavage through oro-gastric tube with normal saline, followed by N-acetylcysteine led to regression of the lactobezoar after 6 days, and 3 days respectively. Total parenteral nutrition was given during the first, but enteral nutrition was maintained during the second occurrence. Therapy for Zidovudin (AZT) treatment and had a history of pulmonary hemorrhage. Plain X-rays for abdominal distension without significant residues and abdominal ultrasonography allowed diagnosis based on typical radiological features.

Repeated gastric lavage through oro-gastric tube with normal saline, followed by N-acetylcysteine led to regression of the lactobezoar after 6 days, and 3 days respectively. Total parenteral nutrition was given during the first, but enteral nutrition was maintained during the second occurrence. Therapy for Zidovudin (AZT) treatment and had a history of pulmonary hemorrhage. Plain X-rays for abdominal distension without significant residues and abdominal ultrasonography allowed diagnosis based on typical radiological features.

Conclusions: GLB is considered exceedingly rare, but may be under-diagnosed in premature infants with abdominal distension and obstruction. For the diagnosis and follow-up of GLB standard X-rays and abdominal ultrasonography are necessary. Although utilization of the protein-cleaving enzyme N-acetylcysteine has been described for treatment of GLB in toddlers and in term neonates, we report probably the first successful treatment of a GLB with enteral N-acetylcysteine in an ELBW infant. A possible association of a GLB with AZT treatment remains speculative.

Ultrasonic cardiac output monitor for cardiac output measurement: is it equal to conventional echocardiography?

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Background: Measurement of cardiac output as an additional parameter in assessing the circulatory status of premature and term infants has become more and more useful in guiding therapy of circulatory compromised babies. Echocardiography is the gold standard to do so but requires time and expertise. Ultrasonic cardiac output monitor (USCOM) is a rapidly available method to estimate cardiac output. However, it’s accuracy for use in a neonatal intensive care unit (NICU) needs to be determined.

Methods: Cardiac output measurements of left ventricular cardiac output by echocardiography and USCOM were done paired. Measurements were obtained for premature as well as for term born infants (n = 49). Measurements were then compared.

Results: Mean USCOM measurement differed from echocardiography in measuring left ventricular cardiac output by –36.6 ml/kg/min (p = 0.003). The Bland-Altman plot shows low measuring agreement (fig. 1). Variations for single results were up to 265 ml/kg/min.

Conclusions: Agreement between the ultrasonic cardiac output monitor and echocardiography for left ventricular cardiac output measurement is poor. At this point USCOM measurement of left ventricular cardiac output as stand alone assessment tool in a NICU can not be recommended.

Sturge-Weber syndrome, Phakomatosis pigmentovascularis and Down Syndrom in a Newborn

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Introduction: Sturge-Weber syndrome (SWS) is a neurocutaneous disorder affecting the skin, the central nervous system and the eyes. SWS is characterized by the classic triad of facial capillary malformations, known as port wine stains, leptomeningeal angiomatosis and glaucoma. Seizures and mental retardation occur in most cases with neurological involvement. Phakomatosis pigmentovascularis is another neurocutaneous disorder with an association of cutaneous and extracutaneous (viscer al, muscular, neurologic or ocular) abnormalities. We present a newborn African boy with SWS with unusual distribution of port wine stains and additional multiple Mongolian spots as well as leptomeningeal involvement. Last but not least, he is diagnosed trisomy 21.
showed multiple port wine stains in uncommon locations and unusual sizes. The leptomeningeal angiomatosis supports our diagnosis of Phakomatosis pigmentovascularis (PP) (type II) – is diagnosed. The multiple Mongolian spots, an additional neurocutaneous disorder case reports about patients with both SWS and Down syndrome. After association of both disorders is reported in the literature. There are few a thorough search in the medical literature this is the only case of a combined manifestation of all three disorders (SWS, PP & Down syndrome).

Bilateral, congenital chylothoraces in a preterm infant; etiologies and therapeutic strategies of a rare disease

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Chylothorax is defined as an abnormal accumulation of lymphatic fluid in the pleural space. This is a rare condition in neonates but is nevertheless the most common cause of congenital pleural effusion in fetuses and newborns. Differential diagnosis includes a wide variety of disorders with changes of the pulmonary venous hydrostatic pressure, lymphatic pressure, and blood oncotic pressure, or with local tissue trauma or inflammation. Depending on the extend of fluid accumulation at birth, the affected neonates suffer from various degrees of respiratory distress to complete respiratory failure, resulting in a substantial morbidity and mortality. Antenatal management of chylothorax consists of thoracocentesis or pleuro-aminocytic shunts to prevent pulmonary hypoplasia. In the postnatal period, the management of the pleural effusion can be either conservative or surgical.

In our case report, we describe a preterm infant of 36 weeks gestational age with antenatal diagnosed bilateral pleural effusions. Immediately after birth, a chest tube had to be inserted without influencing severe respiratory distress resulting in nasotracheal intubation at the age of 6 minutes. Shortly, a second tube had to be inserted, so as to drain a total volume of 110 ml, of which laboratory findings confirmed the diagnosis of bilateral, congenital chylothoraces. Based on various but overall unremarkable examinations to identify the origin of the disease, the etiology remained unknown, however a temporary and self-limiting malformation of the thoracic duct is hypothesized. A conservative treatment consisting of a diet with medium-chain triglycerides was started, which lead to a complete resolution of pleural effusion within 7 days. The infant could be extubated at the 4th day of life. A new trial to mother's milk exposure after 3 weeks was successful with no consequent relapse of pleural effusion.

Antenatal knowledge of this pathology is crucial and potentially life saving. We therefore discuss implications for the neonatologist attending delivery and present different therapeutic strategies based on the extent and origin of the disease.

Newborn boy with ring chromosome 9

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Background: Ring chromosome 9 is a very rare chromosome disorder where the chromosome 9 is formed as a ring by its ends joining with or without losing genetic information. Although usually appearing as a spontaneous error, the risk is higher having a parent with a change in chromosome 9. The phenotype can be very variable, therefore there is not a specific clinic and the maturation profile differs a lot. We present an early-born twin boy with ring chromosome 9, mos46 XY, r(9) (p23q34.3).

Case study: The twins were born by caesarean to a 33year old third gravida in the 30 1/7 postconceptional weeks, after premature rupture of his twin sisters membranes. Otherwise the pregnancy was uneventful, the serology was unremarkable. The boys birth weight was 1100 g (P 10-25), length was 34cm (<P3). He adapted with an Apgar of 2.2 kg and the baby required immediate intubation due to poor adaptation. Clinical examination revealed a profoundly distended abdomen, skin edema and multiple protruding skin nodules. The baby's subsequent clinical course was marked by severe respiratory distress, abdominal compartment syndrome, acute renal failure and severe hemodynamic instability. The skin nodules, most likely representing tumor metastasis, were biopsied and the histology results raised suspicion of metastatic rhabdomyosarcoma. After multidisciplinary discussions with the family, the child received palliative care due therapeutic limitations and very poor prognosis. Post-mortem tumor biopsy revealed a highly mitotic tumor of the rhabdomyosarcoma family.

Discussion: In-depth evaluation of fetal hydrops is inevitable and rare, malignant congenital tumors such as neuroblastoma, teratoma or rhabdomyosarcoma are found. Tumor staging includes histology of the placenta, but fetomaternal tumor spreading is uncommon. Oncologic treatment differs markedly depending on the tumor entity and may be impossible due to complications related to fetal hydrops, prematurity and organ dysfunction. Multidisciplinary team approaches are inevitable in rare causes of fetal hydrops.
abdomen confirmed slight organomegaly, normal liver morphology with well visualized biliary tree and vesicle. Over the next days he developed a more pronounced hepatopathy without liver failure. The search for Enterovirus, CMV, PV- B 16 was negative. Repeat maternal serologies showed a profound seroconversion for THPA and VDRL. Upon further questioning she remembered a non-pruritic bruise-coloured flat rash on her forearm one month prior to delivery compatible with secondary syphilis. His long bone x-rays confirmed metaphyseal osteoporosis i.e. for 10 days was given for confirmed early congenital syphilis.

**Discussion:** The baby showed signs of an early onset sepsis on the one hand. But on the other he definitely presented signs of an antenatal infection. Retrospectively the palmo-plantar lesions with direct hyper-bilirubinemia, thrombopenia and organomegaly are pathognomonic for early congenital syphilis. The lessons learned with this case are that serologic screening in early pregnancy should not defer this differential diagnosis, that congenital syphilis can manifest with curious eruptions indeed and that careful history taking will almost always lead to the proper diagnosis.

**The effect of prematurity on auditory processing during EEG**

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**Background and aims:** Premature birth has an impact on brain maturation that can be measured at term equivalent age (TEA) with neuroimaging techniques. The aim of our study is to determine the neural pathways and processes that are activated in term babies and preterm infants (GA <32 wks) at term after listening to their mother's voice and a stranger's voice with EEG and IMRI techniques. Our secondary aim is to differentiate innate (genetically determined) and acquired (determined by experience) networks. Here we present the results of the EEG analysis and preliminary results of IMRI in normals.

**Methods:** High-density EEG (109-channel) and IMRI (Siemens 3T) recordings were performed for subsequent analysis on newborns while listening to their mother's voice and the voice of an unknown woman. Two groups were tested: premature newborns tested at TEA (GA: 28.7 wks) and full term controls (GA: 40 wks).

**Results:** For preterm and full-babies, the event related potentials results showed significant differences on left temporal electrodes during the first 200 msec when they listened to their mother's voice compared to a stranger's voice (t-test; p < 0.05). The topographic maps showed that the mother voice implies an almost similar map for preterm and full-babies, however the unknown voice seems to be clearly processed only in the preterm group. Preliminary IMRI results will be presented.

**Conclusions:** By showing specific activation in preterm babies at term equivalent age we listened to a known and a stranger voice, our results suggest that the maturation of the auditory network can be influenced by these early ex-utero experiences resulting in an early differentiation between their mother's voice and the voice of a stranger.

**Cortical thickness in preterm infants**

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During the normal perinatal and early postnatal period it is known that the cerebral cortex undergoes substantial reorganisation. Nevertheless, it still remains challenging to answer the question to which extent early change in environment (premature birth) affects the reorganisation of the cerebral cortex and establishment of the adult like cytoarchitecture. In order to first answer the question how premature birth affects the cortical thickness at school age we have analyzed 42 T1 MRI images of prematurely born children aged 6 years. Gestational age at birth within all subjects showed positive correlation with cortical thickness measurements (in areas of bilateral prefrontus, right medial temporal gyrus, right cuneus, left inferior parietal lobule and left parieto-occipital junction). Furthermore, in order to identify the longitudinal changes of the cortical thickness in the children born prematurely we have analyzed longitudinal T1 MRI scans of 5 children acquired at birth (30–34 GW), at term at age 4 years and at 6 years. We have used novel automatic method for the cerebral tissue segmentation, afterwards we have manually detected the CSF in the subarachnoid space. Finally we have computed grey matter surface mesh and measured the cortical thickness between corresponding 40,962 vertices of the pial and cortical/white matter surface using the advanced MRI image processing tools developed at MNI. Mean cortical thickness from birth to school age showed two-fold increase while regional variations of the cortical thickness indicated that the limbic cortex is the first one that thickens while the frontal cortex lacks behind. The measurements of the mean cortical thickness at all three time points showed positive correlation with gestational age at birth. This is the first reported analysis of longitudinal changes of cortical thickness from birth to the school age that might serve as a biomarker of cortical reorganisation during early development and following the preterm birth.

**Intrathecal antibody responses in Mycoplasma pneumoniae encephalitis**

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**Introduction:** We aimed to test for the presence of the rarely analyzed specific intrathecal antibody responses in patients with Mycoplasma pneumoniae encephalitis (MPE) as they may be diagnostic and have an impact on course severity.

**Methods:** Two patients fulfilling the etiological case definition for confirmed MPE [Epidemiol Infect 2010;138:783–800] were enrolled between 11/2010 and 11/2012.
Familial hemiplegic migraine type 2 – a case report

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Case report: 16-year old girl who has suffered from migraine attacks with complex aura since 7 years of age. First hospitalisation for the following sequence of symptoms: paresthesia, headache and vomiting, somnolence, fever, neck-stiffness and left-sided hemiplegia. Complete septic workup (incl. LP) was negative. Imaging (CT/MRI) revealed mild right-sided cerebral edema, while excluding ischemia, thrombosis and mass. EEG showed diffuse unilateral slowing. Recovery was rapid, but partial amnesia of the acute episode and mild focal deficits were still present one month later. Family history was positive for migraine with cataplexy and frequency and duration of attacks was observed. Though she always recovered eventually, focal symptoms took longer to resolve than before and she started to complain about difficulties involving speech, writing and reading. In light of this unexplained and ongoing aggravation we performed a new evaluation (MRI, EEG, neuropsychological testing, ophthalmologic exam) with unremarkable results.

Discussion: Whereas migraine is very common, FHM is rare (prevalence ~1:10000). Diagnosis is clinical, but can be challenging. Imaging, laboratory and genetic testing are often useful to rule out other etiologies and to confirm a causative mutation. The major subtypes (FHM 1–3) are related to channelopathies. Inheritance is autosomal-dominant. There is little evidence to support one pharmacologic treatment as opposed to another, especially for prophylaxis; use of triptans, ergotamine and beta-blockers is considered as initial mechanistic basis of metabolic programming. Poor fetal growth, also known as intrauterine growth restriction (IUGR), is a worldwide health concern. IUGR is commonly associated with both an increased risk in perinatal mortality and a higher prevalence of developing chronic metabolic diseases later in life. Obesity, type 2 diabetes or metabolic syndrome could result from noxious "metabolic programming." In order to better understand early alterations involved in metabolic programming, we modeled IUGR rat pups through either prenatal exposure to synthetic glucocorticoid (dams infused with dexamethasone 100 μg/kg/day, DEX) or prenat al undernutrition (dams feeding restricted to 30% of ad libitum intake, UN). Physiological (glucose and insulin tolerance), morphometric (automated tissue image analysis) and transcriptomic (quantitative PCR) approaches were combined during early life of these IUGR pups with a special focus on their endocrine pancreas and adipose tissue development. In conclusion, these results show that before any catch-up growth, IUGR rats present early physiologic, morphologic and transcriptomic defects, which can be considered as initial mechanistic basis of metabolic programming.
Protective effects of maternal nutritional supplementation with lactoferrin on growth and hippocampal metabolism in dexamethasone-induced IUGR rats

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Background: Bovine lactoferrin (bLf) is a milk glycoprotein considered as a pleiotropic functional nutrient recently shown to improve neonatal immunity. Impact of maternal supplementation with bLf on intrauterine growth restriction (IUGR)-induced sequelae, such as inadequate growth and altered cerebral development, remains unknown.

Methods: IUGR was induced through maternal dexamethasone infusion (100 μg/kg during last gestational week) in Sprague-Dawley rats. Maternal supplementation with bLf (0.85% in food pellet) was provided during both gestation and lactation. Body weight of dams and pups were monitored weekly. At postnatal day (PND) 7, pup hippocampal metabolism and gene expression were studied using in vivo 1H nuclear magnetic resonance (NMR) spectroscopy, quantitative PCR and microarray.

Results: Maternal bLf supplementation did not change gestational weight but increased the birth body weight (b.w.) of control pups (4%) with no effect on the IUGR pups. Intrauterine bLf supplementation allowed IUGR pups to recover a normalized weight at PND21 (weaning). Hippocampal levels of metabolites (GABA, glutamate, N-acetylaspartate, N-acetylaspartylglutamate) and transcripts (BDNF, DMT-1 and glutamate receptors) were altered in IUGR pups but normalized with maternal bLf supplementation.

Conclusion: Our data suggest that maternal bLf supplementation could be viewed as a beneficial nutritional intervention able to revert some of the IUGR-induced sequelae.

Asymptomatic dural venous sinus thrombosis after skull fracture

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Introduction: Dural venous sinus thrombosis (DVST) is an uncommon finding in children head trauma. We report a case of asymptomatic marginal thrombosis of the sagittal sinus associated with a frontal bone fracture in a 3 year old child.

Case report: A healthy 3 years old boy is admitted for cranio-cerebral trauma after falling from the roof of a camping car. He presents initial sleepiness, one episode of vomiting, but no loss of consciousness. Initial Glasgow coma score is 13/15 (E3, M5, V5). Native CT-scan of the skull shows a non displaced frontal bone fracture crossing the anterior part of the superior sagittal sinus. An angio-CT-scan performed two days later reveals a marginal, non-occlusive thrombosis of the sagittal sinus.

The child receives enoxaparin 14 mg daily (1.2 mg/kg) subcutaneous for one month. Repeated MRI shows a complete radiologic resolution of the thrombosis. Interestingly, two months after the accident, the child presents with a two days history of headache, sunken eyes and facial swelling suggestive of relapse. A new MRI shows no sign of thrombosis or venous edema and the symptoms disappear spontaneously.

Discussion: Radiologic studies in adults show that DVST complicates up to 40% of skull fracture crossing dural sinuses [1]. Although rare after childhood head trauma (only 2% of cases [2]), sinus thrombosis should be excluded in all children with such skull fractures. Anticoagulation to prevent extension is probably beneficial, despite lack of specific clinical trials to support this therapy.

Conclusion: Imaging to exclude DVST should be performed on all children presenting with a skull fracture crossing a cranial venous sinus, because specific treatment can be indicated.

Limp, seizures and behavioural change in a young girl: autoimmune encephalitis?

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Case report: 19-months old girl was hospitalised for right motor deficit without fever. Other symptoms were crying, sleeplessness, language, behaviour and feeding disturbances, seizures, then agitation, dyskinesias, and finally loss of walking. Cerebral MRI was normal. EEG showed asymmetric slow waves. CSF lymphocytic pleocytosis (13g/l) were found. In absence of infectious and metabolic aetiologies, autoimmunity was evoked and CSF antibodies against N-Méthyl D-Aspartate receptor (aNMDAR) were later confirmed by neurologic and ophthalmologic consults. One month after the trauma, double images are abating but still affecting the patient, especially when she is tired.

Discussion: Patients with trochlear palsy mainly complain about binocular double vision. Also, blurred vision, vertigo and disturbance of gait can occur. Constrained head posture is a frequent clinical finding. Pointer test and Bielschowsky phenomenon are easy and reliable

Limp, seizures and behavioural change in a young girl: autoimmune encephalitis?

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Introduction: Examination of the cranial nerves is a basic part of the evaluation after head injury. Due to unique features like a long intracranial course and emergence from the dorsal aspect of the brain stem, the 4th cranial nerve (trochlear) is especially susceptible to damage resulting from head trauma. As one of three oculomotor cranial nerves, the trochlear nerve innervates the superior oblique muscle and is responsible for the downward and inward rotation of the eye.

Case report: A 13 year old girl was admitted to our emergency department four hours after she fell from her horse. Her head protection had been broken due to the fall. She did not lose consciousness, had no amnesia, headache or nausea but complained of blurred vision. First clinical examination revealed a slight tenderness over both zygomatic bones and the upper cervical spine only. In particular, no abnormalities of eye position or movement were documented during primary assessment. Cranial CT revealed no intracranial haemorrhage, X-ray of the cervical spine was normal. The following day, the girl could specify that diplopic images were obliquely following the right eye. The pointer test and Bielschowsky phenomenon were easy and reliable

Discussion: NMDAR are glycine and glutamine receptors, highly expressed in GABAergic neurons. ANMDAR induce reversible internalisation of the receptors, but complete pathophysiology of the disease is still partially understood. ANMDAR are found in autoimmune encephalitis. First description was in 2007, in women with ovarian teratoma. Several hundred cases have since been reported. It was found also in children and adolescents, often without tumour, with girl predominance. Main expression is neuropsychiatric: abnormal behaviour, memory loss, hallucinations, dyskinesia, dysautonomia, seizures, decreasing consciousness. EEG is usually slowed and disorganised. Moderate pleocytosis in CSF and hyperproteinorachy are common, sometimes with oligoclonal bands. MRI is normal in 50% of cases. Ovarian or testicular tumour, neuroblastoma and lymphoma must be ruled out. Improvement takes several months. Recovery or persisting moderate sequelae occur in 75% of cases, with less than 5% mortality. First-step treatment includes steroid bolus and IVlg, followed by rituximab and/or cyclophosphamide and finally plasma exchanges. Others immunomodulators may be used, such as methotrexate, micophenolate mofetil, or azathioprine.

Conclusion: When acute neuropsychiatric symptoms occur in children, autoimmune encephalitis must be suspected, even if MRI is normal. Hallmarks are the presence of ANMDAR, which kinetic can be used for follow-up.
diagnostic bed-side tools. Documentation of the squint angle is recommended for follow-up. Traumatic troclear palsy can last up to a year and still regeneration is often incomplete. Therapy consists of optic measures like the use of prism or dimmed foil in the lower part of glasses, occlusion or, ultimately, surgical correction.

**Conclusion:** Double vision after a traumatic head injury can be temporary. However, when double images persist, troclear nerve palsy should be ruled out by detailed ophthalmologic examination.

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**Riboﬂavin in cyclic vomiting:** efﬁcacy in 3 patients

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**Introduction:** Cyclic Vomiting Syndrome (CVS) is an episodic disorder characterized by recurrent transient nausea and vomiting episodes, considered as a migraine variant in the International Classiﬁcation of Headache Disorders. One of the hypothetic causes of migraine is a deﬁcient mitochondrial energy reserve. Based on this hypothesis, riboﬂavin (or vitamin B2, a cofactor involved in the mitochondrial electron transport chain) has been considered a ﬁrst-intention prophylactic. We present two children with severe recurrent vomiting, refractory to any currently available treatment. Both children improved after riboﬂavin treatment.

**Case reports:**

**Patient 1:** A 13-year-old healthy boy who presented recurrent attacks of retching and loss of appetite, of a duration of 24–36 hours, every two weeks. An extensive imaging and laboratory work-up came back normal. No single event was observed during the 4 months that followed riboﬂavin treatment onset.

**Patient 2:** A 12-year-old girl, known for esophageal narrowing operated early in life, who presented with monthly recurrent vomiting attacks since the age of 10 years, each lasting for 2–4 days. Family history was positive for migraines. A normal esophageal transit excluded recurrence of the narrowing. PHmetry, cerebral imaging, and vestibular function were all normal. No single event was observed during the 4 months that followed riboﬂavin treatment onset.

**Patient 3:** A 4-year-old girl, known for perinatal intraventricular hemorrhage and ventriculo-peritoneal shunting, presented recurrent vomiting attacks lasting for 24–36 hours every 2–3 weeks during 6 months. Family history was positive for migraines. Multiple cerebral CT-scans and a revision of the shunting system did not bring any improvement. She was treated with riboﬂavin for 12 months, and has not presented any event since, after a follow-up of 5 years.

**Conclusion:** In our patients, Riboflavin is a safe and effective prophylactic treatment for children and adolescents with CVS. Larger-scale prospective studies are necessary to conﬁrm our observations.

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**Severe neurological complications of sinusitis in 2 children**

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**Introduction:** Neurological complications of sinusitis are rare in children. We present two boys, with a previous history of sinusitis, who presented with severe neurological symptoms, revealing underlying intracranial suppurative complications.

**Case description:**

**Patient 1:** A 9-year-old boy, who presented with a focal seizure, left hemiparesis and a severe frontal syndrome in the context of high fever. The C-reactive protein was 200 mg/l. The MRI revealed maxillary and ethmoidal sinusitis, frontal parenchymal abscesses and frontal subdural empyema. Intravenous antibiotics and multiple sinus and intracranial abscess drainage allowed complete recovery. Patient 1 presented with a focal seizure and meningeal signs. The initial laboratory tests revealed hypoglycorrhachia, hyperproteinorachia and the cell recount was 650/mm³ leucocytes with 93% of neutrophils. No germe was detected on GCS Gram stain. The level of blood procollactin was 103 μg/l and the C-reactive protein was 190 mg/l. The MRI revealed pansinusitis complicated by frontal and parietal subdural collections, sagittal venous thrombosis and an intra-orbital collection. Surgical drainage and intracranial antibiotics allowing a waking up and progressive recovery. Both patients were previously in good health, and had a history of sinusitis treated by oral antibiotics since several days.

**Discussion:** Although rare, neurological complications of sinusitis must be feared in children, even in those who are immunocompetent. An early diagnosis is essential to start adequate therapeutic measures and improve prognosis, and a high index of suspicion is required.

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**Headache and obesity without papilldemma:** lumbar puncture or not?

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**Introduction:** Children with severe headaches are often sent for further evaluation to emergency departments. Should a lumbar puncture be performed in the presence of a normal neurological examination and neuroradiological examination? We present hereafter a case, where the lumbar puncture led to the diagnosis of idiopathic intracranial hypertension without papilledema (IIH/WOP).

**Case:** A 13 year old girl presented with severe headache lasting for seven days that would wake her in the night. She was not febrile and did not complain of nausea or vomiting. Apart from obesity with a body mass index of 29.8 kg/m² the pediatric and neurological examination were completely normal, including vision and visual fields. Cranial MRI did not reveal any pathological findings. Idiopathic intracranial hypertension (IIH) was suspected due to the obesity. A lumbar puncture was performed in sedation and showed an opening pressure of 53 cm H2O. Cytology and chemical analysis were normal.

The patient was treated with 250 mg acetazolamide twice daily and headache improved signiﬁcantly. Two weeks later she presented again with severe headache. Lumbar puncture was repeated in sedation. The opening pressure was found to be 47 cm H2O. Acetazolamide dosis was raised to 500 mg twice daily. Due to secondary electrolyte disturbances leading to a respiratory compensated metabolic acidosis, she was supplemented with sodiumhydrogenbicarbonate. Treatment with acetazolamide ceased and a gradual decrease in BMI was observed. At month 5 of the treatment she had only a few headaches per month and successfully tapered off. Currently she complains of slight frontal headache which does not influence her daily activities.

**Conclusion:** Obesity in adolescent girls is a risk factor for idiopathic intracranial hypertension. Cerebrospinal Fluid (CSF) production is increased by performing a lumbar puncture. This procedure is diagnostic as well as therapeutic. According to the literature a lumbar puncture in patients with severe intractable headache, normal neurological and neuroradiological examination should be considered/performed when BMI is around 30 in order not to miss the diagnosis of IIH/WOP and its therapeutic consequences.

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**Metabolic and Genetic Research into Early Onset Epileptic Encephalopathies**

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**Introduction:** Early onset epileptic encephalopathies represent a heterogeneous group of rare disorders that constitute a major diagnostic and therapeutic challenge and the majority of patients still remain without a clear diagnosis. Recent research has unravelled a growing number of inborn errors of metabolism but also sporadic de novo mutations in neuronal genes as the underlying causes of epileptic encephalopathies. Due to the rarity of the single disease entities knowledge on clinical phenotypes is very limited.

**Methods:** The division of Child neurology at the Kinderspital Zurich now has access to the EEG archive of 120 children, which cares for 40 to 50 cases with early onset epileptic encephalopathy of unclear etiology. For this cohort the EEG archive holds detailed long-term records of seizure semiology and ictal EEGs. Inclusion criteria: onset of epilepsy before age 4 years, difficult to treat seizures for more than 6 months, normal microarray and normal sequencing of the SCN1A gene. Exclusion criteria: morphological changes involving brain cortex. Previous metabolic and genetic testing will be compiled in a newly established database. According to the research protocol, patients will undergo a defined neuro-metabolic and genetic work-up. Metabolic analysis will include screening for a panel of known biomarkers in order to identify inborn errors of metabolism affecting CNS metabolism as well as determination of vitamin compounds in CSF to identify new disease entities, affecting cofactor metabolism. Those with inconclusive biochemical work-up will undergo whole exome sequencing.

**Conclusion:** Beyond the detection of rare defects in metabolic pathways or in one of the several genes known to date, this project has the potential to identify new inborn errors as well as new candidate genes causing early onset epileptic encephalopathy. For both scenarios the EEG archive will allow detailed clinical characterization of the individual patient. In case of novel monogenetic disorders stored body fluids will allow a targeted search for new biomarkers.
Anterior spinal artery syndrome – a rare but important differential diagnosis in children with acute flaccid paraparesis

Introduction: Hospital, Berne, Switzerland
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Case report: We report on a 2 4/12 year old boy presenting in emergency for acute lower extremity weakness and bladder dysfunction without preceding trauma or infection. On neurological examination he showed flaccid paraparesis, extinct tendon reflexes, sensory level and loss of abdominal reflex below level Th10. Diagnostic workup including spinal MRI showed edematous medullary conus with signal alteration in T2 weighted images and diffusion restriction. There was a slight increase of antiphospholipid antibodies, but no further risk factors for inflammatory or thromboembolic events. Platelet antiaggregation with acetylsalicylic acid was started. Due to differential diagnosis, an intensive neuropediatric rehabilitation program was started. Three weeks after the acute onset, nerve conductions of peroneal and tibial nerve showed no motor action potential at high distal latencies, pointing towards an ischemic event of anterior horn. Six weeks after the acute event T2 weighted MRI showed localized hyperintensity of anterior horns in the medullary conus (“snake-bite lesions”), a finding consistent with ischemia in the vascular territory of the anterior spinal artery. Two months after initial manifestation the boy showed minimal improvements with persistent paraparesis and bladder dysfunction and was transferred to a pediatric rehabilitation centre for long term rehabilitation.

Conclusion: Although rare, anterior spinal artery syndrome is an important differential diagnosis in children with acute flaccid paraparesis with a sensory level and bladder dysfunction. Early neuroimaging is important, but frequently follow up imaging is needed to confirm ischemic etiology. Outcome of spinal cord ischemia is prognostically not as good as for transverse myelitis.

Optic neuritis in a 5 yr old boy: neuromyelitis optica or acute disseminated encephalomyelitis?

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Introduction: Optic neuritis (ON) is rare in paediatric patients. Differential diagnoses include various infectious and autoimmune disorders. Demyelinating ON can present as isolated ON or can be associated with acute disseminated encephalomyelitis (ADEM). Multiple sclerosis (MS) or neuromyelitis optica (NMO). NMO-diagnosis is based on 2 major criteria, ON and myelitis of ≥3 consecutive circumscribed symptoms of NMO or MS, but the prominent manifestation of ADEM. Specific antibodies against neuronal structures may help to differ between these demyelinating disorders.

Case report: A 5 yr old Tamil boy presented twice with prolonged seizures during a febrile respiratory infection between 6 days. EEG demonstrated encephalopathic changes, CSF revealed slight pleocytosis (31/µl), cranial MRI was normal. Comprehensive investigations did not reveal an infectious agent. After a period of 3 weeks with fever and fatigue he developed painful eye movements and loss of vision within 2 days, demonstrating ON in the right eye and disc swelling in the left optic nerve. Additionally, he showed symmetrical hyperreflexia and bilateral Babinski signs. Second cranial MRI revealed high signal abnormality of both optic nerves, especially on the right, as well as a small, subcortical white matter lesion. Spinal imaging with T2 hyperintensity over 3 vertebral segments was consistent with longitudinal extensive transverse myelitis, fulfilling criteria for NMO despite negative NMO-antibodies, but high titre of ADEM-antibodies, and negative oligoclonal bands in CSF. After high-dose steroid treatment, the visual acuity improved from <10% to 100% within 4 weeks.

Conclusion: ON in children should prompt further diagnostic steps for demyelinating causes, including spinal imaging and analysis of specific antibodies. Our patient demonstrates the whole spectrum of so called “acquired demyelinating syndromes” with encephalopathy and seizures as well as confirmed diagnosis of NMO, whereas specific antibodies point more to ADEM. Specific neuronal antibodies don’t allow definite diagnosis of demyelinating diseases in every patient, but may play an important role for therapeutic decisions in future, especially indication for long-term-immunosuppression.

The relevance of neuropsychological evaluation in the follow-up of children with cerebral palsy

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Introduction: The vast majority of children with cerebral palsy (CP) exhibit not only motor deficits but also mild to moderate cognitive deficits, that may cause severe learning difficulties. In particular, children with CP are at risk of visual-spatial and constructional processing skills impairments, weaknesses in attention and executive functioning (planning, anticipatory skills, inhibitory control), that contrast with preserved competencies in other domains (verbal reasoning and knowledge, motivational and social skills).

Methods: A detailed neuropsychological evaluation was conducted in 16 children with CP including 9 hemiplegic and 7 diplegic children (age range 6 to 12 years). A battery of standardized tests was performed to confirm ischemic etiology. Outcome of spinal cord ischemia is prognostically not as good as for transverse myelitis.

Results: Results confirm that despite different lesion loci and various form of motor disability, most of the children suffer from with visual-spatial, attention skills and executive function deficits that underlie specific learning disability.

Conclusion: An integrated medical and pedagogical reflection has to be implemented to elaborate individualized training and educational programs, in order to make sure that the integration of children with CP is a successful. The main obstacles to ensure that these children can later accomplish satisfactory vocational training curriculum.

Recent transient ischemic attacks in a child associated with post-varicella vasulopathy

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Introduction: Most often children with arterial ischemic strokes or transient ischemic attacks have multiple risk factors such as infection, trauma, vasculopathy, coagulation disorders, dehydration or metabolic diseases. We present a case with recurrent transient ischemic attacks (TIA) associated with a post-varicella arteriopathy and a MTHFR homozygote mutation 677TT as a risk factor.

Casereport: A 20 month old boy had a two week history of transient loss of balance and unsteady gait. Just 24 hours prior to presentation he had 4 short lived (3–5 minutes) episodes of right facial palsy. A common cold without fever 10 days ago and a primary uncomplicated varicella (VZV) infection 3 months earlier are worth mentioning from the past medical history. During emergency consultation a sudden onset of a central facial palsy accompanied by a right-sided ptosis and hemiparesis could be observed. The signs completely disappeared after 5 minutes. Brain MRI showed an acute ischemia of the left globus pallidus and stenoses of multiple intracranial vessels. To prevent additional ischemic episodes anticoagulation with acetylsalicylic acid was started and the patient was transferred to a pediatric tertiary center with a stroke unit. Further in patient work-up showed increased velocities on neurovascular ultrasound corresponding with the MRI symptoms of NMO or MS. Vascular VZV was suspected and a treatment with high dose acyclovir for two weeks. As a further risk factor for thromboembolic events the boy was found to have a MTHFR homozygote mutation 677TT.

Conclusion: Post varicella arteriopathy is a rare but well described entity. There is little evidence regarding treatment with antivirals and corticosteroids in children. With the homocytog MTHFR mutation and the recent common cold this case has additional risk factors for thromboembolic events. TIAs are a rare finding in children but should be considered in the differential diagnosis of paroxysmal neurological symptoms. Early diagnosis is important to optimise treatment and the neurological outcome.
Influenza-associated mild encephalopathy with a reversible splenial lesion: a case report
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Introduction: Influenza-associated mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a relatively rare clinical entity in children. Initially described in Japanese children, this clinical-radiological syndrome is characterised by an encephalopathy at the onset, minimal to absent pleocytosis, prompt and complete clinical recovery with reversible involvement of the splenium of the corpus callosum.

Case report: We report a 3-year-old Caucasian girl known for a global developmental delay and antecedent convulsions but not on antiepileptic treatment, who presented with fever and status epilepticus in the context of a viral infection confirmed to be Influenza B. Brain MRI on day 1 showed a hyperintense lesion in the splenium of the corpus callosum on diffusion weighted imaging and T2 FLAIR without associated contrast enhancement, EEG showed evidence of severe diffuse non reactive encephalopathy with no epileptiform discharges. She was treated with antiviral medication (oseltamivir) for 5 days and recovered completely.

Conclusion: This case illustrates that an isolated reversible splenial lesion in Influenza B encephalopathy could be considered as a good prognostic factor, predicting rapid and complete clinical and radiological resolution.

Post-infectious cerebellar ataxia, Cerebellitis, ADEM or Clinically isolated syndrome (CIS) after varicella virus infection: a matter of terminology?
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Introduction: Post-infectious cerebellar ataxia is a well-known neurological complication, developing immediately after a varicella infection, while post-varicella acute demyelinating encephalomyelitis (ADEM) has rarely been reported in children.

Case report: We present a 4-year-old child who presented with instability of gait associated with a mild dysarthria 4 weeks after a varicella eruption. She had persistent fever, loss of appetite and irritability, without signs of altered consciousness or other neurological symptoms. Clinical examination revealed an isolated ataxia. A diagnosis of post-infectious cerebellar ataxia was initially considered, however, due to some atypical features (unusual long interval after the varicella infection, persistent fever), a cerebral MRI as well as a CSF study were performed. MRI revealed the presence of multiple areas of demyelination located mainly in the thalamus, the basal ganglia and in the cerebellum, suggesting a diagnosis of ADEM (Acute demyelinating encephalomyelitis). The cerebrospinal fluid analysis showed a discrete pleocytosis without evidence of oligoclonal bands. She was treated with intravenous corticosteroids followed by oral prednisolone with a rapidly favorable evolution. At the follow-up examination after 1 month, she was asymptomatic with a normal neurological examination.

Discussion: The relatively late occurrence of ataxia after varicella in our child associated with a prolonged fever is unusual, leading us to perform neuroradiological investigations. This showed radiological features compatible with ADEM. However, our patient had no clinical signs of encephalopathy, an essential criterion for the diagnosis of ADEM as well as cerebellitis. In this context, we finally retained the diagnosis of a clinically isolated syndrome (CIS), which implies a higher risk of recurrent demyelination or evolution towards multiple sclerosis.

Conclusion: A rigorous nosological classification of post-infectious neurological complications is important for a proper clinical and radiological follow-up in view of the different prognostic implications.
Severe hyperkalemia, metabolic acidosis and arterial hypertension – is this Gordon’s Syndrome?

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Background: Pseudohypoaldosteronism type II (PHAII), also known as Gordon’s syndrome, is a rare (mainly) autosomal-dominant disease characterized by hypertension with hyperkalemia despite normal renal glomerular function, and metabolic acidosis, suppressed plasma renin activity and inappropriately low or normal aldosterone. There is genetic heterogeneity with mutations in at least 5 loci (PHAII A-E) incl. WNK1. Wild-type WNK1 enhances, whereas WNK4 inhibits the thiazide-sensitive Na-Cl co-transporter in the distal tubule; mutations lead to gain of function and increased activity of the Na-Cl transporter with reduced potassium excretion by inhibiting ROMK activity in the renal tubule whereas urinary calcium excretion is increased. Life-long therapy with thiazide is effective.

Case Report: A 14-year-old boy was referred for occasionally detected arterial hypertension (128/56 mm Hg, >95th percentile). Clinical examination was normal. Blood tests revealed hyper-kalemia (6.8 mmol/l), metabolic hyperchloremic acidosis (pH 7.32, chloride 114 mmol/l, bicarbonate 17 mmol/l, BE –9 mmol/l), normal renal function (creatinine 56 µmol/l) and low renin and aldosterone levels. Urinalysis showed normal calciumuria. Renal sonography and echocardiography were normal. Ambulatory 24-hour blood pressure measurements revealed elevated daytime pressures (mean 131/70 mm Hg) with normal dipping at night. Hydrochlorothiazide (1 mg/kg body weight = 50 mg) quickly normalized blood pressure, potassium and metabolic acidosis. Genetic testing revealed a previously unknown mutation in WNK1 (NM_001262.11 (A179G) c.538A>G) confirmed by our clinical diagnosis. One uncle has arterial hypertension too. The father has been on a beta-blocker since two years; eight years ago, he had kidney stones. Genetic analysis of the father is pending.

Conclusion: The hallmark of Gordon's syndrome (PHAII) is hypertension without proteinuria in the presence of normal glomerular renal function and low renin and aldosterone levels. These features are consistent with the mirror image (“Spiegelbild”) of Gitelman's syndrome with loss-of-function of the NaCl co-transporter.

Tumor-associated FGF-23 induced hypophosphatemic rickets in an eight year old boy

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Introduction: Tumor-associated Fibroblast Growth Factor 23 (FGF-23) induced hypophosphatemic osteomalacia has primarily been described in adults. On very rare occasions this entity may also be the cause of renal phosphate wasting and rickets in children, resulting from local production of phosphatases by various benign and malignant mesenchymal tumors.

Case Report: An eight year old boy was investigated for suspected unilateral painless limping. Radiographic evaluation showed a large and polylobulated cystic lesion in the left iliac bone and acetabulum. Further typical clinical signs of rickets and the respective radiographic and laboratory signs including severe renal phosphate wasting were detected. Biopsy of the iliac lesion suggested a primary solitary bone cyst overlaid by a secondary solid aneurysmatic bone cyst. Laboratory findings, i.e. hypophosphatemia, renal tubular phosphate wasting, normal parathormone and normal calcitriol levels were not compatible with common forms of rickets in childhood. Tumor associated rickets was therefore suspected and investigated with various methods, including PET-Scan and FGF-23 measurement in plasma. A causal lesion other than the iliac tumor or clearly abnormal FGF-23 could not be found. A complete curettage and stabilization of the acetabulum cyst was performed and local FGF-23 production was finally proven by immunohistochemistry in solid portions of the cyst. After surgery, tubular phosphate absorption normalized immediately and clinical and radiological signs of rickets quickly resolved without any further need for substitution or other interventions.

Discussion and Conclusion: Tumor-associated rickets have only rarely been described in children. Nevertheless this diagnosis has to be considered in pediatric patients who present with acquired hypophosphatemic rickets beyond infancy.

A paediatric case of lipoprotein glomerulopathy

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Introduction: Lipoprotein glomerulopathy is a rare cause of nephrotic syndrome and renal failure in Asian patients. Few paediatric and/or European cases are described.

Case report: A 14-year-old boy was referred for asymptomatic hypertension (158/102 mm Hg) detected during mass screening at school. Retrospectively, he had swollen ankles and proteinuria for O.U.L.3, a center for children. Life-long therapy with thiazide was ineffective. Clinical examination was normal except bilateral ankle oedema. Laboratory evaluation revealed nephrotic (serum albumin: 27 g/l, total cholesterol: 9.5 mmol/l, proteinuria: 596 g/mol creatinine) and nephritic (microhematuria; mildly raised plasma creatinine: 71 µmol/l) signs. Hepatitis B and C were excluded (HBs-antigen and hepatitis C PCR negative), auto-antibodies (ANA, ANCA, anti-ds-DNA, Anti-PR3, Anti-MPO) were negative. Renal biopsy showed glomerular capillary dilatation by the onset lipoprotein glomerulopathy. Analysis of apolipoprotein E revealed E3/E3 genotype. Echocardiography showed mild left-ventricular hypertrophy. Symptomatic therapy with ACE-inhibitor (Enalapril: 1 x 10 mg/d) and lipid-lowering agent (Atorvastatin: 1 x 20 mg/d) was started. Family history revealed a Swiss-Asian background: the Balinese father was healthy (normal blood pressure and urine) whereas his paternal grandfather had undergone kidney transplantation for unknown reasons.

Pathophysiology: Lipoprotein glomerulopathy is inherited as an autosomal dominant trait with complete penetrance and phenotypic variability ranging from mild proteinuria to end-stage renal failure in young adulthood with recurrence after renal transplantation. Aetiology is uncertain, but elevated concentrations of apolipoprotein E with E3/E3 genotype play a crucial role. Most patients are Asian, mainly Japanese adults. There is no causal treatment and no role for immunosuppression.

Conclusions: Significant proteinuria and hypertension can be asymptomatic in children and adolescents. Precise examination and history taking are crucial. Global migration expands the spectrum of diseases. Treatment of lipoprotein glomerulopathy is symptomatic with ACE-inhibitor and statin.

Fatal cerebral thrombotic macroangiopathy in hemolytic uremic syndrome

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Introduction: The hemolytic uremic syndrome (HUS) is clinically characterized by the triad of hemolytic anemia, thrombocytopenia and renal failure. In >90% of cases, the disease is triggered by an infection with Shiga toxin–producing Escherichia coli (STEC) harboring specific Shiga toxin and often presents with prodromal bloody diarrhea (STEC-HUS). Neurological involvement may occur during the acute phase of the disease and is associated with high morbidity and mortality.

Methods: Description of a STEC-HUS case with unusually severe cerebral complications.

Case presentation: In a 3½ year old boy the diagnosis of HUS was made based on bloody diarrhea and the classical HUS triad (hemoglobin 86 g/l, LDH 5055 UI, platelets 9 G/l, creatinine 125 µmol/l). Urinalysis showed pathologically increased proteinuria and hematuria. Blood pressure was within the normal range. During the first two days anemia and renal failure worsened despite adequate hydration; however, blood transfusions or renal replacement therapy were not needed. On day three, suddenly, dysphasia was observed. A cerebral MRI scan with angiography showed normal results and clinically the symptoms of dysphasia disappeared. On day four red blood cell transfusion was needed (hemoglobin 40 g/l) and again, the boy developed dysphasia and agitation with eye deviation to the left. The EEG indicated slowed general activity without epileptogenic potentials. At this time, cerebral imaging studies (including MR scan, MR-angiography and transcranial Doppler) showed signs of cerebral complications. On day five, headache and speech disorders developed and the patient was referred to our neurology unit. Computed tomography of the brain showed a left-sided parieto-occipital hemorrhage. A complete curettage and stabilization of the acetabulum cyst were performed and local FGF-23 production was finally proven by immunohistochemistry in solid portions of the cyst. After surgery, tubular phosphate absorption normalized immediately and clinical and radiological signs of rickets quickly resolved without any further need for substitution or other interventions.

Discussion and Conclusion: Tumor-associated rickets have only rarely been described in children. Nevertheless this diagnosis has to be considered in pediatric patients who present with acquired hypophosphatemic rickets beyond infancy.

Fatal cerebral thrombotic macroangiopathy in hemolytic uremic syndrome

Conclusions: HUS is characterized by a systemic microangiopathy, but rarely, thrombotic vasculopathy of large vessels with severe neurological involvement may occur. Cerebral complications are associated with high morbidity and mortality. In a Swiss survey mortality of STEC-HUS was 4% and always associated with severe cerebral complications (Eur J Pediatr 2010;169:591–8).
Severe Hypernatremia associated with Rhabdomyolysis in a 3.5 year old girl
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Introduction: Severe hypernatremia (Plasma Sodium >190 mmol/l) is rare in children and is associated with high morbidity and even mortality. Clinical symptoms encompass behavioural disturbances (e.g. agitation), impaired consciousness and convulsions. Rhabdomyolysis has been reported in a few patients. We review the clinical and laboratory features in a disabled patient with severe hypernatremia associated with rhabdomyolysis.

Case report: A 3.5 year old girl with known mosaic trisomy 14 presented in the emergency department with an increasingly apathetic state. She had suffered from diarrhoea since one week, fever or vomiting were absent. Because of failure to thrive as part of her underlying disease, she was fed via gastrostomy PEG-button with a commercial liquid food. Regular daily intake included 300 ml of liquid free water (total intake of 1000 ml/day). Nutrition was not changed during the illness. Clinical examination showed weight of 10.2 kg, mild dehydration and cold periphery. The girl was less active as usual but could interact with the parents. Laboratory tests revealed severe hypernatremia (195 mmol/l) and hyperchloremia (164 mmol/l), low bicarbonate (17 mmol/l) and potassium (3.2 mmol/l), and mildly elevated plasma creatinine (43 mmol/l). Urinalysis showed sodium of 71 mmol/l and specific gravity of 1.013. Stool analysis was positive for Norovirus infection. Parenteral rehydration with isotonic NaCl 0.9% (500 ml) was followed by maintenance fluid (1000 ml/day) with isotonic NaCl-free water. As part of the evaluation blood count and LDH were also measured, showing thrombocytopenia (43 G/l) and elevated LDH (2098 U/l) prompting measurement of CK (65792 U/l) revealing rhabdomyolysis. Renal function remained normal; urine dipstix showed 3+ myo-/hemo-globin. Without any specific therapy, blood and urinary values normalized within 1 week.

Conclusion and summary: Severe hypernatremia in children is rare. Patients at risk include breast-fed newborns with dehydration and jaundice, infants with severe gastroenteritis and mentally retarded children fed via gastrostomy. The combination of Noro-virus gastroenteritis and feeding via PEG-button might have contributed to the severe hypernatremia in this patient. Parenteral isotonic rehydration and free water intake enabled a slow and safe normalization of all parameters. Rhabdomyolysis is a rare, even fatal complication of hypernatremia.

Successful treatment of neonatal atypical haemolytic uraemic syndrome with eculizumab
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Introduction: Haemolytic uraemic syndrome (HUS), defined by the triad of microangiopathic hemolytic anemia, thrombocytopenia and renal impairment, is uncommon in children. We report the case of a 18-days-old girl, diagnosed with atypical haemolytic uraemic syndrome (aHUS) revealed by neonatal seizures.

Case Report: A previously healthy 18-days-old baby presented with repeated episodes of clonias of the left arm and deviation of the right eye to the left of 3 to 5 minutes duration. Four days earlier she had frequent watery stools and vomiting without fever and was diagnosed with gastroenteritis. She had an extensive workup including blood, cerebrospinal fluid and stool analysis, and was started on aminophylline, atropine, atenolol and phenobarbital. Cerebral MRI performed 24h after admission showed anemia (120 g/l) with schistocytes, thrombopenia (78 G/l) and renal insufficiency with a creatinine (Cr) value of 102 µmol/l, consistent with HUS. Complement C3 and C4 values were normal. ADAMTS 13 deficiency and an inborn error of cobalamin pathway were excluded.

Shiga-toxin-1 was not found in the stools by PCR and blood IgM and IgG against E.Coli O157 were negative. There was no deficiency in H and I antigens, and negative ADAMTS 13 deficiency and an inborn error of cobalamin pathway were excluded. Cerebral MRI performed 24h after admission showed restricted diffusion in the periventricular region, corpus callosum, claustrum and optic radiations associated with multiple periventricular white matter ischemic-haemorrhagic lesions. Her hemoglobin was 55 g/L and she received 2 transfusions of packed erythrocytes. Platelet count decreased to 30 G/l. She was started on a complement C5 monoclonal antibody (eculizumab) on the second day. Soon after, her Cr improved and the output returned to normal, she did not require dialysis. She improved and did not present any convulsion. Her clinical exam as well as her blood tests were normal with resolution of anemia after 28 days and thrombocytopenia after

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Ashensta and pallor in children and adolescents: think to renal insufficiency

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Introduction: Nephromphasia (NP) is a recessive autosomal tubulo-intestinal nephropathy that belongs to the family of ciliopathies. NP/PH is one of the most frequent genetic disorders responsible for end-stage renal disease (ESRD) leading to transplantation during childhood. Diagnosis is confirmed by genetic analysis. Extra-renal anomalies may be present in 10–15%. ESRD occurs before 5 years (infantile form) or around 13 years (juvenile form). We report here 2 patients referred for anemia, tiredness and pallor and diagnosed with NPH.

Case 1: A 6 y old boy was referred for anemia and pallor since 2 months (M) and eunuresis since 6 M. In his charts, the renal values were noted in the physical exam. Blood examination revealed normal blood pressure (BP) (112/56) and a systolic heart murmur. Blood and urine analyses showed a severe anaemia (59 g/l) and metabolic acidosis (pH 7.02), bicarbonates (BIC) 12 mmol/l and BE (~16 mmol/l), renal failure with a Creatinin (Cr) of 450 µmol/l and an estimated glomerular filtration rate (e-GFR) of 8 ml/min/1.73 m², mild proteinuria (prot/Cr 145 g/mol) and no hematuria. Ultrasound (US) showed unilateral hypertension. The girl was referred for a normal tubular basement membrane (TBM) and global glomerulosclerosis compatible with NPH. Ophthalmologic examination was normal.

The child was started on haemodialysis.

Case 2: A 12 y old girl who presented pallor and anemia since 1 M was referred for anaemia (84 g/l) and renal insufficiency (Cr 411 µmol/l). There was no renal disease in the family. Physical exam was normal except for a BMI -3.2 standard deviation and BP (125/85). Laboratory showed normal pH (7.32) and slightly decreased BIC (19.2 mmol/l), high Cystatin C (3.1 mg/l), hypokaliemia (3.1 mmol/l), reduced e-GFR 15 ml/min/1.73m², microscopic hematuria and mild proteinuria (12 mg/100 ml). Renal US showed a loss of corticomedullary differentiation and 9 cortical cysts <5 mm without hepatic involvement. The biopsy described diffuse tubular interstitial lesions with thickened TBM, tubules duplication and distortion compatible with NPH. Ophthalmologic examination was normal. Pre-emptive intra-familial renal transplantation was performed.

Conclusion: ESRD during Childhood may be present with a few and non specific symptoms. Renal biopsy should be considered as a screening test in children and adolescent presented with persistent tiredness, pallor, anemia noteworthy with enuresis.

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High Bone Mineral Density in Obese Adolescents is related to Fat Mass and Serum Leptin Levels
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Introduction: Obesity has been associated with increased bone mass. The mechanisms involved are still poorly understood. This study aimed to explore the relationship between bone mineral density (BMD) and factors known to influence bone formation, in obese and lean adolescents.

Methods: We recruited 24 obese and 25 lean adolescents in a cross-sectional study. Total body BMD (TBBMD) z-scores and body composition were determined using DXA. We measured vitamin D (25-OH-D), glucose, insulin and leptin concentrations. Physical activity (PA) level was quantified using accelerometer.

Results: TBBMD z-score was higher, while 25-OH-D and PA levels were lower in obese compared to lean subjects (TBBMD z-score: 1.06 ± 0.96 vs. 0.26 ± 0.91, p = .004; 25-OH-D: 9.9 ± 6.4 vs. 18.5 ± 7.4 ng/mL, p <.001; PA: 308.3 ± 22.1 vs. 406.8 ± 29.2 count min-1, p = .01). TBBMD z-score was no related with serum 25-OH-D or PA levels (p >.05), but positively with leptin level and fat mass (p <.05).

Conclusion: Despite lower vitamin D and physical activity levels, bone mineral density was higher in obese adolescents, associated to higher leptin levels. Furthermore, obese adolescents have lower vitamin D concentrations than lean controls, probably owing to its distribution in adipose tissue.

Prevalence of small intestinal bacterial overgrowth in pediatric patients under long-term therapy with proton pump inhibitors
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Dr. Denise Herzog, chief physician HFR

Introduction: In up to 26% of adults taking proton pump inhibitors (PPI) for longer than 2 months, glucose-hydrogen breath test (GHBT) was found to be positive. It is not known whether small intestinal bacterial overgrowth (SIBO) occurs as frequently in children with hypochlorhydria due to long term PPI treatment as in adults in the same condition. We therefore tested our patients under long-term IPP for SIBO using GHBT.

Method: Retrospective chart review of 15 patients who underwent GHBT (Glucose 2 g/kg, H2 measurement every 15 minutes x 2h) after at least 2 months of PPI treatment.

Results: The 15 patients (7f) had a median age of 172 months (77–201), a median BMI for age z-score of 0.5 (–1.9 – +4.4) and a median duration of PPI treatment of 4 months (2–15), and had been prescribed PPI for gastro-esophageal reflux disease in six and for non-ulcerous dyspepsia in nine. GHBT was suggestive of SIBO in 6/15 (40%) patients with a median duration of PPI treatment of 6.5 months (3–12). The maximum H2 concentrations were 22–30 ppm after 15 to 60 min after refeeding another endoscopy showed the PPI treatment.

Conclusion: SIBO is a frequent asymptomatic complication of PPI treatment in pediatric patients. SIBO can lead to malabsorption of a wide range of nutrients, and should therefore not be overlooked.

Severe enterocolitis due to cow’s milk protein allergy: a case report
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Cow’s milk protein allergy in children has many ways of presentation and we chose to report a very severe case, very close to dysimmunity disorders in term of colonic reorganization.

A 7 weeks(w). old baby presented for 10 days diarrhea, with 4 episodes of associated bleeding. No particular medical history was detected in the family nor in the 3 years old brother, especially no allergy, and also pregnancy and birth occurred without complication. Breast feeding begun at birth and 2 w ago a hypoallergenic formula was introduced to those described in former studies, but incomplete concordance with Rome III criteria should be confirmed prospectively. Special attention is required in children commencing their disease after the age of 24 months in order to prevent the development of enteroparasias.

Severe enterocolitis due to cow’s milk protein allergy: a case report
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A rare finding: Cholestatic icterus caused by desmoplastic small round cell tumor in an 8 year old girl


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Introduction: Desmoplastic small round cell tumor (DSRCT) is a very rare type of sarcoma with less than 200 cases described in the world literature. It is predominantly seen in young male adults but there are also reports about children and adolescents attempted. The tumor is highly aggressive, it begins and spreads on the peritoneal surfaces (1, 2, 3).

Case Report: An 8 year old girl initially presented with symptoms of viral ENT infection followed by abdominal pain, nausea, episodes of vomiting, and weight loss. She developed an icterus of the sclera associated with pale stool and dark urine. Liver enzyme values were 3–4 times higher than normal. Further laboratory analysis showed total bilirubin 139 µmol/l and conjugated bilirubin 91 µmol/l. Coagulation factors and liver function tests were normal. Abdominal ultrasound showed dilatation of intra-hepatic bile ducts due to bile duct compression by multiple retroperitoneal ganglions as well as at the hepatic hilum. Initial suspicion of EBV infection with positive Monotest revealed all negative. Abdominal CT and MRI showed a solid sub-capsular infiltration of the liver with heterogeneous tissue infiltration in small pelvis and multiple ganglions which expressed signs of hyper-metabolism on PET-SCAN. Biopsy/excision of abdominal mass, ganglions and liver tissue were realised by abdominal laparotomy. Histology confirmed a desmoplastic small round cell tumour EWSR 1+. Management: A neoadjuvant chemotherapy VIDE (vincristine, ifosfamide, doxorubicin and etoposide) was started. Further treatment will be based on hyperthermic perfusion chemotherapy (HIPEC) with complete surgical debulking, followed by abdominal radiation and another cycle of chemotherapy.

Conclusion: Cholestatic icterus in school children remains a rare finding. Viral infection and/or obstruction are the most common causes. Nevertheless an oncologic etiology should be kept in mind. Because of its rarity, treatment of DSRCT is still not standardised. The prognosis is poor with a survival rate of only 15% over 5 years (1, 2, 3).

Liver transplantation as a treatment option in a child with hepatic embryonal sarcoma

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Introduction: Primary liver tumors represent 1–2% of pediatric liver malignancies. Other tumors include hepatocellular carcinoma, hepatic angiosarcoma and embryonal sarcoma (this latter accounting for 13% of pediatric malignant liver tumors). Embryonal sarcoma is a rare aggressive malignancy with low survival rates unless complete, i.e. R0-resection is achieved. If R0-resection is possible, four year survival rates are around 70–83%. There are few reports in the literature describing cystic fibrosis with liver transplantation as a treatment of this pathology.
Cardiac resynchronization therapy after anatomic repair for congenitally corrected transposition of the great arteries

Methods: From 1992 to 2012, 106 patients (median age at surgery, 14 months; range, 2 months to 43 years) with ccTGA had anatomic repair. A retrospective review of pre-operative variables, surgical procedure, and post-operative outcomes was performed. Sixty-two patients had an atrial switch, 42 patients a Rastelli procedure, and 2 had an aortic translocation. Results: Early mortality was 5.7% (n = 6), and there were 3 late deaths during a median follow-up of 32 months (range, 7 days to 72 years). The early deaths were excluded from further analysis. Twelve patients (12%) developed moderate or severe left ventricular dysfunction. Thirty-eight patients (36%) were pacing at latest follow-up. Seventeen patients had resynchronization therapy (6% as an upgrade from a prior dual chamber system (8.5%) and 8 as a primary pacemaker (75%). Factors associated with LV dysfunction were age at repair > 10 years (P < 0.001), weight > 20 kg (P < 0.001), pacemaker implantation (P < 0.001) and severe neo-aortic regurgitation. Eight of nine patients undergoing secondary cardiac resynchronization therapy (upgrade) improved LV function. None of the 8 patients undergoing primary resynchronization developed LV dysfunction.

Conclusion: Late left ventricular dysfunction after anatomic repair of ccTGA is not uncommon, with higher incidence in older patients and those requiring pacing. Early repair, aggressive management of significant neo-aortic regurgitation and cardiac resynchronization therapy in patients requiring a pacemaker could be of value to prevent the development of left ventricular dysfunction.

Early diagnosis of congenital heart disease – did we improve?

Methods: An identical study was performed as 12 years ago with a prospective evaluation of the time of diagnosis of CHD during a 3-year period ending in June 2011. Only patients with newly diagnosed CHD that required either catheter-interventional or surgical therapy were included. Of note that in between the two studies came the nationwide recommendation for neonatal pulse oximetry (POX) screening of all newborns starting in 2006.

Results: A total of 209 patients were included. 41% of these had cyanotic, 59% acyanotic CHD. According to the study criteria, late diagnosis was observed in 21 patients (10%), 6% (5 of 85) of cyanotic and 13% (16 of 124) of acyanotic CHD. The most frequent heart defects with delayed diagnosis were atrial septal defect and coarctation of the aorta (7 and 1 patients, respectively). Delayed diagnosis resulted in one patient dead (undiagnosed interrupted aortic arch). Compared to the historical study in our referral population, the striking finding was that still 10% of all CHD diagnosis was made late. The main difference was that late diagnosis in cyanotic CHD decreased from 10 to 6%, whereas in acyanotic CHD an increase from 10 to 13% was seen. Moreover an increase in fetal diagnosis was not surprisingly seen to currently 26% of all children with relevant CHD included in the study.

Conclusion: After 12 years of referring physician education and introduction of a nationwide POX screening, the rate of late diagnosis of CHD in our referral population remained stable at 10% of all CHD, only the rate of delayed recognition of cyanotic CHD showed a decline.
Surgical repair of truncal valve regurgitation

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Introduction: Truncal valve regurgitation remains a short and long-term risk factor for patients with truncus arteriosus. There is limited data available on techniques and outcomes of truncal valve repair. The aim of this study is to report our experience with truncal valve repair in patients of all ages.

Methods: From 1997 to 2012, 36 patients (13 neonates, 30 children and 3 adults) underwent truncal valve repair for significant regurgitation.

Results: There were 3 early deaths (8%), all of which were in neonates. 22 patients had a quadricuspid, 13 a tricuspid and 1 a bicuspid truncal valve before repair. Valve repair improved regurgitation in 31 of 36 repairs. The median regurgitation decreased from moderate-severe to mild (P <0.001). During a mean follow-up of 38.3 ± 44.9 months (range 1 month – 15 years), there was 1 late death, 16 patients required reoperation on the truncal valve and 1 patient required a second reoperation. Freedom from reoperation was 91.4 ± 4.8% at 1 year, 55.0 ± 10.4% at 5 and 22.9 ± 12.2% at 10 years.

A quadricuspid valve after repair tended to worse freedom from reoperation (P = 0.15), and tricuspidization tended to improve freedom from reoperation (P = 0.19). Neonatal repair (HR 4.1, P = 0.03) and leaflet thinning (HR 22.5, P = 0.002) were independent predictors of reoperation.

Conclusion: Valve repair for truncal valve regurgitation is feasible with good results. Surgical creation of a tricuspid truncal valve seems to provide the best outcomes in this challenging population.


Introduction: Pentalogy of Cantrell is a rare congenital defect which combines five anomalies: a supraumbilical abdominal wall defect, diaphragmatic pericardium, and cardiac defects. Few patients present the complete spectrum of the original pentalogy.

Case description: We report the case of a 9 month-old Tunisian boy referred for Cantrell’s pentalogy. He was born in Tunisia without complication. A pulsatile epigastric mass with massive umbilical hernia was discovered at birth. Echocardiography showed a large ventricular septal defect (VSD) and a left ventricular (LV) diverticulum, with otherwise normal biventricular function. The diverticulum was protruding in the upper part of the umbilical hernia through the defect of the anterior diaphragm and responsible for the pulsatility of this mass. A CT-scan revealed several extracardiac anomalies consisting of a supraumbilical hernia, a lower sternal defect, a deficiency of the anterior diaphragm and diaphragmatic pericardium, and cardiac defects. Few patients present the complete spectrum of the original pentalogy.

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Congenital central hypoventilation syndrome (Undine syndrome) with recurrent hypcapnia and hypoxia is likely to act as endothelial preconditioning

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**Introduction:** Undine syndrome (US) is a rare disease with severely impaired central autonomic control of breathing and dysfunction of the autonomic nervous system. The incidence is estimated to be at 1 of 200,000 livebirths. Due to recurrent hypcapnia and hypoxia we hypothesized that these patients have higher risk for pulmonary arterial hypertension (PHT) and longterm systemic vascular dysfunction. We examined 7 patients with US at baseline and high altitude in regards to pulmonary artery pressure and systemic vascular disease and compared them with 6 age and sex matched subjects.

**Methods:** 7 patients with US (5 female, 2 male, mean age 19 ± 3 y) and 6 age and sex matched healthy controls (3 female, 3 male, mean age 20 ± 2 y) were examined at 550 m and at 3883 m above sea level with echocardiography (to measure pulmonary artery pressure). Vascular function was measured at 550m by flow mediated dilatation with and without oxygen.

**Results:** All US patients had mild to moderate PHT at 550 m above sea level. PHT was more pronounced in males than in females (41 ± 5 mm Hg vs. 27.4 ± 3 mm Hg) while no PHT was found in the controls. All US patients had high normal systemic vascular function while controls had normal systemic vascular function. In 3863 m above sea level all US subjects showed only mild increase in PHT in regards to baseline while controls developed moderate to severe pulmonary hypertension (PHT) at 550 m vs. 55.6 ± 23.4 mm Hg vs. 55.6 ± 23.4 mm Hg.

**Conclusion:** Despite recurrent hypcapnia US patients show high normal vascular function. We speculate endothelial preconditioning (recurrent hypcapnia as stimulus). Until today recurrent hypcapnia was believed to be most harmful for endothelium function properties. 2. Presence of PHT at 550 m above sea level is not significantly aggravated by high altitude in comparison with healthy controls. This underlines the hypothesis of endothelial preconditioning and identifies environmental hypoxia as key trigger for PHT in these patients.

How to determine the gender of rearing in a patient with a rare disorder of sex development?

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**Introduction:** Sex chromosome mosaicism 45,X/46,XY is rare with an estimated incidence of 1.5 per 10'000. The phenotypes are highly heterogenous ranging from Turner syndrome females to normal males with varying degrees of phenotypical abnormalities. In each case the risk of germ cells tumors has to be assessed.

**Case report:** We report the case of a newborn who presented at birth with undefined genitalia. A 2 cm genital tubercule, an unfused urogenital groove with a proximal urethral meatus and unfused labioscrotal folds were noted.

**Results:** The karyotype showed a 45,X/46,XY mosaicism. Pelvic ultrasound revealed an uterus with a vagina. The endoscopic explorations, confirmed on the left an uterus and a streak gonad; on the right side, a fallopian tube with a gonad macroscopically compatible with an ovotestis. Two orifices were identified with a female type of urethra and a vagina. The biopsy of the right gonad was compatible with a testis. Laboratory results confirmed the presence of testicular tissue with an Anti Mullerian Hormone (AMH) of 95 pmol/l (2.9–9.3 for female) and a total testosterone level of 32 ng/dl (20–64 for female).

**Discussion and Conclusion:** The first question was how to determine the gender of rearing. The child has a vagina and an uterus. The laboratory results revealed a testosterone level, which will allow a spontaneous male pubertal onset. However the gonads will have to be removed later, in risk of malignancy of 50%. In accordance with the family’s wish, it was decided to attribute the female gender and postpone the surgical procedure until the child can participate in the decision according to the Swiss national ethical committee guidelines. In conclusion, most 45,X/46,XY cases remain undiagnosed, but the phenotypes of these patients are vast. So treating each patient individually is the most important step in the clinical management.

Shaping Parents: Impact of Contrasting Professional Counseling on Parents’ Decision-making for Children with Disorders of Sex Development

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**Introduction:** Despite the latest recommendations of the The Swiss Advisory Commission on Biomedical Ethics the management of differences (or disorders) of sex development (DSD, intersex) remains complex, especially with respect to parents’ decision for or against early genitoplasty. Many parents tend to delay decision about sex surgery until the child is old enough to provide its own consent. The origin of this readiness to authorize childhood surgery is unclear.

**Aim:** To identify the determinants of parental decisions for or against early sex assignment surgery in DSD children, and in particular to assess the impact of the initial health professional interview.

**Methods:** Analysis of a focus group discussion between a hospital multidisciplinary DSD team and patient/parent representatives identified two broad approaches to counseling information: one medicalized, the other demedicalized. Two illustrative 6 minute counseling videos were produced on this basis: one medicalized, by an endocrinologist, the other demedicalized, by a psychologist. Third-year medical students (n = 89) were randomized to watch either video as prospective parents and report its impact on their decision in a self-administered questionnaire.

**Main outcome measures:** Statistical analysis of questionnaire responses.

**Results:** 38/89 parents’ (43%) chose early surgery for ‘their’ child including 27/41 parents’ (66%) shown the medicalized video vs. 11/48 (23%) shown the demedicalized video (P <0.001). Desired aims for ‘their’ child (normativity vs. autonomy) also differed significantly depending on the counseling approach viewed. Yet parents’ perceived their personal attitudes as the main influence on their decision.

**Conclusions:** Parental decisions for or against early sex assignment surgery for DSD children depend on the health professional counseling received a degree of which neither parents nor professionals appear fully aware. In the current absence of conclusive data for or against early surgery, there is a danger of medicalized or demedicalized parentalism resulting in irreversible and inadequately grounded decisions. Realizing the consensus statement of 2005 and the subsequent call for multidisciplinary management.

Perinatal Management of Familial Osteogenesis Imperfecta (OI) after Twin Pregnancy

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**Introduction:** Osteogenesis imperfecta (OI) is an inherited disease of connective tissue, based on abnormalities in type I collagen synthesis or processing. Until now mutations in ten different genes have been identified which cause OI, characterised by bone fragility and low bone mass. The management of these patients vary great from severe to mild forms. Until the child is old enough to provide its own consent. The origin of this readiness to authorize childhood surgery is unclear.

**Case report:** At 22 weeks of gemini gestation of a 33 year old women with OI type IV with short stature (141cm), prenatal ultrasound raised suspicion of OI in the boy, due to shortened long bones with bowing of femora, but not in the girl. Prenatal diagnosis was refused. Birth by Caesarean section, clinical examination showed typical features of OI in the boy, such as very large fontanel, short stature –2.2 SD, blue sclerae, reduced muscle strength, bent thigh and lax ligaments. The girl had short stature and bluish sclera.

**Diagnostics:** Imaging confirmed clinical diagnosis in the boy with bowed long bones and Wormian bones. The girl showed an almost normal X-ray result. Umbilical cord blood, tissue samples and urine were collected, also a skin biopsy and urine from the mother. Urine-analysis showed a decreased ratio of lysyl-pyridinoline to hydroxylysylpyridinoline in the boy and mother, suggesting OI. Urinary analysis of the girl was normal. Biochemical and molecular results are pending. Hearing and vision were normal.

**Therapy:** Comprehensive therapy including careful handling and physiotherapy was not sufficient to prevent 3 fractures in the boy. Additional signs of bone pain required orthopaedic surgery with intramedullary Previt nails. Intravenous bisphosphonate therapy with Neridronat was started at the age of 7 weeks. Neridronat, a potent inhibitor of bone resorption, has demonstrated positive effects, in severely affected OI infants, on mineralized bone mass and pain.
Conclusion: Immobility due to bone pain or stabilisation, reduced muscle strength and fractures are concomitant risk factors for further decreasing bone mass. Hence intensive physiotherapy, early intravenous administration of bisphosphonate and careful stabilisation of fractures are of utmost importance in these patients. Only an individualised multidisciplinary approach will meet these needs of this condition with widely variable severity and genetic heterogeneity. Diagnosis is usually suspected clinically but must be confirmed by radiological, biochemical and molecular findings.

Neonatal thyrotoxicosis - potentially life-threatening!
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Background: Neonatal Graves’ disease is a rare but potentially life-threatening condition in offspring of mothers with Graves’ disease and elevated TRAB during pregnancy.

Case report: We report on a female term baby of a mother with highly active Graves’ disease during pregnancy. The baby was presented to our emergency department on day 11 with restlessness, diarrhea and insatiable hunger. The clinical examination was remarkable for tachycardia (up to 214/min), tremor, irritability and hyperthermia.

Laboratory analysis revealed a suppressed TSH and largely elevated thyroid hormone levels (fT3 25.4 pmol/l, fT4 >99 pmol/l) with highly positive TRAB, diagnostic for neonatal Graves’ disease. The baby was admitted to the intensive care unit and started on propanolol, carbimazole and potassium iodide (Lugol’s solution). ECG and echocardiography were normal but for tachycardiac sinus rhythm. Surprisingly the thyroid was not enlarged on ultrasound. Upon treatment, the cardiovascular condition of the patient stabilized quickly. The patient could be discharged after 9 days of hospitalisation, and medication could be weaned over the course of 5 weeks. TRAB titers decreased rapidly. The clinical condition, development and weight gain were normal at the age of 11 weeks.

Conclusion: Early diagnosis and treatment of neonatal thyrotoxicosis are important to avoid serious cardiovascular complications. Therefore every neonate of a mother with Graves’ disease needs careful follow up. Early information (before or right after delivery) of the neonatology care team about the maternal condition by the mother / obstetrician / adult endocrinologist is essential. Involvement of pediatric endocrinologists is recommended, as well as a flow chart for the neonatology care team.

Epidemiology of bronchiolitis in Geneva University Hospital: difference between RSV and non-RSV episodes
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Introduction: Bronchiolitis is associated with a high morbidity in early childhood. Our aim was to describe the episodes of bronchiolitis during two consecutive RSV (respiratory syncytial virus) seasons, from 2010 to 2012 and identify the differences between RSV and non-RSV bronchiolitis.

Methods: Medical records of all patients under one year admitted to the Emergency Department (ED) with bronchiolitis were reviewed for epidemiologic, demographic, clinical, laboratory and radiologic characteristics. Patients with chronic diseases were excluded. Differences between the two groups were evaluated using Student’s t-test and the chi-square test, as appropriate.

Results: We analyzed 479 patients (317M: 162F) and a total of 582 episodes of bronchiolitis. Among children who had blood gas analysis (77 episodes), C-reactive protein (50 episodes) and chest radiograph (73 episodes), the RSV positive had higher PcO2 values (5.9 ± 1.1 versus 5.0 ± 1.1); however they did not differ with respect to the levels of C-reactive protein and percentage of abnormal chest radiographic findings.

Conclusions: RSV bronchiolitis affected younger children and their disease severity was worse. Chest X-ray and C-reactive protein should not be done routinely, as already recommended.
Risk factors associated with longer hospital length of stay in patients with bronchiolitis

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Introduction: Rates of hospitalization for bronchiolitis, hospital length of stay (LOS) values and the costs of hospital admissions have been increasing since 1980. Our objective was to identify some factors contributing to longer LOS in patients with bronchiolitis during two respiratory syncytial virus (RSV) seasons, from 2010 to 2012.

Methods: Medical records of all patients 1 year hospitalized for bronchiolitis were reviewed for epidemiologic, demographic, clinical, laboratory and radiologic characteristics. Patients with chronic diseases were excluded. Univariate linear regression and 95% confidence interval were calculated according to standard methods. The factors associated with longer LOS on the univariate analysis were included in the multivariate model.

Results: Of 479 enrolled patients, 154 (32%) were admitted to the ward and 17 (4%) to the intensive care unit (ICU). Among the patients hospitalized in the ward, 11 (7%) had more than one episode of hospitalization. The mean age of admitted infants was 4.4 ± 3.4 months, with a mean LOS of 4.8 ± 3.4 days. Univariate logistic regression in the ward and ICU are showed in table 1. Factors associated with longer LOS in patients hospitalized with bronchiolitis. In multivariate analysis the risk factors that remained significant were length of NGT, young age (<6 months) and length of oxygen therapy as factors that increased LOS in patients hospitalized with bronchiolitis.

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Impact of different breathing protocols on nitrogen multiple-breath washout in children

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Background: Nitrogen multiple-breath washout (N2MBW) is a useful test to assess ventilation inhomogeneity (VI) in cystic fibrosis (CF) patient. Two breathing protocols are currently used for measurement: Free tidal breathing and one liter tidal volume (VT) which is thought to improve comparability of results between subjects and is widely used in adults. The impact of protocols using fixed VT on results in children is unknown. We assessed whether breathing at one liter VT impacts N2MBW indices in school-aged children.

Methods: Fifteen children with CF and 20 healthy children performed six N2MBW tests using a validated setup (Exhalizer D, Eco Medics, Switzerland). Children performed three baseline N2MBW at free tidal breathing and three N2MBW at increased VT with a target of one liter using an incentive. Outcomes were size and variability of lung clearance index (LCI), functional residual capacity (FRC), Scond and Scond.

Results: All 35 children achieved six N2MBW. Mean (SD) VT at free tidal breathing was 0.5 (0.1) L at fixed VT 1.3 (0.2) L. Comparing free tidal breathing with one liter VT protocol, LCI increased on average (95% CI) 2.0 (0.5–3.5) in CF children and 0.9 (0.3–1.6) in healthy children. FRC decreased significantly. No changes were seen in Sacin. Changes of N2MBW indices were heterogeneous with increasing variability within tests and between subjects.

Conclusion: Fixed breathing protocols impact severely on N2MBW indices as shown for the one liter VT protocol in school-aged children. This needs to be considered when comparing results from different groups or performing future studies.

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Decreased breath-by-breath variability of expired CO2 volume in infants with bronchopulmonary dysplasia

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Introduction: Bronchopulmonary dysplasia (BPD) is characterized by structural alterations of lung periphery which affect ventilation-over-perfusion matching and gas exchange capacity. The aim of this study was to examine the breath-by-breath variability of the expired CO2 volume (VeCO2) and to assess its value in describing disturbances of gas exchange in infants with BPD.

Methods: Lung function parameters from 53 healthy preterm infants and 87 infants with moderate or severe BPD were compared. Breath-by-breath-expiratory capnograms (i.e. plot of the expired CO2 fraction vs. expired volume) were obtained by mainstream capnography and the the area under the CO2 curve was used to calculate the VeCO2. The ratio of the VeCO2 over the expiratory volume (VeCO2/Ve) was used as an index of expired CO2 per breath. The relative VeCO2/Ve change, and the domain areas of the two- and three-dimensional embedding plots of VeCO2/Ve with one-breath lag, were calculated.

Results: All indices of interest differed significantly between the two groups. BPD infants had lower relative VeCO2/Ve change (median 2.5 [IQR 1.0 – 3.1] vs. 2.7 [2.5 – 3.3] P = 0.003), and smaller domain areas for both two-dimensional (12.4 [8.1 – 19.2] vs. 17.2 [11.0 – 22.8] P < 0.001) and three-dimensional embedding (24.3 [13.7 – 50.9] vs. 36.8 [21.4 – 59.1]; P < 0.001).

Conclusions: Infants with BPD had significantly lower breath-by-breath variability of expired CO2 volume as compared to their healthy preterm peers. This finding probably reflects the disease-related alterations in V/Q matching and gas exchange capacity.

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Should empyema with or without necrotizing pneumonia in children be managed differently?

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Introduction: Necrotizing pneumonia (NP) is an increasing complication associated with pleural empyema. However, specific risk factors, clinical features and outcome are not well-known. We aimed to compare children presenting with empyema with or without NP.

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Methods: We retrospectively included all children with a diagnosis of empyema, hospitalized from January 2005 to December 2011. NP was assessed on CT scan. We recorded age, gender, clinical features, biological and radiological findings, pleural tap, surgery, antibiotics, oxygen, length of stay, and outcome. Results: We included 23 children with isolated empyema and 24 with concomitant NP. Median age was 3.74 and 3.76 years, respectively. Main symptoms were fever, cough, lethargy, abdominal and chest pain. 18/23 and 16/24 children showed leukocytes up to 10G/L. Median C-reactive protein was 200 and 199 mg/l, respectively. Pathogens were mostly Streptococcus pneumoniae (14/23, 20/24) and staphylococcus aureus (3/23, 0/24). All patients required intravenous antibiotic (median duration: 11 and 12 days, respectively). 22/23 and 24/24 underwent further oral antibiotic (median duration: 21d), 16/23 and 9/24 needed oxygen (median range: duration: 3–0; 0–40, respectively). Median (range) length of stay was 13 (7–42) and 15d (8–140), respectively. Complications occurred in 2/23 children without NP (pneumothorax, bronchopleural fistula, pneumomediastinum) and 4/24 with NP (3 bronchopleural fistula including 1 leading to lobectomy, multiple chest tubes). After 6 weeks, X-ray was still abnormal in all patients. 4/23 and 4/24 had functional follow-up: normal (3 patients in both group), obstructive (1 without NP) and restrictive syndrome (1 with NP).

Conclusion: No difference in clinical course, treatment and complications was observed, between children with or without risks factors. CT scan might be questionable if done before diagnosis NP. However, long term follow-up may help in defining potential functional sequelae.

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Oral provocation test is the most important test to diagnose beta-lactams allergy in children

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Background: Urticarial or maculo-papular skin rashes are frequently observed in children treated by beta-lactams (BL). Such manifestations are more likely to be related to the underlying infection rather than to an allergic reaction due to the antibiotic (less than 10%). Accurate diagnosis of antibiotic allergy is important not only to prevent life-threatening reactions, but also to avoid unnecessary drug restriction associated with increased resistance and health costs. Based on a large cohort of patients, the aim of this study was to evaluate the utility of clinical diagnostic tests in children developing a benign rash during a BL treatment.

Method: Patients with a history of urticarial or maculo-papular rash during and up to 72 hours after a treatment with BL, and a positive oral provocation test (OPT) with the culprit antibiotic were prospectively recruited at the Geneva University Hospital between 2006 and 2010. Subjects underwent intradermal skin tests (IDT) for BL. In addition, lymphocyte transformation test (LTT) were performed by measuring (3) H-thymidine incorporation after 7 days of incubation with the incubated antibiotic. Basophil activation tests (BAT) were done according to manufacturer protocol (Buhlmann, Switzerland).

Results: We recruited 14 patients from 14 patients with an antibiotic allergy confirmed by a positive OPT (median age of 4.8 years, range 1.1 to 12.3) and 82 negative controls (median age of 1.7 years, range 0.5 to 14.5). Delayed-reading IDT were negative in all tested patients. Immediate-reading IDT were positive in 7 patients with a positive OPT (50%) and 7 patients with a negative OPT (8.5%). The overall sensitivity determined for immediate-reading IDT was 50% and the specificity was 91.5%. The negative and the positive predictive values were 91.5% and 50%, respectively. Data were available for the LTT in 9 patients with a confirmed BL allergy (median age of 2.0 years, range 1.1 to 8.5) and 15 negative controls (median age of 3.1 years, range 0.5 to 11.1). We observed an overall higher lymphocyte proliferation rate in allergic patients compared to non-allergic children (mean counts per minute (cpm) of 2352 and 1355, respectively). The BAT were negative in the 6 tested patients with a positive OPT.

Conclusion: Both skin tests and in vitro tests (i.e. LTT and BAT) are of limited value and an OPT should be considered in all children who develop a delayed-onset urticarial or maculo-papular rash during a treatment with a BL.

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A dangerous night at Lauchernalp...

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Introduction: Bronchopulmonary dysplasia (BPD) is associated with significant morbidity in early life. This is reflected in current recommendations regarding altitude: traveling in altitude or flying on planes is not recommended during the first year. However no clear recommendations exist for later childhood, making it a challenge for the pediatrician to give adequate counseling. We report here an unusual case of a former premature adolescent with acute respiratory failure.

Case report: A 13-year-old boy, born at 27 weeks of gestation with a history of BPD, went for holiday to a ski resort at 2000 m. On the previous days he suffered from acute upper respiratory tract infection with rhinitis. During the first night he developed severe cough, but decided to go skiing the day after. In the afternoon he developed a respiratory distress and produced roncy, gustom and presented to the general practitioner in respiratory failure. The first chest X-ray showed severe hyperinflation. After transfer to the University hospital he needed aggressive bronchodilatation and therapy with diuretics, corticosteroid, and positive airway pressure. The patient fully recovered within 24 hours.

Discussion: Multiple elements explain the origin of this acute respiratory insufficiency. Prematurity with BPD leads to epithelial and capillary dysfunction. The respiratory tract infection contributed to further epithelial and capillary dysfunction and hyperinflation. Sleeping in altitude probably induced capillary leakage and exercise in this situation added to final respiration failure.

Conclusion: Preterm with BPD among others need a regular pulmonary follow-up to ensure a good quality of life on a specific basis.
Acute salt wasting syndrome in a 18-year old patient with CF having a normal BMI and normal pulmonary function – a case report
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Case: A 18-years young and athletic patient with Cystic Fibrosis (CF, compound heterozygote F508del/G524X) showing up to now a stable pulmonary and gastrointestinal history (FEV1 91 %; BMI 20.8 kg/m² / good thrive). Before presenting at the emergency ward he has been staying in Malta for language holidays (outside temperature constantly 30 to 34 °C). On the third day after arrival in Malta he developed abdominal and muscular cramps, with vomiting, no diarrhea. He had a severe dehydration with prolonged decrease of pulmonary function.

Physical examination: Considerably reduced general condition, cardiopulmonary stable, subebrile temperatures and signs of severe dehydration.

Laboratory results: Leukocytes 25,100/µl, CRP 41 mg/l, urea 32.9 mmol/l, creatinine 342 µmol/l, uric acid 1460 µmol/l, sodium 112 mmol/l, chloride 47 mmol/l, potassium 3.4 mmol/l, pH 7.51, HCO₃⁻ 11 mmol/l, CO₂ 21 mmol/l. Diagnosis: Pseudo-Bartter’s syndrome (metabolic alkalosis with hyponaetraemia, hypokalemia and hypochloremia) with prerenal acute renal failure and dehydration in a patient with CF and salt wasting.

Pathophysiology: As a result of high outside temperature and insufficient salt intake and based on the CF basic defect, development of a hyponaetraemia with intensive voring and presentation of a pseudo-Bartter’s syndrome.

Clinical progress: i.v. rehydration and slow electrolyte supplementation resulted in normalization of plasma electrolyte profile and renal- and inflammatory parameters. Discharge in a good general condition after 5 days of hospitalization, with initial stay at intensive care unit. In the further progress normalization of pulmonary function.

Conclusion: Additional salt intake in situations of high environmental temperatures and/or situations of increased sweating is mandatory for CF patients of all age and also in good general consdition. In patients with CF presenting gastrointestinal symptoms, pseudo-Bartter’s syndrome should be included in the differential diagnosis and a BGA should be made.

Table 1
Clinical Signs and radiologic findings in children undergoing bronchoscopy.

<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>CE + (n = 14)</th>
<th>CE – (n = 28)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough, %</td>
<td>100%</td>
<td>93%</td>
<td>0.439</td>
</tr>
<tr>
<td>Hysteria of choking, %</td>
<td>93%</td>
<td>46%</td>
<td>0.003</td>
</tr>
<tr>
<td>Cyanosis, %</td>
<td>50%</td>
<td>21%</td>
<td>0.064</td>
</tr>
<tr>
<td>Stridor, %</td>
<td>14%</td>
<td>11%</td>
<td>0.547</td>
</tr>
<tr>
<td>Dyspnea, %</td>
<td>71%</td>
<td>36%</td>
<td>0.031</td>
</tr>
<tr>
<td>Presence of viral symptoms,%</td>
<td>21%</td>
<td>54%</td>
<td>0.047</td>
</tr>
<tr>
<td>Abnormal clinical signs, %</td>
<td>86%</td>
<td>43%</td>
<td>0.009</td>
</tr>
<tr>
<td>Abnormal chest radiographic findings, %</td>
<td>67%</td>
<td>36%</td>
<td>0.073</td>
</tr>
</tbody>
</table>

Septic origin of stridor associated respiratory failure
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Introduction: Since the advent of vaccination programs the occurrence of septic stridor-associated respiratory failure is very uncommon. We present the case of a 3 years old boy, vaccinated and usually in good health. At the arrival at the hospital the patient showed a severe respiratory distress stridor-associated without fever and good conditions. We interpreted that as viral croup. Administration of inhaled epinephrine and systemic glucocorticoids was not effective. After measurement of a very high procalcitonin we started an empirical antibiotic therapy. We witnessed a sudden deterioration that required intubation and transfer to Pediatrics Intensive Care Unit.

Conclusion: It’s important to suspect a bacterial origin of respiratory failure in a group of patients. The clinical response to inhaled epinephrine and systemic glucocorticoids. In our opinion procalcitonin can be particularly helpful of a possible quickly severe evolution.
The forgotten ones: Healthy siblings of chronically-ill adolescents
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Aims: To determine the impact of adolescents’ chronic illness on their healthy siblings.

Methods: As part of a larger study on chronically-ill adolescents and their parents, we conducted one focus group (FG) with 5 siblings (HS) and one interview with 1 sibling. Siblings did not have a chronic illness (CI).

Results: Most HSs were protective or overprotective of their chronically-ill sibling (CIS). For instance, by putting on a mothering attitude, protecting from peer mockery, or helping overcome CI-related crises. HSs also worried a lot about their CIS for example by being scared of a relapse, when seeing their sibling go out alone, or in difficult moments like an operation. HSs often felt guilty when their CIS did not feel well as it might be their fault. Therefore, they were careful and self-conscious about what they said, not wanting to hurt their CIS; sometimes even letting it out on other HSs.

The CI generally provoked changes in the entire family dynamics. HSs unanimously mentioned how their parents’ attention was much more focused on the CIS and CIs were often received extra material privileges. Albeit feeling resentful towards their parents, HSs did not want to be an extra burden for them. For some HSs, their relationship with their CIS had undergone negative changes due to the CI such as more hostility between them. Others put forward positive changes like growing closer to each other.

Conclusion: The occurrence of a CI affects the lives and feelings of healthy siblings as they are generally the forgotten ones and seem to suffer a great deal from it. Parents must not forget their healthy children. Health professionals should be aware of this impact and acknowledge the siblings as well as help parents deal with a sick child and his/her siblings in an equal manner.

Comparing opinions of chronically-ill adolescents and their parents concerning disclosure of the chronic condition
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Aims: To compare chronically-ill adolescents and their parents’ opinions concerning chronic illness (CI) disclosure.

Methods: In a qualitative study, we conducted 3 focus groups with 11 chronically-ill adolescents (CIA) (9 females) and 5 focus groups with 30 parents (18 mothers).

Results: Both mothers and fathers unanimously complained that their CIA did not want to talk about their CI with anyone, mainly because CIs as wanted to be considered as normal. While some CIA did not want to disclose their CI for the same reason, some did not mind talking about it; and some, although they did not want to talk about it previously, had changed their mind. Parents’ major worry concerned the issue of disclosure in school as some CIAIs needed special arrangements or because they could find themselves in health-threatening situations. As for adolescents, they considered their CI as part of their private life and did not want to be treated differently. Nonetheless, they expressed the importance of having people from the school knowing about it as it made things easier. Interestingly, parents were mentioned as important actors in helping them talk about their CI in school and disclose it.

For mothers, non-disclosure was an important source of distress as they expressed a discrepancy between their needs to talk about it in order to find solutions and those of their CIA. Some fathers also worried that their children did not do their treatment correctly by wanting to hide their CI.

Conclusion: The issue of disclosure was a central difficulty both for parents and adolescents. Health professionals should address this question in consultations and should discuss it both with parents and CIA in order to help them find options.

Plastic Bronchitis in Monozygotic Twins caused by Bocavirus Infection: Coincidence or Proof
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Plastic bronchitis is an extremely rare disease characterized by the formation of tracheobronchial airway casts, which are composed of a fibrous exudate with rubber-like consistency and cause respiratory distress as a result of severe airflow obstruction. We report on monozygotic twins with plastic bronchitis due to human bocavirus. Our case report is the first to describe monozygotic twins simultaneously affected with plastic bronchitis and substantiates the theory of a contributing genetic factor in the pathophysiology of this disease. In this second report related to human bocavirus, we show additional evidence that this condition can be triggered by a simple respiratory tract infection in previously healthy infants. Differentiated initial therapeutic strategies facing a child with atelectasis and suspected plastic bronchitis include immediate bronchoscopy or conservative treatment depending on the clinical and radiographic extent of the disease.
 extending to the pleura with empyema of the pulmonary middle-lobe and multiple adenopathies. IV antibiotic therapy was given during 3 weeks. Collection's puncture detected an MSSA. There were neither traumatisms nor insect bites. No tuberculosis, cat-scratch disease or microcardiopathy was found. Blood cultures were sterile. Despite the decrease of inflammatory parameters, the fever persisted for 4 days. Surgical drainage of the extra-thoracic abscess led to apyrexia and normal labs. MRI at day 9 revealed the persistence of a 2 cm encapsulated intrathoracic collection which was drained under echo-guidance. There were no signs of malignancy in cytologicpathologic exam. Clinical improvement was obvious after the second drainage.

Discussion: Extensive chest wall abscesses are very rare in immunocompetent children. They occur after thoracic surgery, multifocal tuberculosis or purulent pericarditis. They can reveal a tumor, a cat-scratch disease or can be caused by actinomycoses, fusobacterium or parasites. The management request a combination of abscess drainage and prolonged antibiotic therapy.

Conclusion: Chest wall abscesses may be extremely infiltrating and their causative agents difficult to find. MRI and puncture are useful to precise extension of the mass and etiologic diagnosis. They should be aggressively treated by antibiotics and surgical drainage.

Recurrent macrophage activation syndrome in Still's disease
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Introduction: Systemic juvenile idiopathic arthritis (SJIA) or Still's disease is a chronic idiopathic inflammatory disorder with intermittent fever, rash and arthritis. Macrophage activation syndrome (MAS) is a complication seen in about 10% of patients. We report a case with recurrent episodes of MAS.

Case report: A previously healthy 13 y.o. girl with arthralgias/arthritis (wrists, knees, ankles), rash and fever was diagnosed as SJIA. During the hospitalization, a sudden drop of the hemoglobin, platelet count and serum fibrinogen, as well as transaminase and serum ferritin elevation, were observed. The diagnosis of MAS was confirmed by a narrow biopsy showing hemophagocytosis. Steroids and cyclosporine were initiated. During the next 4 years, she presented 5 relapses of SJIA and 2 recurrent episodes of MAS, motivating a combined treatment of glucocorticoids and immunomodulators, anakinra then tocilizumab, with a good response to the latter.

Discussion: MAS is a life-threatening complication caused by the excessive activation of T-lymphocytes and macrophages resulting in the uncontrolled release of inflammatory cytokines. Typically, patients with a chronic condition become acutely ill with persistent fever, lymphadenopathy, hepatosplenomegaly and in severe cases, mental status changes and hemorrhagic syndrome. Clinical symptoms are associated with vascular damage and multiorgan dysfunction, anakinra then tocilizumab, with a good response to the latter.

Conclusion: MAS is a life-threatening complication caused by the excessive activation of T-lymphocytes and macrophages resulting in the uncontrolled release of inflammatory cytokines. Typically, patients with a chronic condition become acutely ill with persistent fever, lymphadenopathy, hepatosplenomegaly and in severe cases, mental status changes and hemorrhagic syndrome. Clinical symptoms are associated with vascular damage and multiorgan dysfunction, anakinra then tocilizumab, with a good response to the latter.

A 15-year-old adolescent girl with a previously uneventful medical history presented with a 3-week history of malaise, fatigue, sore throat, and low grade fever as well as bilateral upper eye-lid swelling in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for hospital discharge after 1 week. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe.

A severe case of EBV associated encephalitis
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Introduction: Thymic T cell development requires a specialized epithelial microenvironment mainly composed of cortical and medullary thymic epithelial cells (TECs). Thymus organogenesis is initiated in the mouse at embryonic day 10.5 when endodermal cells of the thymic anlage have come in contact with the thymus fate. The formation of an epithelial primordium and the subsequent differentiation of TECs into distinct subpopulations constitute the necessary prerequisite for the formation of a thymic microenvironment proficient to support T cell development. The molecular programs governing the differentiation and maintenance of TECs remain elusive.

Methods: To investigate the role of β-catenin, a central molecule in canonical Wnt signalling, in thymus organogenesis and maintenance, we use conditional mouse genome targeting strategy enabling tissue specific deletion of the gene encoding for β-catenin.

Results: Conditional deletion of β-catenin in endodermal cells at early stages of thymus organogenesis precludes the formation of a regular thymus anlage. Deletion of β-catenin specifically in TECs after formation of the thymus anlage leads to thymic hypoplasia and consequently T lymphopenia, although both thymic architecture and T cell development remain normal. However, β-catenin does not compensate for the loss of β-catenin since mice double deficient for these molecules in TECs display a phenotype comparable to that of β-catenin single deficient animals.

Conclusion: These results demonstrate a critical requirement for β-catenin during early thymus organogenesis and later stages of TEC maintenance.

Homeostasis and function of a potent regulatory T cell subset in WT and lymphopenic mice
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Introduction: Regulatory T cells (Treg) play a pivotal role in the maintenance of peripheral tolerance by controlling self-reactive, chronic and homeostatic T cell responses via different effector mechanisms. However, many current working models neglect the fact that the Treg pool consists of different Treg effector populations that are likely involved in different biological processes utilizing distinct regulatory pathways. To investigate this, we have generated and analysed wildtype (WT) and T cell lymphopenic mice for the presence and function of Treg cells.

Methods: Treg isolated from WT and genetically modified lymphopenic mouse strains were characterized and their functional capacity was tested in vitro and in vivo.

Results: Based on the expression of the co-stimulatory molecule ICOS and the CD103+ integrin (CD103), functionally different Treg subpopulations were identified that demonstrate a marked hierarchy in their in vitro and in vivo regulatory potential: ICOS+CD103+ (designated ICOS) and ICOS‒CD103+ (double positive, DP) Treg display a significantly higher degree of CD4 responder inhibition than ICOS‒CD103+ (double negative, DN) Treg and ICOS+CD103+ (CD103) Treg. Further analysis revealed for each of these subpopulations a unique profile of both common and distinct phenotypic and functional features including gene expression profiles, Foxp3 protein concentration, inhibitory cytokine secretion, chemokine receptor expression and proliferation/survival upon stimulation for each of these Treg subpopulation.

Conclusion: These results demonstrate a critical requirement for thymus organogenesis and maintenance.
Don’t forget the C in endoCarditis – a case of chronic Coxiella burnetii infection in an adolescent cardiac patient with a pulmonary valved conduit xenograft

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Introduction: Coxiella burnetii is transmitted by cattle, sheep and goats and infects humans by inhalation of contaminated aerosols. The chronic form of Q-fever can present with endocarditis, glomerulonephritis, and osteomyelitis but is rare in children. Mortality of endocarditis is decreased to 10% if treatment is initiated early.

Case: We report on a 14-year-old boy from Senegal, known for a repaired Fallot tetralogy at the age of 7 years, who was hospitalized for replacement of his calcified and stenosed right ventricle to pulmonary artery. Controversy, the boy had intermittent low-grade fever with hepatosplenomegaly, glomerular hematuria, a high level of blood inflammation, anti-neutrophil cytoplasmic antibodies (ANCA) and a Coombs postive hemolytic anemia. He was treated for a suspected subacute bacterial endocarditis by vancomycin and gentamicin and further investigations were undertaken. Renal biopsy showed a parainfectious mesangioproliferative glomerulonephritis. Blood cultures, Interferon-gamma release assay for tuberculosis, and broncho-alveolar lavage were negative. Serologies for phase I and phase II IgG and IgM were highly positive. This led us to perform a Q-fever serology. Serologies for phase I and phase II IgG and IgM were highly positive. The patient was treated with doxycycline and rifampicin for at least 18 months. Control serologies showed a clearly decreased level of phase I and II IgM antibodies after one month of treatment.

Conclusion: Chronic preexisting valvular heart defects are at risk to develop chronic Q-fever presenting with subacute endocarditis and glomerulonephritis. Early serological testing for phase I and phase II antibodies against Coxiella burnetii is warranted in order to start life-saving treatment rapidly.

Bullous pemphigoid – a rare form of an autoimmune blistering disease in childhood

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Introduction: Bullous pemphigoid (BP) belongs to a heterogeneous group of autoimmune skin diseases presenting with blistering. It predominantly affects elderly individuals and is very rare in the paediatric population. The incidence of BP in childhood is unknown and currently there are less than 100 paediatric cases published in the literature worldwide. The diagnosis is confirmed by histopathology findings from skin and mucous membrane biopsies.

Case Report: We report the case of a 13 year-old girl who presented with itching facial and palmo-plantar erythematous macules and some tiny blisters. She was previously treated for presumed impetigo without clinical improvement. Within two days of admission she developed large tense bullae on her palms and soles. Histopathology of the skin biopsy showed sub-epidermal blisters with eosinophilia and immunofluorescence staining revealed linear deposits of IgG and C3 at the epidermal basal membrane zone. Antibodies against the hemidesmosomes (anti-BP180 and anti-BP230) were negative. The patient responded rapidly to treatment with prednisone. She now continues treatment with a gradual tapered dose of prednisone.

Discussion and Conclusion: BP is a very rare disorder in childhood and therefore a high index of suspicion is needed for early diagnosis. At onset of the disease, biopsy specimens should be sent for Histopathology analysis and specific staining for BP antibodies. Therefore, early scabbing with eosinophilic multiforme. Prognosis is generally good with appropriate treatment and remission is usually achieved within one year.

Extensive pleural effusion in a seven-year-old boy: Maybe it’s TB?

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Introduction: Large pleural effusions in children usually occur as a complication of bacterial pulmonary infections (S.pneumoniae, S.aureus). Other bacterial species, such as group A streptococci and Mycobacteria, or viral infections must be considered. Parapneumonic effusions are found in up to 58% of cases.

Case: A seven-year-old boy from Sri Lanka born in Switzerland was admitted with a history of abdominal pain, vomiting, cough and intermittent fever for one week. Suspecting pneumonia, the GP began an antibiotic treatment with amoxicillin/clavulenate (67 mg/kg). Because of deterioration in general condition and weight loss the child was referred to our emergency. The boy was in acute distress with tachypnea (RR 32/min), his weight was 2 kg < -3SD, and he had reduced breath sounds on the left lung. Chest x-ray showed a white out on the left side. Ultrasound confirmed pleural fluid with multiple septa. Subsequently, intravenous amoxicillin/clavulenate was started on a higher dose (150 mg/kg). The family history revealed that the patient’s mother was treated for active tuberculosis (TB) for five months. Contact investigations were correctly carried out by the Lung League. Our patient had two negative (0/0 mm) tuberculin skin tests (TST) eight weeks apart. We repeated TST (which was documented as negative after 72 hours, but showed an induration of 12 mm after eleven days), took a positive interferon-gamma release assay (QuantiFERON-TB Gold INR, 2753 UI/ml with good mitogen stimulation), aspirated gastric and bronchial fluid (where no acid fast bacilli could be detected in the Ziel-Neelsen stain). Pleurocentesis revealed an exudate (Lc 1470/μl, 93% mononuclear, glucose 1.6 mmol/l, protein 48.4 g/l). Suggesting TB pleuritis we started triple therapy with rifampicin, isoniazid and pyrazinamide. Two weeks later culture of pleural fluid confirmed TB. All symptoms disappeared within three weeks of treatment.

Conclusion: Even if large pleural effusion in children in Switzerland is mostly associated with pneumonia and S. aureus infection, M. tuberculosis must always be considered despite the low TB-prevalence in Switzerland (7.1/100'000), especially in case of suitable history, origin from countries with high TB-prevalence and/or clinical findings. TB pleural effusion generally appears four to twelve months after primary infection. Negative TST, negative IGRA or negative acid-fast stain of gastric or bronchial fluid do not rule out active TB.
Conclusion: In children, subchronic soft tissue and bone infections with Coxiella burnetii can manifest without overt signs of infection. A diagnosis is made possible by eubacterial PCR on normally sterile material as well as serology. Surgery with complete excision and drainage, as presented in this case, may play a crucial role. However, based on the few published case reports, TMP/SMX remains the regimen of choice in this age group. Yet, relapses have been reported and should always be anticipated for several months.

Pruritus as presenting sign in Toxic Shock Syndrome

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Introduction: TSS is a toxin-mediated illness and is classically characterized by fever, rush rapidly progressing to erythroderma (sunburn-like), hypotension and multinorgan involvement. It is mainly caused by toxin-producing strains of *Staph. aureus* and *Streptococcus pyogenes*. We observed a 7 year old boy in excellent clinical condition presenting strong pruritus and slight rash on day 1 after septrhinoplasty, initially interpreted as an allergic reaction, improvement after oral antihistaminic. In addition, arising of erythroderma, fever and septic appearance on day 2. We started antibiotic therapy for TSS and we detected *Staph. aureus* as the cause. We reviewed the literature but we couldn’t find pruritus as a common initial sign of TSS.

Conclusion: TSS can present initially as an acute allergic reaction. But pruritus appears to be an uncommon or insignificant symptom in TSS. It could be explained by the massive T-cell activation mediated by superantigens releasing cytokines.

Necrotizing fasciitis in patient with chickenpox: deficiency in host immunity?

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Introduction: Necrotizing fasciitis (NF) caused by group A *Streptococcus* (GAS) is a well-described and rare complication of chickenpox. However, clusters within a same family are even more seldom. We report two cases of NF in siblings with chickenpox. A genetic deficiency in the hosts’ immune system could explain this unusual presentation.

Case 1: A 6 year-old girl, was admitted with high fever, stiff neck, sore throat, trismus and a left erythematous cervical mass 4 days after onset of chickenpox. Blood analysis revealed high inflammatory markers, and rapid Strept-test was positive. Ultrasound and CT-scan showed signs of NF of the neck. IV co-amoxicillin and clindamycin were started, and surgical debridement was performed as well as hyperbaric oxygen therapy. GAS was found in the throat and on the wound’s culture. Her course was favorable after a total of 14 days of antibiotics.

Case 2: Her 20 months-old sister was admitted 2 weeks later. Chickenpox had started 7 days earlier and she had high grade fever and an erythematous swelling of her left thigh and of the right part of the chest. Suspicion of NF was high. IV co-amoxicillin and clindamycin were started immediately as well as surgical debridement. Wound cultures came back positive for GAS and MSSA, but the throat swab was negative. Because of acute respiratory difficulties and increasing inflammatory parameters in the blood, antibiotic therapy was switched to IV vancomycin, gentamycin and clindamycin. Evolution was subsequently favorable.

Follow-up: Two children in the same family presented with chickenpox complicated by a serious invasive infection by GAS. Both parents and a sibling were also positive for GAS in the throat. GAS decontamination was carried out for them. Certain strains of GAS are believed to be hypervirulent. Concerning the host immune system, we know that Toll-like receptors are involved in innate immunity, with TLR9 playing an important role in host defense against GAS infections. Polymorphism in TLR9 could predispose for a higher rate of invasive GAS infections. Therefore, blood samples were obtained in this family to test for TLR9 mutations.
Hereditary spherocytosis, a neonatal diagnostic challenge

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Introduction: Hereditary spherocytosis (HS) is a congenital haemolytic anemia secondary to an RBC protein membrane defect resulting in spherical cells. Transmission is usually autosomal dominant. With a positive family history diagnosis is easier. We report a case of neonatal spherocytosis without prior family history.

Case Report: A full term newborn of non consanguineous parents developed at H16 neonatal jaundice (bil199 mmol/l) with a constellation and negative Coombs test. He was treated with phototherapy. There was no family history for hemolytic anemia. Systemic examinations showed slight icterus and later, non tender splenomegaly of 2 cm below costal margins. At 1 month, anemia (Hb 49 g/l) with high reticulocytes count (RC) (279 G/l) was present and spherocytes detected on blood film. Osmotic fragility test (OF) was twice normal (5 days & 2 months of age) then positive at 3 months of age (36.8%). Enzyme deficiencies were excluded (G6PD and pyruvate kinase). Ektacytometry, done at 6 months of age after five transfusions, was in favor of spherocytosis. Over the first year, despite well tolerated anemia, nine transfusions were required for Hb level <60 g/l.

Discussion: HS diagnosis may be difficult in newborns. Although transmission is an autosomal dominant, few cases are due to de novo mutations or recessive forms. OF can be falsely negative. The ektacytometry is the most reliable diagnostic test but isn't widespread. A new highly sensitive and specific procedure with flow cytometry is now available.

Conclusion: HS is a heterogeneous disorder regarding clinical severity, protein defects and mode of transmission. Diagnosis is difficult in neonatal period, especially when family history is negative. Diagnostic tests as ektacytometry and flow cytometry are recommended.

Fever without focus? Keep hemophagocytic lymphohistiocytosis in mind

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening group of disease in which an ineffective immune response leads to uncontrolled inflammation. The causes vary widely, from rare genetic mutations to more frequent acquired disease associated to autoimmunity, malignancy, immunodeficiencies or infections. The diagnosis is often delayed because of aspecific symptoms. Most cases present with fever, splenomegaly and cytopenia, which may be disguised as an infectious disease.

Case Report: A 6 weeks old baby, with known medical history, presented with fever without focus. Initial investigations showed isolated moderate thrombopenia and elevated CRP leading to the suspicion of HLH and a treatment was immediately started with dexamethasone, etoposid and ciclosporine, with subsequent addition of antithymoglobulin because of clinical severity. The clinical and laboratory responses were excellent under treatment with almost complete remission. The genetic analyses returned positive for double heterozygous mutation of Munc 13-4, leading to the diagnosis of familial lymphohistiocytosis type 3. The patient is currently planned for hematopoietic stem cell transplantation, the only curative treatment in this situation.

Conclusion: HLH diagnosis is difficult because of the rare prevalence and the non specific clinical presentation. However, early detection is extremely important to enhance the chances of a successful therapy. Therefore, every pediatrician should keep it in mind in its differential diagnosis.

Spherocytosis – no rule without exception

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UKBB

Introduction: Hereditary spherocytosis (HS) is the most common hereditary anaemia in central Europe, due to a red cell membrane defect. It is a result of heterogeneous alterations in one of six genes (most often the ankyrin gene) that encode for proteins involved in vertical associations that tie the membrane skeleton to the lipid bilayer. The incidence is 20 to 30 per 100 000 people per year. We present the case of a girl which was referred to our department for the first time at the age of 5 weeks with a severe anaemia of 4 g/l with normal erythrocytes indices and without increased haemolytic parameters.

Initial investigations revealed inconclusive results. Family history was negative for haemolytic disorders. At the age of 5 months a redcellulocytosis occurred. Finally the suspected chronic membranous haemolytic anemia was demonstrated to be a spherocytosis based on erythrocyte osmotic fragility and ektacytrometry.

Case Report: A 5 week old infant was referred to our department due to a severe normocytic, normochromic anaemia of 4 g/l. No evidence of jaundice or splenomegaly was found. Except anaemia, complete blood count and smear was normal with normal reticulocytes and without spherocytes, infections parameters were normal. Haemolytic parameters were not elevated. Family history was negative for haemolytic disorders. Further investigations revealed a CMV infection, suspected to be a possible cause for the anaemia. Initially, antiviral therapy was not given because the child was considered to be immunocompetent, however severe anaemia persisted and gancyclovir was administered for 3 weeks without normalisation of haemoglobin concentration. Bone marrow investigations, performed at the age of 3 months, excluded a bone marrow failure. Erythrocyte osmotic fragility was initially not suggestive of hereditary spherocytosis, but the osmotic resistance of the parents was completely normal. However further fragility tests became positive together with ektacytrometry. Eosin-5-maleimide test (EMA-test), membrane protein and gene analysis were not performed. Until now 5 packed red blood cells transfusions were needed. Hereditary elliptocytosis, pyropoikilocytosis, stomatocytosis and xeroctyrosis were excluded so far. The majority of patients with HS has a autosomal dominant inheritance. This is a case of a child with an unusual, but in the literature described, presentation of a membranous chronic haemolytic anemia.
Painful Port-a-Cath - a Medical Emergency?
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Introduction: The Port-a-cath (PAC) system is a widely used implantable venous access device. Not only in hematology/oncology but also in various other pediatric subspecialties this device is used to ensure children PAC. Medical problems with these devices include mainly infection and obstruction. However, rare problems such as line leakage, paravasal infusion and disconnection can occur and need urgent evaluation and specific treatment. We present two cases of life-threatening disconnection of the PAC device.
Case reports: A 5-year old boy in first remission 18 months after treatment for an acute b-cell-leukemia developed acute pain during fluid injection into the PAC on a routine exam. 4 months earlier no blood could be drawn from the PAC while injection of normal saline went perfectly well. X-ray exam of the PAC revealed a disconnection of the system. The tube was dislocated into the heart and echocardiography confirmed that the tube had passed the foramen ovale and reached into the left low pulmonary vein. Previous echocardiography did not show any signs for persistent foramen ovale. The tube could be removed via cardiac catherization without any further problems. The patient showed no clinical signs of a Wiskott-Aldrich Syndrome.
Case reports: A 2-year old girl presented with an acute exacerbation of an eating disorder (anorexia nervosa, non-self-induced vomiting and psychogenic polydipsia) diagnosed 3 years earlier. Now she presented with hyperemetic dehydration, due to a diabetes insipidus (DI) accompanied by a growth arrest of her germ cell tumor over the last 2 years and a decreased visual acuity due to chiasmal compression. Brain magnetic resonance imaging (MRI) revealed an enhanced mass in the suprasellar region. j-HCG was increased in both CSF and serum. A subtotal resection revealed the diagnosis of a mixed of NGGCT with germinomatous and chorioncarcinomatous components. Multimodal therapy according to COG protocol AC1012 was started.
Discussion: We hypothesize that the diagnostic delay of 3 years in this patient might have resulted in a transformation from pure germinoma into NGGCT, resulting in an inferior prognosis. This hypothesis is supported by both the 5-year EFS >90%, Malignant NGGCTs have an inferior prognosis with a 5-year EFS that ranges from 10% (choriocarcinoma, embryonal carcinoma) to 70% (mixed NGGCT). Our two cases highlight the importance of immediate work-up of PAC-associated problems. Standard operating procedures for PAC-associated complications like pain, clotted line and disconnection should be available for medical personnel who is in charge of these children. Multidisciplinary approaches are needed in case of PAC disconnection, where intracardiac tube is a rare but life-threatening event which requires transfer to a tertiary care center and immediate removal of the PAC.

Can delay in diagnosing a germinoma result in transformation into a non-secreting germ cell tumour?
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Introduction: Malignant central nervous system germ cell tumours can be divided into two major categories, germinoma and malignant non-germinomatous germ cell tumours (NGGCT). Germinomas are exquisitely radio- and chemosensitive with 5-year event-free survival (EFS) >90%. Malignant NGGCTs have an inferior prognosis with a 5-year EFS that ranges from 10% (choriocarcinoma, embryonal carcinoma) to 70% (mixed NGGCT).
Case report: A 13-year old girl presented with an acute exacerbation of an eating disorder (anorexia nervosa, non-self-induced vomiting and psychogenic polydipsia) diagnosed 3 years earlier. She presented with hyperemetic dehydration, due to a diabetes insipidus (DI) accompanied by a growth arrest of her germ cell tumor over the last 2 years and a decreased visual acuity due to chiasmal compression. Brain magnetic resonance imaging (MRI) revealed an enhanced mass in the suprasellar region. j-HCG was increased in both CSF and serum. A subtotal resection revealed the diagnosis of a mixed of NGGCT with germinomatous and chorioncarcinomatous components. Multimodal therapy according to COG protocol AC1012 was started.
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Langherans cell histiocytosis: an unusual cause of torticollis in children
Laura Cossazzo Franscini1, Veneranda Mattiello1, Pauline Filaine1, Paetite Bernard1, Marc Ansari1, Gerald De Coulon2, Amira Dhour Chariou3, Anne-Laure Hell-Manent-Pidoux4, Fabienne Gumy-Paule8
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Introduction: Torticollis is a common symptom and sign encountered by paediatricians. It may be congenital or acquired. Underlying conditions range in severity from benign to potentially life-threatening disease. We present the case report of a child with Langherans cell histiocytosis.
Case report: A 3-week old boy presented with bloody stools. At the age of 6 weeks he developed blisters, petechiae and serosanguineous crusting on the neck. A computed tomography of the thorax showed a large Langherans cell histiocytosis of 60 G/l with a normal MPV was diagnosed at the age of 7 weeks and decreased in the following weeks to a persistent level between 16–30 G/l. A thrombocytopenia of the newborn was highly suspected. An allimmune thrombocytopenia was excluded. The differential diagnosis of a WAS was discussed, but seemed unlikely, mainly due to the absent hallmark of micro-thrombocytopenia and the atypical dermatological presentation.
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Discussion and Conclusion: Normal MPV values initially argued against a diagnosis of WAS, because micro-thrombocytes are known as a key diagnostic feature, a consistent finding in WAS and XLT. Our patient had a normal or even if giant platelets are present. Rarely, patients with WAS can present with normal or large platelets. Furthermore, automated platelet counting does not pick up small platelets as sensitively as an analysis of a blood film with the specific question of platelet size.

Does a normal mean platelet volume in an infant exclude a Wiskott-Aldrich Syndrome?
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Introduction: Wiskott-Aldrich syndrome (WAS) is a rare X-linked recessive disorder that affects one out of a million boys, typically characterized by the triad of micro-thrombocytopenia, eczematous skin disease, and recurrent infections. Lack of WAS protein expression causes the most severe phenotype (classic WAS), whereas some mutations in the WAS gene allow residual protein expression and cause less severe X-linked thrombocytopenia (XLT). We describe a patient with a diagnostic delay due to a unique phenotype of WAS with an intermediate mean normal platelet volume (MPV) and an initially atypical dermatological presentation.
Case report: A 3-week old boy presented with bloody stools. At the age of 6 weeks he developed blisters, petechiae and serosanguineous crusting on the neck. A computed tomography of the thorax showed a large Langherans cell histiocytosis of 60 G/l with a normal MPV was diagnosed at the age of 7 weeks and decreased in the following weeks to a persistent level between 16–30 G/l. A thrombocytopenia of the newborn was highly suspected. An allimmune thrombocytopenia was excluded. The differential diagnosis of a WAS was discussed, but seemed unlikely, mainly due to the absent hallmark of micro-thrombocytopenia and the atypical dermatological presentation.
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Langherans cell histiocytosis: an unusual cause of torticollis in children
Laura Cossazzo Franscini1, Veneranda Mattiello1, Pauline Filaine1, Fanette Bernard1, Marc Ansari1, Gerald De Coulon2, Amira Dhour Chariou3, Anne-Laure Hell-Manent-Pidoux4, Fabienne Gumy-Paule8
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Administration of rituximab after hematopoietic stem cell transplantation can induce severe and prolonged hypogammaglobulinemia in children

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Geneva University Hospital, Pediatric Onco-Hematology Unit\textsuperscript{1} and Department of Hematology\textsuperscript{2}

A 10-year-old boy received an allogeneic hematopoietic stem cell transplantation (HSCT) for post-haploidal aplastic anemia, from an 9/10 HLA-matched unrelated donor. Engraftment occurred on day 24, and full donor chimerism was achieved on day 29. Early post-transplant complications consisted of a mild thrombotic microangiopathy on day 93 treated by replacing cyclosporine by mycophenolic acid and corticosteroids, and an auto-immune hemolytic anemia on day 180 treated by corticosteroids. Normal CD4+ count and IgM production were achieved after 15 months. Eighteen months post-transplant, a relapse of the autoimmune hemolytic anemia occurred, which did not respond to treatment with corticosteroids. Therefore, the patient received 4 consecutive weekly injections of rituximab (375 mg/m\textsuperscript{2}). Because despite complete B-cell count recovery, IgG levels were low, the patient was supplemented with IV Igs until month 31 post-transplant. At month 40 post-transplant, i.e. 17 months after the last rituximab injection, hypogammaglobulinemia with undetectable IgM levels. Remarkably, he had no infectious complication. T-cell count and function were normal. Immunophenotyping of peripheral B cells showed that CD27+ B-cells (memory B-cells) were virtually absent. Delayed recovery of B-cells maturation and subsequent hypogammaglobulinemia has been described after adjuvant or maintenance rituximab therapy post-autologous HSCT for non-Hodgkin lymphomas. In children, it was reported only in a case of allo-sibling lymphopoietic disorder after allogeneic HSCT. Our report confirms that rituximab can alter B-cells maturation as well as function late after allogeneic HSCT in pediatric patients.

The Role of the mTOR pathway for the development and function of the mouse thymic epithelium

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Introduction: The evolutionary conserved protein mammalian target of rapamycin (mTOR) is a key-regulator of cellular metabolism and consists of two functionally different complexes, named mTORC1 and mTORC2. It serves as a substrate for the immunosuppressant rapamycin – a drug broadly used in clinical transplantation to inhibit T-cell activation. The thymus is the primary lymphoid organ responsible for the differentiation and selection of T cells. This essential role is mainly prompted by cortical and medullary thymic epithelial cells (cTEC and mTEC), which are themselves subject to immunosuppressive therapies.

Methods: To define the role of mTOR signalling in TEC, we generated mice, deficient for either mTORC1 or mTORC2 function or for a complete loss of mTOR activity. These experimental models were achieved using tissue-controlled, Cre recombinase-mediated gene deletion targeted to the TEC-specific transcription factor Foxn1. Results: In each of the loss-of-function models, a significant reduction in total TEC cellularity, thymic lymphopenia and decreased thymic output was observed, though the extent of these changes was dependent on the gene targeted for deletion. Loss of mTORC2 resulted in a 50%-reduction of total thymic cellularity, whereas a lack of mTORC1 or total mTOR activity caused a cellular decrease of 66% and 99%, respectively, when compared to wild type mice. As a consequence of disturbed mTORC1 signalling, there was a significant reduction in medullary but not cortical TEC cellularity, a diminution of cell size, decreased TEC cell cycle activity, an increased fibrotic remodelling of the thymic microenvironment and a reduction in the transcription of TEC-specific chemokine production. Delayed recovery of B-cells maturation and subsequent hypogammaglobulinemia has been described after adjuvant or maintenance rituximab therapy post-autologous HSCT for non-Hodgkin lymphomas. In children, it was reported only in a case of allo-sibling lymphopoietic disorder after allogeneic HSCT. Our report confirms that rituximab can alter B-cells maturation as well as function late after allogeneic HSCT in pediatric patients.

Green leaves are not always healthy

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Introduction: Nerium oleander is an ornamental plant of the dogbane family. Apocynaceae found in the Mediterranean region, Arabian Peninsula and southern Asia but also as ornamental household plants in Switzerland. It is known to be one of the most poisonous plants as each of its parts contains oleander, a non digitalic glycoside.

Case report: After tasting a basil-tomato salad, a healthy 3-years-old girl was found by her brother eating green leaves from different plants on the family terrace including nerium oleander. She was asymptomatic in the emergency unit. Physical exam was normal; she received 1 g/kg activated charcoal and was admitted for surveillance. As potassium level, ECG and cardiac monitoring were normal, she was discharged 12 hours later.

Discussion: Nerium oleander toxicity is similar to digitalic overdose. Oleander is a cardiac glycoside containing oleandrine, oleandroside, digitoxigenin and nerin which inhibit Na-K-ATPase. This provokes increased intracellular calcium and hyperkalemia leading to delayed depolarization, premature contraction, AV-block and ventricular arrhythmia. Cardiac manifestations may include bradycardia, hypotension, and potentially death. Mucosal irritation, gastro-intestinal and neurological symptoms may occur as well. First line treatment consists in administration of multiple doses of activated charcoal, that binds cardiac glycosides in the intestinal lumen, promotes their elimination and interrupt the entero-hepatic circulation. In case of circulatory instability, hemodynamic support and anti-digitoxin antibody fragments should be used.

Conclusion: Nerium oleander is a common ornamental plant and its ingestion is mostly accidental. In children, intoxication may be fatal even with absorption of a very small amount of its components and prompt management is advised in all cases.
Derivation of a decision algorithm to predict acute pyelonephritis in febrile children without source
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Background: The identification of acute pyelonephritis (APN) in children with fever without source (FWS) would be of interest as APN represent half of bacterial infections among those children. Procalcitonin was demonstrated to be significantly associated to APN, and urinary dipstick, a specific screening test for urinary tract infection, could be helpful. We aimed to derive a decision algorithm to predict APN among febrile children without source using simple examinations immediately available (procalcitonin and urine dipstick) at the Emergency Department.

Methods: Data from bi-centre cohort studies of children with FWS were analysed using multilevel regression modelling.

Results: 582 children (15% APN) were included. Procalcitonin, leucocytes and nitrates on dipstick urine were associated with APN in univariate and multivariate analysis. A model was derived based on the logistic regression equation, and yielded an AUC ROC of 0.94 [0.91–0.97] significantly higher than procalcitonin and CRP alone (p <0.001). According to a decision curve analysis, the model also offered a better net benefit than those based on biomarkers considered alone. Dichotomizing the model on an interesting threshold, the model achieved 97% [93–99] sensitivity, 54% [49–59] specificity, 40% [35–45] positive predictive value, and 98% [96–100] negative predictive value.

Conclusion: The derived decision algorithm predicted APN with high sensitivity and negative predictive value, meaning that very few patients were misdiagnosed. The good specificity could allow to identify children who really need further invasive diagnostic procedure such as reference techniques for urine collection or early DMGA scan. These results need further abstraction validation.

Caught in a trap!
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Introduction: Transmeselecteric intestinal hernia is a rare cause of small bowel obstruction, occurring most frequently postoperatively or after abdominal trauma, but also rarely due to congenital mesenteric defects. Even though adults make up most of the reported cases, they represent up to 5% of small bowel obstructions in children. Clinical presentation and laboratory findings are not specific. Imaging studies only demonstrate signs of small bowel obstruction. Therefore, this condition is most often missed by the treating surgeons. However, a delay in the diagnosis can lead to extensive small bowel necrosis or even death.

Case report: A 4-year-old girl presented to the Pediatric Emergency Department with a 48-hour history of abdominal pain, nausea and episodic non bilious vomiting. Two hours before admission, she complained about increasing abdominal pain and started with bloody non bilious emesis. Her past medical history revealed chronic constipation but no previous abdominal surgery. On physical examination, she had fever (38.3 °C) and the abdomen showed diffuse muscular tenderness and guarding with no palpable mass and no bowel sounds on auscultation. A compensated shock (HR 190/min, BP 107/67) was treated with 40 ml/kg NaCl 0.9%. A nasogastric tube was inserted and iv ceftriaxone, metronidazole and omeprazole were started. Laboratory findings showed an elevated bowel distension in the left hemiabdomen. Abdominal ultrasonad demonstrated abundant peri toneal fluid with dilated small bowel loops and thickened intestinal walls, showing antiperistaltic movements. Emergent surgery was performed. Exploratory laparoscopy revealed a 150 cm-length necrotic ileum. On laparotomy, a 2 cm-wide mesenteric defect was found in Treves’ Field. The stranguulation was carefully relieved, and the necrotic portion of the bowel resected. An end-to-end ileo-jejunal anastomosis was performed and the congenital mesenteric defect was sutured.

Conclusion: This case describes a Treves’ Field congenital hernia in a child. Although pediatricians should not forget incarcerations internal intestinal hernia through a mesenteric defect as a potential cause of small bowel obstruction. If suspected, immediate proper surgical exploration should be performed.

The Moral Iceberg behind Vitamin K Prophylaxis
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Introduction: Vitamin K prophylaxis was introduced as early as 1939 to prevent Vitamin K Deficiency Bleeding (VKDB) in the first month of life. The risk of vitamin K deficiency in newborns and high risk populations (breast fed newborns for example) and its routine substitution is well understood and medically applied by pediatricians and neonatologists worldwide. Unfortunately, rare isolated cases of VKDB are still encountered in developed countries, as vitamin K prophylaxis recommendations are not always followed according to local guidelines.

Case Report: We report the case of a 2 month old boy, presenting to the Emergency Department with hematemesis and clinical signs raising the suspicion of intracranial, cutaneous and intra-abdominal haemorrhage accompanied by hypovolemic and septic choc. Laboratory work up revealed prolonged PTT at 120 seconds. Late VKDB was immediately recognized as the infant was born at home, at 2 months of age had not yet received any medical attention other than a midwife at birth and had not received Vitamin K substitution since birth. The parents were strict vegetarians with an alternative family life style. Multiple discussions were necessary with the parents, as they initially refused all treatment including Vitamin K. Repeatedly, the medical staff was required to rationalize the importance of each treatment. The parental authority was threatened on several occasions. The infant was finally accepted, received intravenous Vitamin K 2 mg/day, volume and appropriate intravenous antibiotics. He rapidly recovered over 48 hours and remained hospitalized for 6 days. Vitamin K was continued per os as 2 mg/day for 10 days. Blood and urinary cultures remained sterile and antibiotics were discontinued after 72 hours.

Conclusion: This case illustrates the importance of 1. midwife education regarding VKDB; 2. parental education concerning the risk to the newborn of Vitamin K prophylaxis; and 3. maintaining an open dialogue with parents and keeping in mind the cultural and personnel beliefs whilst considering the vital risk for the patient at hand.
Etiological Diagnosis of Pediatric Pneumonia at the Emergency Department

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Introduction: International reviews consider clinical or radiological findings alone inaccurate to distinguish typical, atypical bacterial or viral pediatric pneumonias. The vast majority do not present with positive blood or pleural cultures. Inflammatory markers are still controversial. These considerations often lead to inappropriate antibiotic prescriptions. A step-by-step approach seems to help.

Methods: This prospective cohort study enrolled 142 children with clinical and radiological pneumonia in the Geneva, Lausanne and Sion Hospitals. Radiological lobar consolidation was the reference for typical bacterial pneumonia in the prediction model. Step-by-step, we compared it to a clinical model (unilateral hyperventilation, bronchial breathing, grunting, and absence of wheezing), to inflammatory markers (C-Reactive Protein [CRP] and Procalcitonin [PCT]), and then to nasopharyngeal-viral-PCR and blood-pneumococcal-PCR.

Results: We confirmed that the clinical model strongly predicts the radiological lobar pneumonia (Odds-ratio 2.46; 95% CI: 1.17–5.17), but positive and negative likelihood ratios (LR+, LR−) were rather weak. Bedside inflammatory markers were showing negative predictive values and LR −0.32 and 0.11 respectively for typical lobar and complicated pneumonia (bacteremia/effusion). Specificity and post-test probabilities were strongly improved (≥94%) with combination (CRP+ >0 mg/dl, negative nasopharyngeal-viral and positive blood-pneumococcal-PCR).

Conclusion: A step-by-step approach allows narrowing the diagnosis of “pneumococcal pediatric pneumonia”. This can be achieved by using first the clinical model, it is important to have a negative effect on growth and bone mineral density (BMD). The aim of this study was to analyze the impact of cumulative doses of corticosteroids on growth and BMD of children with nephrotic syndrome.

Methods: A retrospective chart review in children with NS, followed at the Geneva Children Hospital from 1992 to 2011 was carried out. The mean cumulative dose of prednisone received by the patients in [mg/kg/day] was divided in 3 dose levels: low dose (<0.2 mg/kg/day; n = 9), medium dose (0.2 to 0.4 mg/kg/day; n = 15), and high dose (>0.4 mg/kg/day; n = 6). Growth was evaluated using children’s initial and final height expressed in standard deviation (SD) Z-score. Bone mineralization was assessed by dual energy X-ray absorptiometry (DXA) and expressed in bone mineral density (BMD) of the rachis in [g/cm2] and rachis Z-score. Impact of cumulative doses of prednisone was assessed using linear regression.

Results: Thirty patients were included (21 boys, 9 girls). They were 3.7 years-old (interquartile range (IQR) 2.6–4.8) at onset of nephrotic syndrome and were followed during 9.8 years (IQR 6.6–11.7) during 3.7 years-old (IQR 2.6–4.8) at onset of nephrotic syndrome. Growth was negatively associated to the cumulative dose of prednisone (p = 0.037), but the difference was not statistically significant among the groups of different prednisone dose level.

Conclusions: In our cohort, cumulative dose of prednisone was significantly associated with a decrease in growth and BMD Z-scores. Low cumulative dose of prednisone <0.2 mg/kg/day had no effect on growth, whereas this effect was significant for doses >0.2 mg/kg/day.

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Impact on growth and bone of long-term steroid treatment in nephrotic syndrome: the more you get, the less you grow

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Introduction: Idiopathic nephrotic syndrome is the main cause of nephrotic syndrome (NS) in children. Corticosteroid (prednisone) is the treatment of choice to induce remission and treat subsequent relapsing episodes, it is known to have a negative effect on growth and bone mineral density (BMD). The aim of this study was to analyze the impact of cumulative doses of corticosteroids on growth and BMD of children with nephrotic syndrome.

Methods: A retrospective chart review in children with NS, followed at the Geneva Children Hospital from 1992 to 2011 was carried out. The mean cumulative dose of prednisone received by the patients in [mg/kg/day] was divided in 3 dose levels: low dose (<0.2 mg/kg/day; n = 9), medium dose (0.2 to 0.4 mg/kg/day; n = 15), and high dose (>0.4 mg/kg/day; n = 6). Growth was evaluated using children’s initial and final height expressed in standard deviation (SD) Z-score. Bone mineralization was assessed by dual energy X-ray absorptiometry (DXA) and expressed in bone mineral density (BMD) of the rachis in [g/cm2] and rachis Z-score. Impact of cumulative doses of prednisone was assessed using linear regression.

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Conclusions: In our cohort, cumulative dose of prednisone was significantly associated with a decrease in growth and BMD Z-scores. Low cumulative dose of prednisone <0.2 mg/kg/day had no effect on growth, whereas this effect was significant for doses >0.2 mg/kg/day.

Abnormal small airways function in children with mild asthma and normal spirometry

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Background: Small airways disease is a hallmark in adults with persistent asthma but little is known in children with mild asthma and normal spirometry.

Objective: To assess ventilation heterogeneity, a marker of small airways function, using an easy single-breath washout (SBW) technique in school-aged children with mild asthma and normal FEV1 and healthy age-matched controls.

Methods: Primary outcome was the double-tracer gas phase III slope (SDTG), an index of ventilation heterogeneity in peripheral acinar airways derived from the tidal double-tracer gas SBW test. SBW testing was done with normal tidal breathing. Double-tracer gas constitutes 28.3% helium and 5% sulfur hexafluoride. Triplicate SBW and spirometry tests were performed in all children (n = 66) at baseline and after bronchodilatation in asthmatic children (n = 31).

Results: Acinar ventilation heterogeneity (SDTG) was significantly increased in asthma compared to controls. SDTG was abnormal (≥2 z-scores) in 11/31 asthmatic children, FEV130% in 3/31 and FEV1 in 0/31. After bronchodilatation SDTG, FEV1 and FEV1 significantly changed; Average (95% CI) change given as percentage from baseline was 38 (16–56)%), 17 (9–25)% and 23 (10–36)% respectively.

Conclusion: Abnormal acinar ventilation heterogeneity in one third of children suggests that small airways disease may be present despite rare and mild asthma symptoms and normal spirometry. The easy tidal SBW technique has potential as a clinical and research outcome in children with asthma.
The Swiss Pediatric Sepsis Study – obstacles and opportunities in establishing a national obstetric patient cohort in Switzerland


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Background: Sepsis remains one of the leading causes of infant and childhood death worldwide. Only last year did the WHO, in its attempt to provide an overview of the current status of knowledge on sepsis and its treatment, produce a consensus document to help guide clinical care of critically ill children. Preclinical studies of clearly defined populations will have sufficient power to investigate the immunologic and genetic background of sepsis. However, the regional fragmentation of pediatric clinics in Switzerland, low case numbers, and insufficient access to full-time study nurses are obstacles to clinical research.

Aims: The Swiss Pediatric Sepsis Study was designed to 1. assess epidemiology of pediatric sepsis in Switzerland, 2. identify single nucleotide polymorphisms that increase susceptibility to sepsis in children using chip-based GWAS, 3. discover rare genetic variations sequencing, 4. build-up a pediatric sepsis biobank for future research projects.

Methods: Prospective observational cohort study of all Swiss pediatric A-level clinics, supported by the Pediatric Infectious Diseases Group Switzerland including newborns and children <17 years with proven sepsis/severe septic shock. Since 1.9.2011, over 300 children with sepsis (mortality 6%) were recorded, with an inclusion rate of 80%.

Correlation of twenty virulence genes of Staphylococcus aureus with severity of atopic dermatitis in children as compared to healthy individuals

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Principles: Patients with atopic dermatitis (AD) have a higher susceptibility for colonization and infection with Staphylococcus aureus (S. aureus). S. aureus are capable of expressing a multitude of virulence factors including superantigens which may act to modulate the host immune response and affect the course of infection. This study determines the genetic repertoire of S. aureus isolated from children with atopic dermatitis and compares it to healthy controls and to pathogenic S. aureus isolated from cutaneous skin infections.

Materials: Bacteria from 24 AD patients between 7 months and 18 years and 24 uninstructed controls. PCR and DNA sequence analysis were used to determine microbial surface components recognizing adhesive matrix molecules (MSCRAMM) patterns, staphylococcus protein A, spa types, and the presence of the genes for 20 virulence factors, the gene for methicillin resistance, mecA. Virulence factor gene patterns from AD associated S. aureus were compared with gene patterns from control group isolates and with 72 S. aureus isolates previously characterized from infected skin lesions not associated with AD.

Results: MRSA SCCmec type IVA made up approximately 8% of both AD and control isolates. There was no difference in the prevalence of any MSCRAMM or virulence factor gene pattern analyzed in AD isolates in comparison to the healthy control group except for a higher prevalence of chemotaxis inhibitory protein, chp, in control group. Isolates of AD patients compared to those of infected skin lesions were more likely to carry the gene for staphylococcal enterotoxin A, sea (p = 0.032), which encodes for an enterotoxin known to act as a superantigen. Prevalence of the genes encoding for exfoliative toxin A and B, eta and etb, were significantly associated with organisms isolated from non-AD infected lesions (eta: p = 0.0003, etb: p = 0.0001). No significant factor gene was found to be specifically associated with severity of AD lesions.

Conclusions: The genotypes of S. aureus strains colonizing AD patients do not differ significantly from the genotypes of strains colonizing healthy individuals. Isolates infecting patients without AD express significantly more eta and etb and therefore seem to be more virulent to overcome the intact skin barrier.

Clinical Gene Therapy for X-linked Chronic Granulomatous Disease

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Background: X-linked chronic granulomatous disease (X-CGD) is a primary immunodeficiency caused by deficient phagocyte nicotinamide adenine dinucleotide phosphate (NADPH) oxidase subunit gp91phox. Patients suffer from recurrent life threatening infections with bacteria and fungi, often requiring a lifelong bone marrow transplantation. In case no matched bone marrow donor is available, the only alternative treatment option is gene therapy to autologous haematopoietic stem cells.

Methods: A recent Swiss-German clinical trial for X-CGD using a gamma-retroviral vector has demonstrated clear therapeutic benefits in four patients although complicated by enhancer-mediated mutagenesis and diminution of effectiveness over time due to silencing of the p21 long terminal repeat. In collaboration with other centers in Europe a new lentiviral SIN (self-inactivated) gene transfer vector for X-CGD has therefore been developed to improve efficacy and safety. In this vector expression of the therapeutic transgene gp91phox is mediated by a chimeric promoter – a synthetic fusion of two myeloid promoter elements.

Results: This vector results in high levels of gp91phox expression and normal NADPH oxidase activity in committed myeloid cells and granulocytes from transduced human X-CGD CD34+ cells.

Conclusion: Based on these results the chimeric vector was selected for large scale GMP-production in a joint effort between labs in Zürich, Frankfurt, London and Paris aiming at a multicenter clinical gene therapy trial phase I/II. First children are planned to be treated by 2013 in Zürich in this EU-FP7 funded trial.

Prevalence of vitamin D insufficiency in Swiss teenagers with appendicular fractures: a prospective study of 100 cases

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Introduction: The significance of subclinical vitamin D deficiency in the pathogenesis of fractures in children and adolescents remains currently unclear. We aimed to determine the prevalence of vitamin D insufficiency and its effect on bone mineral density and content values in a collective of Swiss Caucasian children with a first episode of appendicular fracture.

Methods: One hundred teenagers with a first episode of appendicular fracture (group 1) and 50 healthy controls (group 2) were recruited into a cross-sectional study. Bone mineral content (BMC) and bone mineral density (BMD) values were measured by dual-energy x-ray absorptiometry, and serum 25-hydroxyvitamin D was assessed by electrochemiluminescence immunosassays.

Results: From the 100 injured teenagers in the study, 12% had deficient vitamin D levels (<20 ng/mL; <50 nmol/L) and 36% had insufficient levels (20 <30 ng/mL; 50 <75 nmol/L). Vitamin D deficiency was associated with appendicular fracture: a prospective study of 100 cases.

Conclusion: Vitamin D supplementation may have a role in the prevention of fractures in children and adolescents.

Safety, immunogenicity and efficiency of the VZV vaccine after pediatric liver transplantation


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Introduction: Varicella is a serious threat for pediatric liver transplant (LT) recipient, since 1) varicella zoster virus (VZV) is very contagious and endemic in Switzerland, and 2) infection is more severe and frequently complicated in immunocompromized individuals. Unfortunately, prevention with the live-attenuated VZV vaccine is
The “blue infant”, a case report of methemoglobinemia

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Hôpital Intercantonal de la Broye

Methemoglobinemia is a rare condition due to an imbalance consisting of either increased methemoglobin (MetHb) production or decreased iron in the ferric state to functional hemoglobin (hemoglobin with iron in the ferrous state). Affected patients appear cyanotic but are not an increased production of methemoglobin. A thorough history and an early clinical recognition are critical, as clinically important symptoms may appear. A 3.5 year-old boy treated by cyclophosphamide and doxorubicin for nephroblastoma. He was started on ceftriaxone on day 6. Antibiomicrobial susceptibility testing revealed a resistance to ceftriaxone, and treatment was switched to imipenem replaced TMP-SMX in order to have a bactericidal effect for B. holmesii. The patient’s brother was the likely source.

Discussion: This first report of B. holmesii infection in Switzerland confirms that this microorganism also circulates in our country. Diagnosing B. holmesii is not easy: 1) diagnostic is often delayed, as it is a slow growing organism by culture; 2) in pertussis-like illness, as it is a slow growing organism by culture; 3) in pertussis-like illness, B. holmesii is not easy: 1) diagnostic is often delayed, as it is a slow growing organism by culture; 2) in pertussis-like illness, is a recently identified organism that does not correlate with the incidence of invasive osteoarticular infections. Our case aims to describe this case of methemoglobinemia in order to raise awareness among practitioners of this diagnosis and share our observations.

Conclusion: Bordetella holmesii is a recently identified organism that pediatriticians should be aware of since it can cause invasive disease, and is often difficult to diagnose and treat.

Purpose: The aim of this study was to investigate the changes of oropharyngeal K. kingae carriage rate during the first four years of life, its seasonal evolution and to analyze whether these fluctuations in carriage rate correlate with the incidence of invasive osteoarticular infections (OAI) due to this microorganism.

Methods: The oropharyngeal bacterial carriage of K. kingae was screened in 756 healthy children aged 5 to 48 months between January 1, 2009 and December 31, 2012. Oropharyngeal swabs were analysed by real-time polymerase chain reaction (rt-PCR) assay targeting the DNA of K. kingae RTX toxin, and the epidemiological characteristics of the asymptomatic carriage were calculated. In parallel the age related- and seasonal incidence of invasive K. kingae OAI diagnosed in our setting were recorded.

Results: K. kingae oropharyngeal carriage rate was higher among male children (10.6% vs 6.4% in females; p <0.001), and between the ages of 13 and 24 months (10% vs. 6.1%, 9.8% and 76% among, 6–12 month-, 25–36 month- and 37–48 month – old children respectively). Carriage rate was greater in spring (10.2%) and autumn (9.3%) than during the other seasons. OAI incidence was significantly higher in the 13–24 month age group than the 6–12 month-, 25–36 month- and 37–48 month age group and during the autumn and summer. However the OAI incidence did not correlate with the oropharyngeal carriage rate.

Conclusion: Although oropharyngeal colonization with K. kingae is a prerequisite for further invasive infection, the carriage rate does not correlate with the incidence of OAI. Therefore further investigations are needed to elucidate which other factors play a role in the pathogenesis of invasive infections.

The oropharyngeal bacterial carriage of K. kingae during the first four years of life is seasonal and correlates with the incidence of invasive osteoarticular infections.
Effectiveness of an exercise intervention on health-related quality of life and well-being in parents from a randomized-controlled trial

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Aims: The hospitalization of an own child is a highly emotional burden for parents, often resulting in stress, fear and a reduced mental state. This randomized, controlled trial intended to evaluate whether acute well-being and quality of life (QoL) in parents of children with severe illness while they are hospitalized can be influenced by an exercise program.

Methods: Parents whose children were hospitalized over seven days or more were recruited and assigned to an intervention (IG) or control group (CG) by drawing lots in relation 2:1. The exercise lessons took place five times a week for an hour. Mental health (SCL-27+), quality of life (SF-36) and the impact of chronic disease on the family (IFS) were assessed prior and after the intervention that ended when the parents left the hospital. Acute well-being pre and post the exercise lessons were measured by the acute well-being score (BI-S).

Results: Forty-one parents (38 ± 6 years, 36 mothers) were randomized into an IG (n = 22) and CG (n = 19). There was a significant positive effect of the intervention on the mental summary score of the SF-36 in favor of the IG (about 10% difference in change, p < 0.02) while groups did not differ for the physical summary score or the global score of the SCL-27+. Acute well-being by BI-S improved consistently in response of the exercise lessons.

Conclusion: These results show that parents mental QoL can be improved by an exercise program that is provided for free while their children with severe illness are hospitalized. However, these results should be considered with caution due to the very high numbers of non-participation and the dropout rate.

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Epigeneatics in Thymic Epithelial Cells: The Role of DNA Methylation

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Introduction: The thymus stromal microenvironment is mainly comprised of cortical and medullary subsets of thymic epithelial cells (TEC) that in aggregate provide immature T progenitor cells with the cell bound and soluble factors required for their commitment and maturation to fully functional T-cells. DNA methylation is an evolutionary conserved and important epigenetic mark that is involved in the organization of the genome and the regulation of gene expression. In mammals, this DNA modification is mainly established by the de novo DNA Methyltransferases (Dnmt) 3a and Dnmt3b during early embryogenesis and is required for proper tissue specification and cellular differentiation. The removal of methyl groups on cytosine residues involved in DNA methylation that critically requires the DNA repair enzyme Thymine DNA Glycosylase (TDG).

Methods: To investigate the role of DNA methylation in thymus organogenesis and maintenance we established mouse models with a thymus epithelial targeted, conditional deletion of the Dnmt1a, Dnmt3b and TDG.

Results: Mice deficient for both de novo Dnmt show no changes in thymus organogenesis and maintenance during the first weeks of life. With age, Dnmt-deficient mice reveal a smaller thymus size and an increase in relative and absolute numbers of cortical TEC. These changes are accompanied by the upregulation of cortical markers in the medulla and a reduced capacity of the cortex to positively select developing thymocytes. The deletion of TDG in TEC results in normal thymus organogenesis and function during the first weeks of life. A decrease in the central tolerance inducing medullary TEC appears in adulthood, which is associated with the development, without signs of the emergence of an autoimmune phenotype until 20 weeks of life.

Conclusion: Our results demonstrate a requirement for DNA methylation modulating enzymes for thymus maintenance in aged mice.

The role of continued Foxn1 expression in thymus organogenesis and maintenance

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Introduction: The transcription factor Foxn1 is essential for thymic epithelial cell differentiation and the functional loss of Foxn1 results in athymia and a complete absence of T cells. However, the precise molecular function and the gene network controlled by Foxn1 remains unknown. The aim of this study is to define the temporal and quantitative requirements of continued Foxn1 expression for the correct development and maintenance of a normal thymus.

Methods: Two different experimental mouse models have been created: (i) mice that express a non-functional Foxn1 lacking the DNA binding domain once a thymus anlage has normally formed, and (ii) mice that express a hypomorphic Foxn1 allele. The first model allows to investigate the consequences of a loss of Foxn1 function, whereas the second model investigates the importance of the quantity of Foxn1 expression.

Results: In both models the thymus was significantly reduced in size, cystic and the regular microarchitecture was lost when compared to wild type mice. Thymopoietic activity was not detected in the post-natal thymus of either model and the mice displayed severe peripheral lymphopenia, which is aggravated with age. Both types of mice developed severe enterocolitis at adult age, which was T-cell dependent as the disease could be adoptively transferred by CD4+ T cells.

Conclusion: TEC differentiation and maintenance depend on both continuous and adequate Foxn1 expression as short-term or low level Foxn1 expression are insufficient to sustain regular thymus development and function. Inadequate expression of Foxn1 expression results in a T cell repertoire that reveals its autoreactivity over time by causing severe colitis.

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Epithelial cytoreduction sustains ectopic expression of thymus-restricted antigens in thymus medulla during acute graft-versus-host disease

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Introduction: The development of acute graft-versus-host disease (aGVHD) predisposes to chronic GVHD whose autoimmune manifestations are integral components of disease. It remains uncertain, however, whether and how aGVHD is linked to antecedent alloimmunity. A hallmark of murine aGVHD is the de novo generation of autoreactive T cells from donor HSC, suggesting a defect in thymic central tolerance. Essential for clonal deletion is the ectopic expression of a full scope of tissue-restricted peripheral self-antigens (TRAs) which is a distinct property of mature medullary thymic epithelial cells (mTEC)1,2. Since the thymus epithelium is a target of donor T-cell alloimmunity we hypothesized that thymic aGVHD interfered with the mTEC1,2 capacity to sustain TRA diversity.

Methods: Ectopic expression of TRAs was tested in a murine alloenogeneic transplantation model.

Results: We found that reductions in mTEC1,2 compartment sizes were universal manifestations of thymic aGVHD in murine models of haploidentical and fully MHC-disparate transplantation. Contraction of the total mTEC1,2 pool corresponded to a progressive decrease in the subset which expresses autoreactive regulator (Aire), a key regulator of TRA expression. When testing entire residual mTEC1,2 cell pools we found that aGVHD altered expression of ubiquitous genes (Ub) and TRAs, however, at different frequencies. The most substantially reduced TRAs were expressed for genes specifically for known target tissues of chronic GVHD. Fibroblast-growth-factor-7 rescued mTEC1,2 numbers and fewer TRAs were repressed.

Conclusion: Our data provide a mechanism for how autoimmunity develops in the context of aGVHD. Moreover, approaches for epithelial cytoreduction may prove to prevent the emergence of thymus-dependent autoreactive T cells.

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Macro-ASAT – how to avoid diagnostic escalation in children

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Introduction: In certain cases of isolated elevated serum enzymes no pathologic cause can be found. Increased activity can be dissembled by so-called macroenzymes, enzymes that form high-molecular-mass complexes by binding immunoglobulins (type I) or by self-polymerisation or binding to other proteins (type II). Serum activity can be elevated due to decelerated renal clearance or hepatic elimination. Macro-creatinkinase (macro-CK) or macro-amylase are well-known uncertain, however, whether and how autoimmunity is linked to antecedent alloimmunity. A hallmark of murine aGVHD is the de novo generation of autoreactive T cells from donor HSC, suggesting a defect in thymic central tolerance. Essential for clonal deletion is the ectopic expression of a full scope of tissue-restricted peripheral self-antigens (TRAs) which is a distinct property of mature medullary thymic epithelial cells (mTEC)1,2. Since the thymus epithelium is a target of donor T-cell alloimmunity we hypothesized that thymic aGVHD interfered with the mTEC1,2 capacity to sustain TRA diversity.

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P 143

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Jochmann A.¹, Skendaj R.², Furlano R.¹, Schifferli A.¹
1University Children’s Hospital Basel; 2University Hospital Basel

Introduction: In certain cases of isolated elevated serum enzymes no pathologic cause can be found. Increased activity can be dissembled by so-called macroenzymes, enzymes that form high-molecular-mass complexes by binding immunoglobulins (type I) or by self-polymerisation or binding to other proteins (type II). Serum activity can be elevated due to decelerated renal clearance or hepatic elimination. Macro-creatinkinase (macro-CK) or macro-amylase are well-known macroenzymes, enzymes that form high-molecular-mass complexes by binding immunoglobulins (type I) or by self-polymerisation or binding to other proteins (type II). Serum activity can be elevated due to decelerated renal clearance or hepatic elimination. Macro-creatinkinase (macro-CK) or macro-amylase are well-known with a prevalence of up to 10%. Macro-ASAT was rarely described in case reports. In contrast to other macroenzymes, macro-ASAT can be seen in younger persons, even in children, mostly without any clinical relevance. Routine laboratory analysis is not able to distinguish between increased plasma enzyme activity and the presence of macroenzymes which may lead to further investigations.

Case report: A thirteen year old boy was referred to our hematologic department for persistent elevation of ASAT over several years. He declared no symptoms except for intermittent abdominal pain. He had a medical history of asthma treated with montelukast once a day. Family history revealed elevated copper values in childhood in a maternal aunt and two cousins which were not followed up further. Several investigations including laboratory tests had already been performed: Extended serological and immunological laboratory testsings for infective or autoimmune hepatitis were negative. Coeruloplasmin and copper were within the reference range. Abdominal ultrasound showed...
Influenza Vaccination in Pregnant Women: Better late than never

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Introduction: Pregnant women and newborns are at higher risk of complications when infected by influenza virus. Immunization of mothers during pregnancy allows protection of the newborn after birth through the passive transfer of maternal antibodies.

Methods: This was a cross-sectional study performed in Geneva in the post-pandemic 2010/2011 winter season to measure the titers of maternal antibodies by hemagglutination inhibition (HAI) against the H1N1, H3N2 and B 2010/2011 seasonal influenza strains in the umbilical cord blood of newborns from vaccinated and unvaccinated mothers. Seroprotection was defined as HAI titer ≥40.

Results: A total of 188 women were enrolled, including 101 vaccinated during pregnancy. Among the babies of the vaccinated mothers, between 84–86% were seroprotected depending of the influenza strains. In comparison, there were significant less seroprotected babies of non vaccinated women (between 29–33%) (p<0.001).

Adjusting for various factors and using multivariate regression analysis, vaccination during pregnancy increased the geometric mean titre (GMT) by 3.3 to 17 times and the probability of seroprotection by 4.4 to 24.4 times depending of the strains of influenza and of the time between vaccination and delivery. Vaccinating pregnant women one month before delivery was still better than no vaccination (GMT increase between 3.3–4.6 times and likelihood increase in protection between 3.4–6.8 times).

Conclusion: Vaccination during pregnancy confers seroprotection to the majority of newborns, even when done only one month before delivery.