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CL 1

SwissDRG and pediatric clinics: Conclusions one year after the launch

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Introduction: In 2012, Switzerland launched SwissDRG, a nation-wide 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 baserate 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 reimbursement. 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.

CL 2

Accuracy of infrared ear and contact forehead thermometers in the 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 measurements 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 – 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.

CL 3

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 Michaelson 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 post-graduate 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.

CL 4

Five-Year Experience of Clinical Ethics Consultations in a Pediatric Teaching Hospital

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Objective: We present and evaluate a structure for implementing a hospital-wide ethics culture with reference to its application to clinical ethics consultations (CECs) in pediatrics.
Methods: Description and statistical analysis of the Ethics Forum approach in Zurich University Children's Hospital to clinical ethics decision-making using a 7-step model and its implementation in pediatric CECs.
Results: Ninety-five CECs were held over 5 years for 80 patients. The care team reached a consensus treatment recommendation after one session in 75 cases (89%) and on 82 of 84 ethical issues (98%) after two or more sessions (11 repeats). Fifty-seven CECs (60%) recommended limited treatment, and 23 (24%) maximal treatment. Team recommendations were agreed outright by parents and/or patient in 59/73 cases (81%). Initial dissent yielded to explanatory discussion or repeat CEC in seven cases (10%). In a further seven cases (10%), no solution was found within the CEC framework: five (7%) required involvement of the child protection service, and in two cases (3%) the parents took their child elsewhere. Eventual team-parent/patient consensus was reached in 66/73 families (90%) with documented parental/patient decisions (missing data: n = 11). Patient preference was assessable in ten CECs (11%). Patient autonomy was part of the ethical dilemma in three CECs (3%).
Conclusion: The Zurich clinical ethics structure produced a 98% intra-team consensus rate in 95 CECs and reduced initial team-parent dissensus from 21% to 10%. Success depends closely on an underlying institutional clinical ethics framework embodied in a standardized CEC protocol, with regular evaluation of decisions and their consequences for care team and families.

CL 5

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 from the intestine into 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-Iso received a diet isocaloric to the Lf (n = 6) and a Sham group (n = 3). At P3 pups from HI-Lf and HI-Iso groups underwent HI injury. At P25, Multimodal MRI with conventional T2W images, ^{1}H-MRSpectroscopy and Diffusiin imaging (DWI, DTI) were performed. A Mann-Whitney test was used to compare values between the different groups.
Results: When compared to HI-Iso group, the number of rats injured (51% vs. 61%), the percentage of injured cortex at P3 (4.9 ± 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 ^{1}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-Iso 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.

CL 6

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-pro ANP) 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 2nd 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 1/7 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) and to children successfully treated with indomethacine (n = 17; 663 (534–899) pmol/L; p <0.05).
Conclusions: MR-proANP and CT-proET-1 may play a supportive role in diagnostic and treatment surveillance of PDA in very preterm infants.

CL 7

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 after injection. NPC survival and differentiation was evaluated by immunohistochemistry and myelination was monitored using luxol fast blue (LFB) and myelin basic protein (MBP) stainings 10 and 30 days post-treatment. RT-qPCR was performed on stroked hemispheres in NPC- and saline-treated groups. Functional recovery was assessed using the elevated plus maze (EPM) and novel object recognition (NOR) at P40.
Results: BLI demonstrated homing of NPC to the stroked hemisphere and histology further confirmed their localization to the corpus callosum and cortex at 3, 10 and 30 days after treatment. LFB and MBP staining demonstrated greater myelination in the corpus callosum (p = 0.022, p = 0.049) and the striatum (p = 0.017, p = 0.001) at 10 and 30 days after cell-treatment. Increased expression of transcripts specific for myelination (NRG2, GalR1, GDNF), cell proliferation (TGFb1, p53, Stat3) and immunomodulation (IL10, ApoE, Hspb1) were observed in the stroked hemisphere of cell-treated animals. Neonates transplanted with NPC demonstrated better performance on EPM (p = 0.050) and NOR (p = 0.016).
Conclusion: Intra-arterial NPC delivery following HI in neonatal rats resulted in early NPC homing to the injured brain and maintenance for up to a month upon treatment. Behavioral performance suggests cell-treated animals have 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, we here suggest that one potential mechanism of action is the functional repair of white matter tracts.

CL 8

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 perioperative lesions and neurodevelopmental outcome. The objective of this study was to determine the correlation between perioperative cerebral injuries detected on cerebral MRI (cMRI) 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 bypass 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 combined WMI and stroke in two. Lesions were mostly small. Postoperatively, two infants (7%) manifested new cerebral lesions, both minimal WMI's. One infant developed an isolated vena galena 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 and motor domain. Perioperative cerebral lesions did not correlate with neurodevelopmental outcome parameters. This may be due to the small sample size and to the fact that functional impairments associated with these lesions may not manifest until later in life.

CL 9

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 corticomotoneuronal 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: MT differentially modulates corticomotoneuronal excitability in the M1 projecting to the affected (non-dominant) hand depending on the task performed. The specific increase in corticomotoneuronal excitability was more pronounced during bimanual training. This preliminary finding provides neurophysiological evidence supporting the application of MT in children and adolescents with hemiparesis.

CL 10

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 Provvida 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 discontinuous. Indeed, a given child can show no development at all for many years and then suddenly encounter a "development jump", especially in the active language and autonomy areas. However, the long-term development linearity hypothesis seemed to hold true in our study.
Conclusions: 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 long-term repeated follow-up data concerning 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.

CL 11

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 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.

CL 12

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 adolescent. 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 assigned 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 (IL1-Ra) 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 376.2 mA) and decreased in A (397.1 vs 384.9

mA), but the comparison between the two groups for each parameter didn't reach significance (P = 0.09 for MCP-1 vs P = 0.07 for ETP).
Discussion and Conclusion: The statins tended to lower the pro-inflammatory MCP-1 levels and the ETP. MCP-1 is known to be the most increased pro-inflammatory parameter in obese children and since inflammatory markers predict future atherosclerosis, therapies that modify their concentrations or actions could lead to cardiovascular protection and might be an interesting therapeutic tool.

CL 13

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 results, is an accurate tool for SBI prediction. We aimed 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 79.7% (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 6.64 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 28.2% 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.

CL 14

Laughing gas in the emergency department – fun for all "participants"

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Background: Laughing gas (nitrous oxide) either as equimolar mixture with oxygen or in higher concentration up to 70% with a blender is a well known medication against pain. Especially in children it is an approved method for short painful procedures because it is efficient and well tolerated by the children and their parents. Studies from the use of nitrous oxide in anaesthetics show a reduced level of vitamin B 12 (Vit B 12) dependent metabolism in the anaestetic staff. The aim of this study is to examine the Vit B 12 dependent metabolism of medical staff that is working with nitrous oxide for short painful procedures in a pediatric emergency department (ER).
Methods: All members of the pediatric ER of the University Children's Hospital of Zurich who are working over 1 year in the department were asked to participate in the study. As a control group we asked the same number of medical staff working in the intensive care unit (ICU) in the same hospital. In the ICU they don't use nitrous oxide at all. In the blood of all participants we examined the Vit B 12 dependent metabolism (homocysteine, methyl malonic acid, Vit B 12 –level, blood count).
Results: n = 29 participants from the ER, n = 31 from the ICU. The mean of Vit B 12 (ER 339 versus ICU 309 ng/l); blood count (Hb 138 versus 132 g/l; MCV 86 versus 85 fl), homocysteine (9.3 versus 9.2 umol/l) and methyl malonic acid (215 versus 177 mmol/l) showed normal values and no statistical difference.
Conclusions: No signs of impairment of Vit B 12 metabolism was detected in the staff using laughing gas in our ER. In the way and frequency the laughing gas is used in our department for short painful procedures it is safe for the staff with regard to their Vit B 12 dependent metabolism. Therefore we can continue to use laughing gas as a very save analgetic-sedative medication for short painful procedures.

CL 15

Performance of a rapid antigen detection test in group A β-haemolytic streptococcal pharyngitis in comparison with three clinical decision rule in a tertiary paediatric emergency department

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Objectives: Main objective: Compare the performance of a rapid antigen detection test (RADT) of group A β-haemolytic streptococcus (GABHS) to three clinical assessment, McIsaac score, WHO Acute Respiratory Infection (ARI) guideline and Integrated Management of Childhood illness (IMCI) Marocco in children with a acute pharyngitis presenting to a paediatric emergency department.
Methods: Children aged 3–18 years with sore throat were included prospectively between May to July 2012. All children were evaluated clinically. Two pharyngeal swabs were obtained, one for rapid antigen detection and one for throat culture. Diagnostic performance of the RADT and clinical assessment were compared to throat culture (reference test) and were expressed by sensitivity, specificity with a 95% confidence interval (95%CI).
Results: Altogether 193 patients were included. Prevalence of GABHS is 37% based on culture results. With reference to culture results, RADT sensibility is 84% (95%CI 75-93) and specificity 91% (95%CI 86-96) McIsaac Score (>2) sensibility is 97% and specificity is 17% (95%CI 10-23). WHO ARI criteria sensibility is 20% (95%CI 10-30) and specificity is 91% (95%CI 86-97). IMCI Maroc sensibility is 33% (95%CI 21-45) and specificity is 68% (95%CI 59-77).
Conclusion: Rapid diagnostic test showed its superiority over three different clinical assessments for the diagnosis of acute streptococcal pharyngitis. McIsaac score, WHO ARI and IMCI Marocco had low global diagnostic performance.

CL 16

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 care 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 rates of hospitalisation of a period prior and another 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 Mai 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 <0.05) 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 results were 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.

CL 17

Comparison of family-based behavioral therapy in group or individual setting in obese adolescents

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Introduction: Actually, only 19 multidisciplinary group therapy programs are certified in Switzerland, which is insufficient to treat about 250'000 overweight youth. Therefore, the aim of this study was to compare changes in body mass index (BMI) after a family-based behavioral therapy in group or in individual setting.

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 = .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 = .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.

CL 18

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 people between the ages of 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 problem 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 (≥1 joint/week) 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.

CL 19

Fatal rhabdomyolysis in a child with LPIN1 mutation

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Introduction: Autosomal recessive mutations in the LPIN1 gene coding for the nuclear protein Lipin-1 involved in the metabolism of fatty acids at different levels, have recently been described as a cause of severe/fatal rhabdomyolysis in early childhood.
Case report: A two year old previously healthy girl suffered from acute rhabdomyolysis (creatine kinase: CK 653'000 U/L, normal <170 U/L) associated with Rotavirus infection and transient renal insufficiency (maximal plasma creatinine 96 umol/l) prompting further evaluation. Carnitine palmitoyltransferase II deficiency, mitochondrial fatty acid β-oxidation defects (FAO) and renal tubulopathy were ruled out. The further clinical course was uneventful apart from a persistently mildly elevated CK (minimal value 233 U/l); thus muscle biopsy was not performed. The non-consanguineous parents were healthy; family history was unremarkable. At the age of 3 9/12 years, the girl woke up with a mild viral infection of the upper airways with rhinitis and cough. Two hours later – on the drive-in to the hospital – the girl rapidly deteriorated with progressive fatigue and muscle weakness. On arrival, she presented in poor general condition with somnolence, spontaneous breathing with low oxygen saturation (67%), no measurable blood pressure and low body temperature (34.8 °C). A few minutes after admission she had a cardiorespiratory arrest with immediate cardiopulmonary resuscitation. 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 Hum Genet 2008) prompted analysis of the LPIN1 gene revealing a homozygous deletion (c.2295-866_2410-30del) 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 incl severe hypokalemia, carnitine palmitoyltransferase 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 illnesses 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.

CL 20

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 (TIKSS).
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 misunderstanding 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 pediatricians should be sensitized to these risk factors. Families at risk should be early 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.

CL 21

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 increase 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.

CL 22

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 (1.7–17.9 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 lipids disturbance ($r = 0.115$, $p = .053$), and ischemic events or T2DM were correlated with the total number of cardiovascular risk factors present in the child ($r = 0.074$, $p = .046$; $r = 0.09$, $p = .038$, 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 signs 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.

CL 23

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 therefore, there are few data available, defining the annual incidence of SCA in childhood . As many studies suggest, the outcome of pediatric cardiopulmonary 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 Berne 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 cardiopulmonary 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 cardiopulmonary 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.

CL 24

Drug-induced fetal renin-angiotensin system blockade syndrome: a systematic review of the literature

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Background and objective: The objective was to analyze the outcome following prenatal exposure to drugs that block the renin-angiotensin system, either angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor antagonists (ARBs).
Methods: A systematic review of published cases reports and case series dealing with intrauterine exposure to ACE-Is or to ARBs using Medline as source of data was performed. The publications retained for analysis included patients who were described individually, revealing at minimum the gestational age, substance used, period of medication intake and the outcome.
Results: In total, 72 reports were included; 37 articles (118 well-documented cases) described the prenatal exposure to ACE-Is and 35 articles (68 cases) described the prenatal exposure to ARBs. Overall, 52% of the newborns exposed to ACE-Is and 13% of the newborns exposed to ARBs did not exhibit any complications ($p < 0.0001$). Neonatal complications were more frequent following exposure to ARBs and included renal failure, oligohydramnios, death, arterial hypotension, intrauterine growth retardation, respiratory distress syndrome, pulmonary hypoplasia, hypocalvaria, limb defects, persistent patent ductus arteriosus or cerebral complications. The long-term outcome is described as positive in only 50% of the exposed children.
Conclusions: Fetopathy caused by exposure to ACE-Is or ARBs has relevant neonatal and long-term complications. The outcome is poorer following exposure to ARBs. We propose the term "fetal renin-angiotensin system blockade syndrome" to describe the related clinical findings. Thirty years after the first description of ACE-I fetopathy, relevant complications are at present regularly described, indicating that the awareness of the deleterious effect of prenatal exposure to drugs inhibiting the renin-angiotensin system should be improved (Bullo M et al. Hypertension 2012;60:444–50).

CL 25

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 no 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 severity of dysfunctional voiding (DV) 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 time of 9.4 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.

CL 26

Herpes simplex virus – The "bad player" in chemotherapeutic 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 lesions to detect positive patients (PCR+) early, 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.

HSV IgG (n = 50)		Patients with chemotherapy	Chemotherapeutic associated OM	HSV-PCR positive OM	HSV-PCR negative OM	Total OM episodes
positive	11	7	6 (86%)	6	0	24
negative	39	30	11 (30%)	0	11	14

Methods and results: We performed a retrospective study of 50 pediatric patients with potential oncological diseases to evaluate the prevalence of HSV IgG+/IgG- in patients with/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.

CL 27

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 pre-pubertal 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 two patient's parents. The surgical procedure was combined with another surgery for all patients but one. No complications were reported. The patients' diagnoses were: 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 pre-pubertal pediatric cancer patients. As the methods of fertility restoration are still experimental, accurate information should be provided to patients and their parents. A multidisciplinary approach and the follow-up using a patient registry are indispensable.

CL 28

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.
Patients and methods: All children with EA born September 2005 to October 2010 were included. Proton pump inhibitors (PPI) or histamine-receptor antagonists (H2RA) were introduced post-operatively and stopped after 12 months in patients without esophageal stricture (ES) and normal 24-hour-pH-monitoring. Upper endoscopy was performed <4 years of age.
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 36 children after surgery. Treatment was stopped in 17 patients (45.9%) at a median age of 17 months (current age 4.8 years). Among them, 3 had history of ES with a normal repeat pH-monitoring and endoscopy. The 14 others had normal pH-study and 9 underwent endoscopy with normal findings. Twenty children still needed antacid treatment (current age 3.1 years), including 12 with ES requiring ≥2 dilatations. Of the 20 patients with persistent need for antacids, 13 had a pH study performed and all were abnormal. Fifteen had ≥1 endoscopy which was abnormal in 5 children with ES (3 gastric metaplasia, 4 moderate-to-severe esophagitis, 2 hiatal hernia).
Conclusion: Our data suggest that although GER is common in children treated for EA, a sizeable proportion have a favourable evolution in the first years of life, with no GER thus allowing cessation of antacids. On-going follow-up is needed to confirm these observations.

CL 29

LeCompte Maneuver for Airway Compression Management in Late-presenting Absent Pulmonary Valve Syndrome

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Introduction: Patients with absent pulmonary valve syndrome (APV) 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 bronchi. The LeCompte maneuver has been proposed to address this issue, although there is limited data available. This study reviews our recent experience in managing APV 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 Fallow and APV from 2000 to 2012 at our institution. Patients with clinical evidence of airway compression undergo systematic pre- and post-operative bronchoscopy. The primary endpoints were post-operative bronchoscopic 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 4.1 ± 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, totally anomalous pulmonary venous return and infradiaphragmatic MAPCA to the right lung, and 1 patient with 22q11 microdeletion. There were no perioperative deaths. 8 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 1 had improved compression (P = 1.0). 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 APV 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.

CL 30

Necrotizing Fasciitis: a 4-year review of cases of a single-institution

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Aim: Necrotizing fasciitis (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 outcomes 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 total body surface area of skin excised was 0.5% (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 septic shock, 2 coagulation perturbations and 1 agranulocytosis. Intensive care stay for an average of 6.5 ± 1.4 days was necessary for 6/7 patients, and 5/7 patients required intubation for 5.2 ± 1.2 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.

CL 31

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, ERJ 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 similar in infants with CF (mean 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.

CL 32

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 peanut 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 with a mean age of 5.9 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], angiooedema [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 892 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, particulary with a cut of level of greater than 11.0 kU/l.

CL 33

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 N02-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.

CL 34

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

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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 tour pediatric cohort, in order to identify pre- and per- 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, pneumothorax, or diaphragmatic paralysis. No delayed (1 to 3 month) pulmonary complication occurred. In long termate (>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 because of a lung-related complication.
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.

CL 35

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 not only more and more patients, family members and doctors are concerned, but also nurseries, kindergardens and schools have more often to deal with the problem. Knowledge about risk factors, elicitors, augmentation factors and symptoms 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 evaulate 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 allergolo-gy 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-question-naire 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 symp-toms were accepted. Data included demographic data, personal and familiy atopy histo-ry, clinical features, place of occurence, elicitating allergen, diagnostic tests, aggrava-ting or triggering factors, the emergency treatment including drug, drug 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 anaphy-laxis were food allergens, followed by hymenoptera sting and drugs. Medical treatement included antihistamines and corticosteroides 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.

CL 36

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 consulting a 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 = 1.25; 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.
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.

CL 37

Campagne de vaccination contre la coqueluche à l'Hôpital du Chablais
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.

P 1

Sub-aponeurotic fluid collections in young infants

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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 isointens with 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 liquid 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 may cause minor 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 diagnose 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.

P 2

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, perniose 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. A systematic search of the literature was also performed.
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 easy recognizable variant of polymorphic light eruption. Outbreaks 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.

P 3

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 mean subjects' weight, 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.

P 4

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 Geneva University Hospitals. Medical history and evolution of 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.

P 5

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 7.6% and 4.6%, severe and excruciating pain 5.7% and 8% for groups 1 and 2, respectively, χ^2 = ns), nor for parent satisfaction (satisfied and very satisfied 85.1% and 86.5%, unsatisfied and very unsatisfied 5.4% and 3.4%, χ^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.

P 6

Does additional topical anesthesia improve the analgesic efficacy of inhaled nitrous oxide/Oxygen mixture?

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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®) anesthesia (TA).
Method: Retrospective analysis of 532 questionnaires including 11 questions asked to the patients aged 2–191 months and/or to their parents between January 2004 and December 2011. After exclusion of procedures not accessible for topical anesthesia (voiding cystourethrograms, removal of sutures, bandage changes, ENT examinations), questionnaires of 113 patients with, and 168 patients without additional topical anesthesia could be analyzed.
Results:

	Lumbar puncture			**Venous puncture**		
Topical anesthesia	+ EMLA®	– EMLA®	p	+ EMLA®	– EMLA®	p
Gender (m/f)	16 m, 12 f	16 m 11 f	ns	62 m 23 f	109 m, 32 f	ns
Pain score (0–10)						
– No or slight pain (0–2)	71.8%	63%	ns	77.6%	72.3%	ns
– Moderate or severe (3–10)	17.9%	18.5%		9.1%	9.9%	
– missing	10.3%	18.5		15.2%	17.7%	

Conclusion: pain perception during lumbar or venous puncture was not different between patients with or without additional topical anesthesia.

P 7

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 Tafers or Riaz and 4 transferred to Bern or Lausanne, 66 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 (R2 = 0.07, p = 0.04) but not for complications (R2 = 0.02, p = 0.4), and in-hospital delay was not a predictor, neither for complications nor for the duration of hospital stay (r2 = 0.02, p = 0.3, and r2 = 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.

P 8

Transient benign hyperphophatasemia 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-Analyses statement.
Results: The 142 reports retained 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 ≈70% 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.

P 9

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 few municipalities, the 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, 1003 in 2008, 2398 in 2009, 2705 in 2010, 3154 in 2011 and 3398 in 2012; the number of schools increased from three in 2006 to 68 in 2012. In 2012 about 10% of the Geneva state population between 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 children liked to participate to the program and the race. Participating teachers were generally very positive.
Conclusion: The increase in participation of children and the retention of knowledge of healthy eating habits suggest an adequate design of the program. The implementation in schools with support from the government was decisive to reach these goals. Whether these changes are accompanied by changes in behavior remains unknown but recent statistics of the State Juvenile Health Services indicating a trend for a decline in obesity prevalence in this age group favor continuation of the program.

P 10

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 –9.2 – 1.3%) 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, demonstrating the possible usefulness of this device for the assessment of dehydration. Future larger studies are needed to assess the clinical usefulness of these devices in clinical practice. (Acta Paediatr. 2012 Oct;101(10):e479–8).

P 11

Making Sense of the Best Interest Standard in Pediatrics: Results from an empirical study

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Introduction: Existing recommendations contain vague or even conflicting identification of the best interests of the child and empirical data about the interpretation of the concept by professionals in clinical practice are almost completely missing. The following study examines the different explanations and interpretations used in practice by specialists in the area of pediatrics.
Methods: We conducted 12 semi-structured interviews with health care professionals in pediatrics. Data were evaluated by means of the interpretative phenomenological analysis.
Results: Semi-structured interviews showed a context-dependent and multifaceted interpretation of the Best Interests Standard widely confirming an earlier theoretical classification by Loretta Kopelman concerning an ideal-dimension, a standard of reasonableness and a threshold value.
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.

P 12

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 umbilic 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 fistulas. 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).

P 13

Pelvic cyst in a teenager, a radiological and surgical challenge

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Introduction: Ovarian cystadenofibromas (CAF) are benign tumors originating from the surface 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 a papillary formation in connection with the right fallopian tube, and no calcifications. Laparoscopic exploration showed a torsion of a right adnexial mass caused by the large heterogenous cyst and a right 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.

P 14

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 dehydration and weight loss due to profuse vomiting lasting 24 hours associated with discomfort but 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.

P 15

Ovarian torsion – delayed diagnosis in a prepubertal girl

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Background: Ovarian torsion (OT) in children is an uncommon condition. Although there is a higher incidence after puberty, it does occur in younger girls and should be considered in the differential diagnosis of all females with lower abdominal pain. Right sided OT is diagnosed more often than left-sided OT, therefore appendicitis is the most common differential for OT. 58% of the OTs are associated with benign mass (35% ovarian cyst, 23% benign neoplasm). The clinical and laboratory findings are unspecific. Therefore and also because of diagnostic uncertainty the treatment of ovarian torsion is often delayed.
Case report: We report the case of an eight year old girl who complained of right lower quadrant abdominal pain and vomiting. Suspecting an acute appendicitis, the girl was sent to a peripheral hospital for an ultrasound on the second day which revealed a cystic lesion. The following day the ovarian cyst was confirmed with magnetic resonance imaging. An ovarian torsion could neither be excluded nor confirmed. Therefore the girl was referred to our hospital. A diagnostic laparoscopy was performed the same day. With a delay of three days after onset of the symptoms, the ischemic right ovary was derotated and the cyst was fenestrated. A sonographic follow-up at four weeks postoperatively showed a well perfused ovary.
Conclusion: OT especially in prepubertal girls is most likely underdiagnosed. It is estimated that over half of the cases of OT are initially missed. Right-sided OT is diagnosed more commonly than left-sided OT, which may be owed to a lower threshold for investigation when appendicitis is a differential. Additionally, the diagnosis is often delayed. Girls with suspected OT wait more than twice as long for imaging and surgical intervention than boys with suspected testicular torsion. Early sonography should be considered in all girls with lower abdominal pain to prevent diagnostic delay and loss of the ovary.

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P 16

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), for median age (43.7 (8-157) and 64.6 (5-180) months, p = 0.07), median weight for age z-score (0.2 (–1.5 -+4) and 0.5 (1.9-+4), p = ns), and delay between FB ingestion and consultation at the ER (1.13 hours (0.5–120) and 1.6 (0.3-192), 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.

P 17

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 abdominal pain and subfebrile temperature persisting for two days. MPH treatment had been initiated several months ago; regular clinical check-up's incl. blood pressure were normal. The dose had been gradually increased up to 60 mg per day. As behavioral problems and poor school results persisted, dosing was further escalated up to 90 mg per day. The boy had tolerated the dose increase well with the exception of 2 days of transient headache disappearing without any intervention. Finally – one week prior to hospital admission – the daily dose was increased to 120 mg (= 3 x 40 mg; 5.2 mg/kg body weight). The boy had taken the last MPH dose 26 hours prior to admission. Initial clinical examination incl. fundoscopy was unremarkable and the abdomen was not tender. Vital parameters revealed arterial hypertension with maximal blood pressure of 168/111 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. Further 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.

P 18

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/Prinicpal 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 hip joint) 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 assessment and splinting treatment of DDH led to mature hips in all children followed up. Procedures are feasible and will be continued.

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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 intensive 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 having taken a hot tub bath with his parents and siblings. The rash was disseminated with predominance on the trunk and the swimsuit area. He reported no other symptoms. The other family members complained of a similar rash. 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* the most frequently isolated microorganism from 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 spontaneous within 4–10 days. Needless to say the patient should seek advice in order to decontaminate their hot tub.

P 20

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 unexplainable 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 by the end 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 hematologic 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.

P 21

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

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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 and adolescents as they may present differently than in adults. Recently researchers have proposed ten adapted criteria for measuring BED in children. The purpose of this study was to develop a brief auto administered scale (ADO-BEDS) to measure BED in adolescents according to these ten criteria, and to validate this scale against a clinical interview administered by a psychologist using the BED module of the Structured Clinical Interview for the Diagnosis of DSM-IV Disorders.
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.

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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 de 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 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. which 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.

P 23

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.

P 24

Effects of family-based group therapy on physical activity and eating habits of overweight children and their parents: the KIDSSTEP study

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Introduction: Children's physical activity and eating habits are largely influenced by their environment and the family plays an important role in the development of overweight in youth. The purpose of this study was to determine the effects of a family-based behavioral group therapy on physical activity and eating habits of overweight children and adolescents and their parents.
Method: Before therapy and at 1 year, longitudinal data of 201 children (12.4 ± 2.3 years) of the ongoing Swiss multicenter cohort study KIDSSTEP, the Family Eating and Activity Questionnaire (Golan 1998) was completed by the parents. It included 4 scales most likely to be associated with their child's weight change: 1) activity level, 2) stimulus exposure, 3) eating related to hunger, 4) eating style. The body mass index standard deviation score (BMI-SDS) of children was also determined.
Results: Results at 1 year showed beneficial changes in stimulus exposure and family eating style scores reported by both parents (–3 to –13%, p <.0006). Stimulus exposure (–13%, p <.0001) and eating related to hunger scores (–11%, p <.0001) were also improved in children. However, the physical activity score did not significantly change. The total family score decreased at 1 year (–12%, p <.0001) and correlated positively with BMI-SDS differences (r = 0.4, p <.0001).
Conclusion: Multidisciplinary family-based behavioral group therapy results in improvement in child's and parents eating habits and consequently may contribute to the reduction of the degree of obesity in the child. However, changes in physical activity level remain to be demonstrated by objective measures. *Source of funding: FOPH grant #09.004211/204.0001/-629*

P 25

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 topic 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 investigation and therapy. Clinical examination showed in the 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 dosed amoxicillin/clavulanic acid. After 36 hours of treatment the area of inflammation extended rapidly and progressively to a multiple 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, fasciitis 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 inflammation are possible complications using NSAID in patients with acute varicella zoster infection. Therefore caution is recommended for the use of NSAID in this context.
Literature: Y. Mikaeloff et al., Nonsteroidal anti-inflammatory drug use and the risk of severe skin and soft tissue complications in patients with varicella or zoster disease. BJCP 200: 65:2; 203–209.

P 26

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. Children usually present with chronic headache as 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 Acetazolamid controlled symptoms, but ICH did not resolve. One year later the boy complained of lower limb pain. Radiological work-up revealed gross multilocular metaphyseal non-ossifying lesions of the long bones. Because of these lesions OD was suspected. Manifestation of this extremely rare genetic trait 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.

P 27

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 theses adolescent girls. The core risk factor is the quality to mentalize, and it becomes more important when moderated with other risk factors.
Conclusions: The better the capacity to mentalize, the quality of attachment and the absence of an ill-treating environment, the less the aggressiveness in theses adolescent girls. Taken separately mentalization has a large influence on the quantity of aggressiveness observed, but taken together with other risk factors such as attachment and ill treatment, the variance explained is much higher. The importance of the number of risk factors on the psychopathology is a classical clinical conclusion, but what has emerged from the results of this research and that is innovative, is the importance of the quality to mentalise. It is of such importance that if the quality is good (enough), the attachement quality and ill treatment no longer influence the quantity of aggressiveness. Thus, mentalization is a major risk factor but also a factor that can protect from developing psychopathological traits such as major aggressiveness. As a global clinical conclusion, and to open on to further studies and practice, this study shows that increasing the capacity to mentalize could help diminish the aggressive traits in adolescent girls.

P 28

Teaching basic interviewing skills to medical and nursing students using simulated adolescent patients: opportunities for an interprofessional education module?

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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 multidisicplinary 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 appropriatness of training material for their students. A training in group facilitation with adolescent simulated patients was developed based 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' feed back 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 address issues of profesionnal 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 interprofessional education programs of Geneva University and Health school in Geneva.

P 29

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

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Introduction: Training of health professionals is crucial to address adolescent's specific health needs: developmentally appropriate communication skills, role of parents, confidential care, identifying risk and protective health factors. The aim of this project was to test the benefit of using adolescent simulated patients to improve interviewing skills of medical students.
Method: Since 2008, all 4th year medical students in the university of Geneva attend a two hours workshop in small groups with one simulated patient and a facilitator. Facilitators were specifically trained and gave personnal feedback. In 2009, before the workshop all students filled a short open questionnaire (T0). In the year following the workshop they filled a self assessment questionnaire (T1) issued from T0.
Results: Participation was high (80% questionnaires filled, N = 122 students). Students felt more at ease addressing substance use and contraception than sexual orientation, suicide or family issues. Simulated patients and facilitator's interventions were highly appreciated. Facilitators' feed back was positive on attending prior specific training. Small group with simulated patients allowed effective role play and interactive learning on intimate topics.
Conclusions: This method provides an adapted training environment to improve medical students' skills in identifying adolescent's health needs. Adequate training of simulated patients and facilitators is crucial. Content was adapted to match students needs (i.e adding a vignette on sexual orientation). Further steps will focus on objective evaluation methods of such training compared to other formats.

P 30

Training general practitioners to assess young people's mental health needs: impact on general practitioner's detection of mental health issues

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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 consultation. Mental health need was defined as a score above 20 on Kessler's scale of emotional distress (K10) and/or young people's 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: There was no significant difference between the two arms in GPs' identification of young people's mental health needs (OR: 0.87; 95%CI: 0.60 to 1.25). Accuracy of detection was comparable between intervention and control arms (sensitivity: 0.37; 95%CI: 0.27 to 0.47 and 0.37; 95%CI: 0.26 to 0.49 respectively and positive predictive values: 0.56; 95%CI: 0.46 to 0.65 and 0.60; 95%CI: 0.50 to 0.70 respectively).
Conclusion: There was no evidence that a 9-hour training intervention in screening and motivational interviewing followed by two follow-up visits to practices were better than a brief standard talk at increasing GPs' detection of mental health needs among young people. Yet, primary care physicians are well placed to respond to the enormous burden of disease associated with mental disorders in young people. In this study, high level of unmet need persisted regardless of whether GPs received training in screening and motivational interviewing or not. Seeing 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 screening young people in primary care appears warranted before further intervention trials.

P 31

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.
Seventeen (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 most 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.

Genetics – Metabolic Diseases – Neonatology – Neurology

P 32

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.
Discussion: Hypokalemic periodic paralysis is a rare channelopathy characterized by periodic muscle weakness or paralysis as kalemia 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. 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 kalemia suggests this diagnosis, especially when family history is positive, but needs to be confirmed with a genetic test. Treatment is symptomatic.

P 33

Acute respiratory decompensation in a previously healthy 3-year old boy leading to 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

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 polyneuropathia/myopathia was suspected (CIPNM). A congenital myasthenic 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.

P 34

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.

P 35

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. The GLB did not recur after stopping AZT treatment.
Conclusions: GLB is considered excessively rare, but may be under-diagnosed in premature infants with abdominal distension and obstruction. For the diagnosis and follow-up of GBL 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 GBL with AZT treatment remains speculative.

P 36

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

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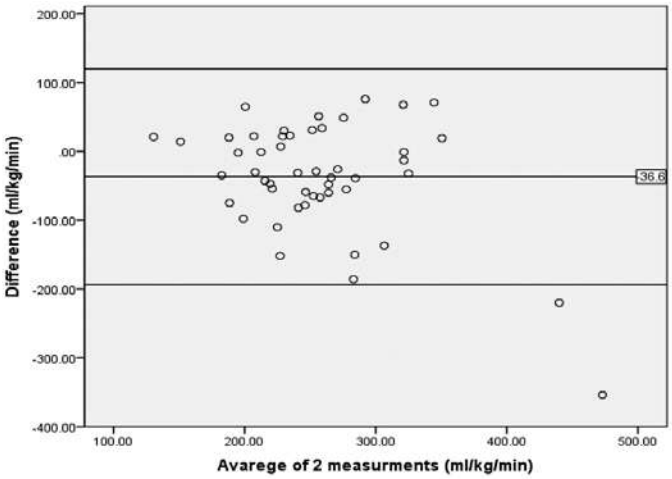
Background: Measurement of cardiac output as an additional parameter in assessing the circulatory status of premature and term infants has become more and more useful in guiding therapy of circulatory compromised babies. Echocardiography is the gold standard to do so but requires time and expertise. 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.



Figur 1

Results: Mean USCOM measurement differed from echocardiography in measuring left ventricular cardiac output by –36.6 ml/kg/min (p = 0.003). The Bland-Altmann 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.

P 37

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 occure in most cases with neurological involvement. Phakomatosis pigmentovacularis is another neurocutaneous disorder with an association of cutaneous and extracutaneous (visceral, 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.
Case-report: In our neonatal unit, a term neonate of African decent presented with multiple port wine stains located all over his body. Furthermore, numerous Mongolian spots of huge sizes were spread over his body. Moreover, the boy showed typical stigmata of Down syndrome. Chromosomal analysis showed a free Trisomy 21. The port wine stains raised our suspicion of SWS. A cranial MRI showed signs of meningeal angiomatosis compatible with neurological manifestation of SWS. Eyeexamination was normal. During hospitalization, the boy demonstrated no other noticeable neurological problem but muscular hypotonia. He showed a good drinking performance.
Discussion: Sturge-Weber syndrome typically presents with facial port wine stains (in the distribution of the trigeminal nerve). Our patient

showed multiple port wine stains in uncommon locations and unusual sizes. The leptomeningeal angiomatosis supports our diagnosis of SWS. Considering the widespread capillary malformations and multiple Mongolian spots, an additional neurocutaneous disorder – Phakomatosis pigmentovascularis (PP) (type II) – is diagnosed. The association of both disorders is reported in the literature. There are few case reports about patients with both SWS and Down syndrome. After a thorough search in the medical literature this is the only case of a combined manifestation of all three disorders (SWS, PP & Down syndrome).

P 38

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-amniotic 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 45 minutes. Soon after, 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.

P 39

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 postconceptionel 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 6-4-6 and needed assisted breathing with additional oxygen, while his sister adapted uneventful. Clinically our patient showed obvious abnormalities such as penile hypospadia, cryptorchidism, short fingers, pes equinovarus right and pes adducutus left sided, dark eyebrows, microcephaly and an inguinal hernia. Genetic analysis was initiated, which showed mosaic 46 XY with a ring chromosome 9(p23q34.3). Further investigations displayed normal cardiac anatomy in echocardiography, immature gyri and small temporal cysts both side in cerebral ultrasound, missing testes in abdominal ultrasound, as well as an ophthalmologic examination suspicious for opticushypoplasia. Results concerning an endocrine disorder (e.g. hypopituitarism) are pending, TSH in the newborn screening was normal. During the cause, nasogastric feeding was needed until 43 3/7 postconceptional weeks, gastro-oesophageal reflux disease led to repeated apnoea. Furthermore oxygen supply is ongoing needed due to a chronic long disease.
Conclusion: Ring chromosome 9 is a rare disorder important to be considered when a child has multiple abnormalities such as growth restriction, microcephaly and underdeveloped male genitals. Moreover feeding problems and gastro-oesphageal reflux are common. A genetic analysis for further pregnancy is strongly recommended.

P 40

A rare cause of fetal hydrops

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Introduction: The differential diagnosis of fetal hydrops remains a challenge. Congenital tumors can be a rare cause of fetal hydrops, and diagnostic work-up is inevitable. Rhabdomyosarcomas are rarely diagnosed in the prenatal or early neonatal period. Despite improvements in therapy regimens, prognosis for patients with metastatic rhabdomyosarcomas continues to be poor. This relates particularly to preterm neonates, in whom anti-cancer therapies (i.e. chemo- and radiotherapy) remain a challenge or cannot be applied for various reasons.
Case report: We present a preterm infant of 29 6/7 weeks of gestational age who presented with fetal hydrops and a large abdominal mass. Fetal MRI demonstrated a huge retroperitoneal tumor. Cesarian section was done for restricted CTG. Birth weight was 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 rarely, 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.

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A Chameleon in the Night

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Case report: This male infant born vaginally at 38 4/7 weeks gestation (BW 2980 g) to a healthy 22 year old G2P1 mother of central African origin, but living in CH since early adolescence (with known homozygous alpha + Thalassemia) presented at 8 hours of age with a dusky colour, subtle respiratory distress, capillary refill <2 seconds, hypothermia (35.8 °C), hypoglycaemia (1.4 mmol/L) and listlessness. Abdomen had slight organomegaly, was distended but non-tender. His skin presented multiple erythematous maculae (maximum 5 mm diameter), with a blueish center and hyperpigmented border on palmo-plantar surfaces with some desquamation. Timely antibiotic prophylaxis for positive GBS screen had been applied. Mother›s first trimester serologies were negative for lues, HIV, hepatitis B and C. We admitted the infant with suspected early onset sepsis for immediate antibiotic (Amioxicillin/Amikacin) treatment. At 9 h of age the CRP was 178 mg/l, Il-6 <50 pg/mL, and CBC 25.3 G/l with a marked left shift (53%). CXR and CSF were normal. Within 12 hours of life he presented an elevated direct bilirubin (104 umol/L for a total at 124 umol/L) with normal transaminases, coagulation screen, γ-GT and a thrombocytopenia (minimal 27000 G/L) requiring 3 platelet transfusions. Echocardiography revealed a moderate pulmonary hypertension. His circulatory function remained stable. US of the

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 TPHA and VDRL. Upon further questioning she remembered a non-pruritic bronze-coloured flat rash on her forearms one month prior to delivery compatible with secondary syphilis. His long bone x-rays confirmed metaphyseal osteitis. Penicillin i.v. 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-bilirubinaemia, 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.

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The effect of prematurity on auditory processing using EEG and fMRI

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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 fMRI 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 fMRI in newborns.
Methods: High-density EEG (109-channel) and fMRI (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-term 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 <.05). The topographic maps showed that the mother voice implies an almost similar map for preterm and full-term babies, however the unknown voice seems to be clearly processed only in the preterm group. Preliminary fMRI results will be presented.
Conclusions: By showing specific activation in preterm babies at term equivalent age when they listen a known and an unknown 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.

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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. Neverthless, 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 precuneus, 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 equivalent age 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 extracted gray and white 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 association 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.

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Emotional, attentional and inhibition abilities in very preterm and full-term children at 24 months of age

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Introduction: Children born prematurely are at increased risk of developing cognitive and behavioral problems. Temperamental characteristics (attention, inhibition and emotionality) have been linked to later socio-emotional and behavioral difficulties.
Objective: To compare emotional, attentional and inhibition abilities of very preterm and full-term infants at 24 months of age through experimental design and questionnaire.
Methods: 49 very preterm children (<29 wks gestation) and 27 full-term children were evaluated at 24 months of age. The Early Childhood Behavior Questionnaire (ECBQ) was completed by parents. Four episodes of the Laboratory Temperament Assessment Battery (Lab-TAB; assessing joy, anger, fear and attention) and 3 episodes of the Effortful Control Battery (ECB; assessing inhibition) were administered to the children.
Results: Results of the ECBQ revealed that parents of preterm children reported more negative emotionality in their children compared to full-term children, Preterm children displayed a distinct attentional pattern with an unchanged attentional level during a task. Moreover, ECBQ indicated lower level of focused attention in preterm children compared to full-terms. Inhibition difficulties, measured with the ECB, were observed in preterm children No difference in effortful control was found between both populations according to the questionnaire.
Conclusion: Compared to full-term children, preterm children were rated by their parents as having more negative emotion. The Lab-Tab analysis suggests a distinct attentional pattern among preterm children aged 24 months. Moreover it demonstrated that this population experiences greater difficulties in maintaining inhibitory control than do full-term children. These patterns could be predictive of later behavioral difficulties.

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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.

Results:

Case	15-year-old girl	9-year-old boy
Diagnosis	**Meningoencephalitis**	**Bickerstaff brainstem encephalitis**
Clinical findings	Neck pain, headache, and diplopic images	Meningism, ataxia, ophthalmoplegia, hemiplegia, and coma
Magnetic resonance imaging	Normal	Brainstem encephalitis
Cerebrospinal fluid (CSF)	39 cells/µL (95% mononuclear), normal protein and glucose levels	11 cells/µL, normal protein and glucose levels
M. pneumoniae real-time PCR	Pharyngeal swab: negative **CSF: positive**	**Pharyngeal swab: positive** CSF: negative
M. pneumoniae ELISA (serum) [≤11 U/ml]	IgM 31.7, IgG 15.5, IgA 40.7 U/ml	IgM 67.0, IgG 48.7, IgA 34.3 U/ml
Intrathecal antibody synthesis [Reiber index: cutoff 1.5]	No	**Yes: IgM 15.5, IgG 7.2, IgA 5.4**
Treatment	Azithromycin PO (5 days)	Doxycycline IV (1 week), IVIG (1 g/kg once), Prednisolone IV (5 days)
Sequelae	No	Yes

Conclusion: Our observations show that intrathecal specific antibody responses may help ascertaining etiological diagnosis of MPE. Furthermore, they may contribute to a more severe course, and in their absence, MPE can be self-limiting despite microbial invasion of the CNS.

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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 motor aura in the father. Genetic testing showed ATP1A2 mutation, confirming the diagnosis of FHM 2. After a 4-year period of relative calm an increase in 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, ophtalmologic 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 controversial. Prognosis is variable, severe CNS complications (cerebral infarction, cognitive decline) are rare.
Conclusion: Recognition of FHM in affected individuals is crucial, as it can mimic other acute CNS disorders and needs highly individualized management. Difficulties involve the indication for imaging, the choice of medication and genetic counseling. Family history is the key to diagnosis.

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Pseudotumor Cerebri is not always idiopathic

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Introduction: Pseudotumor cerebri (PTC) is characterized by signs and symptoms of increased intracranial pressure (IIP) without space occupying lesion. PTC should be divided into idiopathic and secondary forms of which we report three cases.
Case Report: Patient 1: 17 y.o. girl, known for Behçet's disease treated with Azathioprine and Cortisone.
Patient 2: 3 y.o. boy, known for scaphocephaly with surgical correction at 9 months of age.
Patient 3: 13 y.o. boy,with no significant medical history.
All 3 patients presented with headache for several weeks or months, vomiting for two of them and phonophobia for one of them. Fundus examination revealed papilledema in all patients. Cerebral MRI ruled out organic lesions. Lumbar puncture showed elevated CSF opening pressure (30–43 cmH_2O). Blood test was positive for Lyme disease in patient 3.
Acetazolamide treatment led to remission of symptoms. Patient 3 with Lyme disease was treated with ceftriaxone and patient 2 with scaphocephaly was planned for a second operation.
Discussion: Physical examination and medical history could help to find diagnosis since causes for PTC are multiple. Precise cause of IIP in PTC is unknown. Excessive CFS, defective CSF absorption, extracellular edema, increased venous sinus pressure, infections, medications and toxics are possible etiologies. Brain MRI is necessary to exclude intracranial processes like tumor or venous thrombosis. PTC diagnosis is confirmed by elevated CSF opening pressure. Most cases of pediatric idiopathic IIP improve with medical treatment.
Conclusion: PTC is not always idiopathic. Pediatric IIP is associated with infections, collagenoses, hematologic diseases, endocrine disorders, medications and toxics. Careful medical history and diagnostic test are hallmarks for an etiology.

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Early Metabolic Defects in Dexamethasone-Exposed and Undernourished Intrauterine Growth Restricted Rats

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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 prenatal 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 the absence of catch-up growth before weaning, DEX and UN IUGR pups both presented basal hyperglycaemia, decreased glucose tolerance, and pancreatic islet atrophy. Other early metabolic defects were model-specific: DEX pups presented decreased insulin sensitivity whereas UN pups exhibited lowered glucose-induced insulin secretion and more marked alterations in gene expression of pancreatic islet and adipose tissue development regulators. 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.

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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. In contrast, maternal 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.

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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 episod 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 DSVT complicates up to 40% of skull fracture crossing dural sinuses [1]. Although rare after children 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 DSVT should be performed on all children presenting with a skull fracture crossing a cranial venous sinus, because specific treatment can be indicated.

[1] Delgado Almandoz JE, et al. Radiology. 2010;255(2):570–7.
[2] Holsti M, et al. Pediatr Emerg Care. 2005;21(10):639–44.

P 49

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 pleiocytosis and hyperproteinorachy (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 found. Intravenous Immunoglobulin (IVIg) and steroid bolus had transient effect. Rituximab was poorly effective; plasma exchanges were then performed. Four months later she recovered walking with limp, feeding, quietness, orientation and coherence. Partial language and right motor deficit persisted with dystonia
Discussion: NMDAR are glycine and glutamine receptors, highly expressed in GABAergic neurons. ANMDAR induce reversible internalisation of the receptors, but complete pathophysiology of 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 pleiocytosis 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 sequellae occur in 75% of cases, with less than 5% mortality. First-step treatment includes steroid bolus and IVIg, followed by rituximab and/or cyclophosphamide and finally plasma exchanges. Others immunomodulators may be used, such as methotrexate, micophenolate mofetil, or azathioprin.
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.

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Double trouble after minor head injury – traumatic trochlear palsy

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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 about blurry 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 displaced and worst when she was glancing downward. Upon reevaluation, a slight upward drift of the right bulbus and head-tilt posture to the left side led to suspicion of right trochlear palsy, which was 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

diagnostic bed-side tools. Documentation of the squint angle is recommended for follow-up. Traumatic trochlear 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, trochlear 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 treatment in children suffering migraines. To our knowledge, there are no studies about riboflavin prophylaxis in pediatric CVS. We here describe the effectiveness and tolerability of riboflavin in 3 children with CVS.
Case reports: Patient 1: A 13 year-old healthy boy who presented recurrent attacks of nausea, vomiting and headache, of a mean 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. PH-metry, cerebral imaging, and vestibular functions were 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 for 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: 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 2: 15 year-old boy, who presented with a focal seizure and meningeal signs. The initial laboratory tests revealed hypoglycorrhachia, hyperproteinorachia and the cell recount was 650/mm^3 leukocytes with 93% of neutrophils. No germe was detected on CSF Gram stain. The level of blood procalcitonin was 103 ug/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 intravenous antibiotics allowed rapid improvement 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 papilledema: lumbar puncture or not?

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Introduction: Children with severe headaches are often sent for further evaluation to emergency departements. Should a lumbar puncture be performed in the presence of a normal neurological/ neuroradiological examination? We present herewith a case, where the lumbar puncture led to the diagnosis of idiopathic intracranial hypertension without papilledema (IIHWOP).
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 vomitting. Apart from obesity with a body mass index of 29.8 kg/m^2 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 33 cm H20. Cytology and chemical analysis were normal. The patient was treated with 250 mg acetozolamide 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 H20. Acetozolamide dosis was raised to 500 mg twice daily. Due to secondary elektrolyte disturbances leading to a respiratory compensated metabolic acidosis, she was supplemented with sodiumhydrogenbicarbonate. Treatment with acetozolamide was continued thereafter for 2 months 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. The diagnosis of IIHWOP could only be made 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 IIHWOP and its therapeutic consequences.

Literature:
Vieira DS, et al. IIH with and without papilledema in a cosecutive seires of patients with chronic migraine. Cephalgia, 28(6):609–13, 2008 June
Brara S, et al. Pediatric IIH and extreme childhood obesity. Journal of Pediatrics, 161(4):602–7, 2102 Oct.

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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 inherited 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 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.

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Anterior spinal artery syndrome – a rare but important differential diagnosis in children with acute flaccid paraparesis

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Introduction: Spinal cord ischemia (SCI) is a rare event during childhood and has a high morbidity for longterm motor and bladder problems. Most commonly spinal cord ischemia results from an ischemic event in the vascular territory of the anterior spinal artery.
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 insecurity concerning myelitis as etiology a parallel steroid treatment was initiated at presentation. 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 stimulation, pointing to axonal degeneration 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.

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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 vertebral segments. Encephalopathy and seizures are less 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 inbetween 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 longitudinally extensive transverse myelitis, fullfilling 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 "aquired 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.

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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).
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.
Discussion: 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 in regular classrooms is successful. The main objective is to ensure that these children can later accomplish satisfactory vocational training curriculum.

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Recurrent 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 677T 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 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 findings. Vasculitis was suspected and a treatment with methylprednisolon was started. The CSF showed oligoclonal bands and a positive VZV PCR. The decision was made to treat 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 677T.
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 homocygous 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.

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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.

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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 thalami, 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.

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Use in rapid administration of specific antibiotic therapy in severe Mycoplasma pneumoniae encephalitis

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Mycoplasma pneumoniae is a well known cause of acute childhood encephalitis, accounting for a significant proportion of cases. It has been associated with a poor prognosis, neurological complications arising in 15–30% of cases and mortality rates as high as 9%. Physiopathological pathways responsible for the neurological manifestations are not clearly understood, but several different mechanisms, either coexiting or not, are most likely involved: direct invasion of the central nervous system, auto-immunity, cytokine-mediated inflammatory response, neurotoxin production, vasculopathy. The role of antibiotic therapy in the management of acute Mycoplasma pneumoniae encephalitis remains uncertain. Therapeutic success might depend upon the current clinical stage of the disease, a reflection of the different underlying pathological mechanisms.
We report the case of a previously healthy 7-year-old boy with a 7-day history of fever and respiratory symptoms, who presented with sudden onset severe altered level of consciousness and epileptic seizures of bitermporal origin. Evidence of *Mycoplasma pneumoniae* was obtained by PCR in a throat specimen. High levels of cytokines Il-6 and Il-8 were measured in the cerebrospinal fluid. Outcome was favourable following the rapid administration of ciprofloxacine, a fluoroquinolone with high bactericidal activity against *Mycoplasma pneumoniae* as well as good cerebrospinal fluid penetration. The efficiency of this therapeutic strategy suggests the reduction in direct cerebral lesions by *Mycoplasma pneumoniae* or in the inflammatory response secondary to the elimination of the circulating pathogen. Furthermore, it could enable a reduction in the risk of subsequent indirect neurological lesions.

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Transverse Myelitis, Differential Diagnosis

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Introduction/Background: Transverse myelitis (TM) is a clinical syndrome, characterized by acute or subacute spinal cord dysfunction and signs of local inflammation, resulting in paresis, a sensory level, and autonomic (bladder, bowel, sexual) impairment. Differential diagnosis encompasses parainfectious etiologies, acquired demyelinating diseases as well as systemic autoimmune disorders.
Case Report: A 14 year old Caucasian adolescent presented with a sudden onset of bilateral paraesthesias and weakness of the lower limbs for 2 days together with urinary retention, one week after acute airway infection. Physical examination revealed a sensory level at Th8, muscle strength of M4/5 and hyperreflexia with positive Babinsky signs in his lower extremities, and absent anal and cremaster reflexes. Neuroimaging including cranial and repeated spinal MRI showed a T2 hyperintense lesion expanding from Th11 to Th12, suggestive of myelitis, but no brain anomalies. A mild pleocytosis and protein elevation in the cerebrospinal fluid (CSF) confirmed an inflammatory cause. CSF and serological testing couldn't detect neither neuropathogenic infectious agents, nor markers for a demyelinating or autoimmune process, finally fullfilling the inclusion criteria for idiopathic TM. The patient further deteriorated and was started on high dose i.v.-corticosteroids. Following this treatment he showed gradual improvement of sensory and motor functions. However, urinary retention persisted and self-catheterisation had to be maintained, representing a common neurological sequela of TM.
Conclusion: TM is a rare pediatric disease. Acute spinal cord dysfunction represents a medical emergency and should prompt an urgent spinal MRI to run out other causes of myelopathy such as spinal cord compression, neoplasms or vascular disorders. In the next step inflammation should be confirmed by CSF analysis. A cranial MRI and visual evoked potentials as well as analysis of specific antibodies help to run out demyelinating processes (multiple sclerosis, neuromyelitis optica, acute, disseminated encephalomyelitis). Despite a long list of different causes of TM, specific examinations often remain unremarkable, leading to the diagnosis of idiopathic TM in up to 89% of pediatric patients. However, a thorough assessment of these different causes remains crucial because of relevant therapeutic and prognostic consequences.

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Severe hyperkalemia, metabolic acidosis and arterial hypertension – is this Gordon's Syndrome?

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Background: Pseudohypoaldosteronism type II (PHAII), also 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 and WNK4 (with-no-lysine protein kinase), KLHL3 or CUL3 gene. 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 excessive Na-Cl reabsorption and volume expansion; in addition, they reduce 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 (128/58 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 umol/l) and low renin and aldosterone levels. Urinanalysis showed normal calciuria. Renal sonography and echocardiography were normal. Ambulatory 24-hour blood pressure measurement showed elevated daytime values (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 WNK4 gene (c.1691 A>G / p.D564G) confirming 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 with hyperkalemia 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 Na-Cl co-transporter.

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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 phosphatonins 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 iliacal 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 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 of phosphate 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.

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A paediatric case of lipoprotein glomerulopathy

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Introduction: Lipoprotein glomerulopathy is a rare cause of nephrotic syndrome, hypertension 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 reported swollen eyelids in the morning for the last 3 years. 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 (microhaematuria; 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 lipoprotein thrombi consistent with 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 reason.
Pathophysiology: Lipoprotein glomerulopathy is inherited as an autosomal dominant trait with incomplete 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.

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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 U/l, 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 42 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 thrombotic macroangiopathy with high-grade vascular stenosis of the basilar as well as both internal carotid arteries. Despite immediate renal replacement therapy, low-dose heparin and administration of Eculizumab® (Monoclonal antibodies against terminal complement protein C5 (described to be effective against severe cerebral complications of STEC-HUS, N Engl J Med 2011 30;364:2561–3)) the boy died of severe cerebral complications.
Conclusions: HUS is characterized by a thrombotic 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).

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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 diarrhea 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 food (sodium content: 180 mg), home made «seasoned» soups and 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 mmo/l) and hyperchloremia (164 mmol/l), low bicarbonate (17 mmol/l) and potassium (3.2 mmol/l), and mildly elevated plasma creatinine (43 umol/l). Urinalysis showed sodium of 71 mmol/l and specific gravity of 1,013. Stool analysis was positive for Noro-virus infection. Parenteral rehydration with isotonic NaCl 0.9% (500 ml) was followed by maintenance fluid (1000 ml/day) with isotonic Ringerfundin (sodium: 145 mmol/l). Hypernatremia gradually decreased and normalized after 4 days (144 mmol/l). Behaviour and consciousness were not altered as compared to the girl›s usual state. 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 maintenance fluid enabled a slow and safe normalization of all parameters. Rhabdomyolysis is a rare, even fatal complication of hypernatremia.

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Hypertensive emergency secondary to renovascular disease in a 15-years-old boy

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Background: Secondary hypertension is the most common cause of hypertension in children [1, 2]. In children and adolescents with sustained hypertension, renal parenchymal or reno-vascular diseases, aortic coarctation and phaeochromocytoma must be ruled out.
Case report: A 15-year-old boy with subacute onset of blurred vision and headache went to see his ophthalmologist who diagnosed "fundus hypertonicus". Upon referral, blood pressure was 265/165 mm Hg consistent with hypertensive emergency. Clinical examination was normal without abdominal bruit. Laboratory results showed normal renal function, hypokalemia (2.4 mmol/) and metabolic alkalosis (pH 7.61, bicarbonate 31 mmol/l). Immmediate intravenous treatment with an alpha-adrenergic blocking agent (Urapidil) lowered blood pressure within 4 hours to 170/95 mm Hg. Oral therapy with an angio-tensin converting enzyme inhibitor was added (Lisinopril, 1x20 mg/d) and blood pres-sure was further lowered over 5 days to 130–140/75–90 mm Hg. Aortic coarctation was ruled out clinically and by echocardiography. On admission, renin activity (484 mU/l) was markedly elevated and aldosterone level (79 ng/l) was high-normal, suggesting secondary hyperaldosteronism. Phaeochromocytoma was ruled out by normal blood/ urine catecholamines; cortisol was normal. Renal (Doppler) ultrasound did not show any sign of renal artery stenosis. Magnetic resonance angiography (MRA) showed an accessory left renal artery. Finally, conventional angiography revealed a short stenosis of the accessory renal artery which was successfully dilated with balloon angioplasty.
Conclusion: Renovascular disease must be ruled out as cause of secondary hypertension in children. Conventional angiography/ angioplasty are the gold standard for diagnosis/therapy.

1 Arar MY, et al. Etiology of sustained hypertension in children in the southwestern United States. Pediatr Nephrol 1994;8:186. 2 Wyszyńska T, et al. A single pediatric center experience with 1025 children with hypertension. Acta Paediatr. 1992;81:244.

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

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Introduction: Nephronophtisis (NPHP) is a recessive autosomal tubulo-interstitial nephropathy that belongs to the family of ciliopathies. NPHP 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 5y (infantile form) or around 13y (juvenile form). We report here two patients referred for asthenia, tiredness and pallor and diagnosed with NPHP.
Case 1: A 6 y old boy was referred for asthenia and pallor since 2 months (M) and enuresis since 6 M. Neither consanguinity, nor renal diseases were noted in the family. Physical 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 undifferentiated small kidneys. The biopsy revealed abnormal tubular basement membrane (TBM) and global glomerulosclerosis compatible with NPHP. Ophtalmologic examination was normal. The child was started on haemodialysis.
Case 2: A 12 y old girl who presented pallor and asthenia since 1 M was referred for anemia (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 <3rd percentile and BP (125/85). Laboratory showed normal pH (7.32) and slightly decreased BIC (19.2 mmol/l), high Cystatin C (3.2 mg/l), hypokaliemia (3.1 mmol/l), reduced e-GFR 15 ml/min/1.73m2, microscopic hematuria and mild proteinuria (12 mg/kg/j). 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 thicken TBM, tubules duplication and distortion compatible with NPHP. 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 and Creatinin should be measured as a screening test in children and adolescent presented with persistent tiredness, pallor, asthenia noteworthy with enuresis.

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Successful treatment of neonatal atypical haemolytic uremic syndrome with eculizumab

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Introduction: Haemolytic uremic syndrome (HUS), defined by the triad of microangiopathic hemolytic anemia, thrombocytopenia and renal impairment, is uncommon in the neonatal period. We report the case of a 18-days-old girl, diagnosed with atypical haemolytic uremic 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, cerebro-spinal fluid and stool analyses, and was started on phenobarbital, amoxicilline, gentamycine and acyclovir. Her work-up revealed anemia (120 g/l) with schistocytes, thrombopenia (78 G/l) and renal insufficiency with a creatinine (Cr) value of 102 umol/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* 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 protein and no factor H antibodies. The genetic screenings of the CFH gene is pending. 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. After 48 hours 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, her urine output remained stable and 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

4 days. She was discharged from hospital on day 10 with Amoxicilline prophylaxis, Phenytoine, maltofer, vitamin D and Eculizumab every 3 weeks. Her first immunizations were scheduled at 42 days of life.
Conclusion: We report a case of aHUS in a neonate with diarrhea and convulsions who was successfully treated with eculizumab.

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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 (TB-BMD) 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: TB-BMD z-score was higher, while 25-OH-D and PA levels were lower in obese compared to lean subjects (TB-BMD 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-1, p <0.001; PA level: 308.3 ± 22.1 vs. 406.8 ± 29.2 count.min-1, p = .01). TB-BMD z-score was no related with 25-OH-D or PA levels (p >.05), but positively with leptin level and fat mass (p <.05). Vitamin D level was negatively correlated with fat mass (p <.001).
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.

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Chronic constipation in children: clinical characteristics in a Swiss rural population

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Introduction: Chronic functional constipation +/- encopresis are common problems of the paediatric population. Rome III association provides the first internationally accepted diagnostic criteria for this condition. The aim of this study was to assess the clinical characteristics of the Fribourg paediatric population with chronic constipation, seen at the paediatric gastroenterology consultation, applying Rome III criteria.
Method: Retrospective study on 231 charts of patients seen for chronic constipation between 1997 and 2009.
Results: In 121 (52.4%) boys and 110 (46.6%) girls, the disease started at a median age of 24 months, the first specialized consultation was at the age of 47 months, and 52% had a positive family history. Rome III criteria for chronic constipation were met by 86.6%, yet encopresis or fecalome was present in 7 (3%) more. The most frequent complaints were pain during defecation (71%), stool retention (69%), abdominal pain (63%), large volume stool (59%), and fewer than 2 stools per week (56%). Encopresis was present in 95 (41.3%) patients, was more prevalent in boys than in girls (59 (48.8%) and 36 (33.0%) p <0.05), mostly in children with stool retention developing the first symptoms after a mean age of 24 months and with a mean disease duration of 30 months and was inversely associated with present or past anal fissure.
Conclusion: The disease characteristics of our population are similar 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 encopresis.

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Prevalence of small intestinal bacterial overgrowth in pediatric patients under long-term therapy with proton pump inhibitors

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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 median duration of PPI treatment of 4 months (2–15), and had been prescribed PII 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 minutes of glucose ingestion. Four of the six had symptoms such as abdominal pain and flatulence during the test, but only one suffered from abdominal discomfort before and after the test. This latter patient improved under therapy with metronidazole, the remaining 5 stopped or interrupted 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.

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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 for ¼ of the intakes was given. First medical evaluation showed many dehydratation signs on a malnourished baby. Profuse diarrhea with blood, leads to important hydro electrolytic disorders. After fasting and IV rehydratation, the diarrhea stopped within 48 hours. Total Parenteral Nutrition was undergone during 3 w. and feeding with amino-acid based formula was tried. No diarrhea reappeared and TPN weaned within 4 w.
Pan-endoscopy had a normal macroscopy, but pathology (pictures will be available for presentation) showed duodenitis with active and focal neutrophilic inflammation, and severe reorganization of the colonic mucosa: **total extinction of the glands and major eosinophilic inflammation.** Electronic microscopy excluded congenital enteropathies of the mucosa. No infectious agent was detected. Auto-immunity screening including specific antibodies (anti-enterocytes, anti-goblets cells, anti 75kD) was negative, cytometric immunophenotyping, and vaccine responses had normal profils. Fecal elastase in context of transient neutropenia was normal (Schwachman – Diamond's disease). After refeeding another endoscopy showed biopsies with important improvement: light inflammation in the duodenum and colonic regeneration of the glands with still eosinophilic inflammation. Eosinophilic deposition took only place in the colon.
No hypereosinophily in the blood was detected, IgE count and cow's milk protein specific antibodies were normal.
This case reports a severe enterocolitis due to cow's milk protein allergy with complete destruction of the glands. The absence of diarrhea with the amino-acid based formula feeding allowed concluding to recovery of the colonic function. This observation also leads to hospital reintroduction of cow's milk protein formula after one year of age and long-term immunity follow-up.

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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 and presence of stimulated lymphocytes was excluded by PCR. Bacterial broad range PCR, extended virology and fungic tests 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 include hyperthermic intraperitoneal 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].

1 Hayes-Jordan A, Anderson PM. The diagnosis and management of desmoplastic small round cell tumor: a review. Curr Opin Oncol. 2011Jul;23(4):385–9.
2 Jordan AH, Pappo A. Managmenet of desmoplastic small round-cell tumors in children and young adults. J Pediatr Hematol Oncol. 2012 May;34 (Suppl 2):S73–5.
3 Dufresne A, Cassier P, Couraud L, Marec-Bérard P, Meeus P, Alberti L, Blay JY. Desmoplastic small round celle tumor: current management and recent findings. Sarcoma 2012 Mar;2012:714986.

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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 tumors. Hepatoblastoma is the most common among 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 complete hepatectomy with liver transplantation as a treatment of this pathology.
Case presentation: We report the case of a 10 year old boy presenting with abdominal pain and chronic constipation. Abdominal ultrasound followed by CT scan showed a large abdominal mass originating from the liver. Lab work showed thrombocytocis, and normal liver parameters. AFP, beta-HCG and CA-125 levels were also normal. We completed investigations with an MRI that showed a heterogeneous, multifocal mass of the entire liver with vascular extension in the right and middle hepatic veins, only segment II and III were spared, the mass extending to and compressing the left hepatic as well as the left portal vein. Whole-body imaging ruled out extra-abdominal dissemination. A biopsy of the mass confirmed the diagnosis of embryonal sarcoma. The child received chemotherapy according to the CWS-2002P protocol, which resulted in a significant reduction of the mass size. Because of vascular proximity and compression, right lobectomy could not guarantee a R0- resection of the tumor ad liver transplantation was therefore the only surgery offering complete resection. This treatment option is similar to the one applied in cases of hepatoblastoma, where it is well established. The child has recovered well and is completing his postoperative chemotherapy.
Conclusion: The treatment of embryonal liver sarcoma combines pre-operative chemotherapy followed by complete mass resection. Complete hepatectomy and liver transplantation should be considered in cases of unresectable tumors to ensure complete mass removal and thus increase survival probabilities.

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Severe cholestasis and immune deficiency at 1 month of age – an unusual initial presentation of cystic fibrosis

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Introduction: Cystic fibrosis (CF) is one of the most common genetic diseases in the Caucasian population. Cholestasis, pancreatic insufficiency and pulmonary infection are well-documented clinical complications of CF. However, neonatal cholestasis is a rare form of presentation and even rarer in combination with immunodeficiency.
Case: A 1 month old boy presented with feeding difficulties, weight loss >10% of birth weight, repetitive vomiting and discoloured stool. The clinical exam showed jaundice and hepatomegaly of 4 cm. Blood analysis revealed metabolic acidosis with a pH of 7.29. The Quick test was reduced to 29%, and PTT prolonged to 86.5 sec. Liver enzyme and bilirubin levels were elevated and he was admitted with a diagnosis of severe cholestasis. The management and evolution over the next 2 months included:
1 Cholangiography revealed bile slush necessitating a cholecystectomy and the placing of a biliary shunt which had to be removed 3 weeks later due to cholangitis with *E. faecium,* BLSE *Klebsiella pneumoniae* and *P. Aeruginosa.*
2 2 months later portal hypertension and ascites ensued.
3 Life-threatening RSV infection required intubation and bronchoscopy. Cultures revealed *Pneumocystis jiroveci, Strenotrophomonas maltophilia* and *Aspergillus spp.* Associated with neutropenia and low Ig levels this lead to an initial differential of severe combined immunodeficiency (SCID). However low Ig levels were ultimately explained by loss through enteropathy in a context of CF.
4 Exocrine pancreatic insufficiency was evidenced.
5 Newborn screening additionally revealed MCAD deficiency.
The newborn screening for CF (immune-reactive anti-trypsine levels) tested negative 3 consecutive times, and initial genetic analysis did not confirm any of the 19 most common mutations of the CFTR gene. Due to continued elevated clinical suspicion, 2 sweat tests were performed at an interval of 2 days and tested positive. Detailed genetic analyses of CFTR channels are still ongoing.

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Annuloplasty at Atrioventricular Canal Repair Improves Late Left Atrioventricular Valve Function

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Introduction: Annuloplasty at common atrioventricular canal (CAVC) repair has been used to improve left atrioventricular valve (LAVV) function. This report reviews our experience in annuloplasty at CAVC repair.
Methods: The demographic, procedural and outcome data were obtained for all children who underwent biventricular repair for complete CAVC from 2001 to 2011.
Results: 219 patients were included. This was a heterogeneous group of complex diseases, with 22 with heterotaxy, 37 tetralogy of Fallot or double outlet right ventricle, and 56 unbalanced CAVC. The cleft was closed completely in 192 patients (88%). 65 patients had annuloplasty (39 commissural, 32 posterior). There were 5 early deaths (2.3%). At discharge, 4 patients (1.9%) had more than mild regurgitation and no patients had significant inflow gradients. During a follow-up of 2.7 ± 2.1 years, there were 6 late deaths (2.8%) and 16 patients (7.3%) required LAVV reoperation. Two of 65 patients (3.1%) with annuloplasty required reoperation, compared to 14 of 148 without annuloplasty (9.5%, p = 0.16). In propensity-matched analysis, annuloplasty was significantly protective of ≥ moderate LAVV regurgitation (OR 0.19, p = 0.008) and non-significantly of reoperation (OR 0.28, p = 0.099). The propensity score matching was supported by similar findings in 1:1 case-control matched analysis.
Conclusion: LAVV function after CAVC repair continues to decline over time. Annuloplasty stabilizes LAVV function significantly and tends to reduce reoperations.

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Cardiac resynchronization therapy after anatomic repair for congenitally corrected transposition of the great arteries

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Introduction: Early results for anatomic repair of congenitally corrected transposition of the great arteries (ccTGA) are excellent. However, development of left ventricular dysfunction late after repair remains a concern. Ventricular pacing and prolonged QRS have been shown to be risk factors for left ventricular dysfunction. In this study we sought to determine factors leading to late left ventricular dysfunction and the impact of cardiac resynchronization as a primary and secondary (upgrade) mode of pacing.
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 arterial 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 32 months (range, 7 days to 7.2 years). The early deaths were excluded from further analysis. Twelve patients (12%) developed moderate or severe left ventricular dysfunction. Thirty-eight patients (38%) were pacing at latest follow-up. Seventeen patients had resynchronization therapy, 9 as an upgrade from a prior dual chamber system (8.5%) and 8 as a primary pacemaker (7.5%). 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 in 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 preclude the development of left ventricular dysfunction.

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Early diagnosis of congenital heart disease – did we improve?

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Background: 12 years ago, a study was published showing that in our referral population, cardiac diagnosis was made late in 10% of all patients with congenital heart disease (CHD) requiring therapy, resulting in late initiation of therapy according to accepted standards of treatment timing. The rate of late diagnosis was the same in cyanotic and acyanotic CHD with 10% in each.
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 patients) of acyanotic CHD. The 2 most frequent heart defects with delayed diagnosis were atrial septal defect and coarctation (7 and 6 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.

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Impact of Age and Duration of Banding on Left Ventricular Preparation Before Anatomic Repair for Congenitally Corrected Transposition of the Great Arteries

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Introduction: The optimal age and duration of left ventricular (LV) training in congenitally corrected transposition (ccTGA) with an unprepared LV is unknown. The objective of this study is to review the impact of age at pulmonary artery banding (PAB) and duration of ventricular training on LV function and aortic regurgitation (AR) after anatomic repair.
Methods: Retrospective chart review of all patients who underwent PA banding for LV training between 1962 and 2011. The primary endpoints were ≥ moderate LV dysfunction and ≥ moderate AR after anatomic repair.
Results: Twenty-five patients with ccTGA underwent PAB for LV preparation during the study period. There was 1 early death. 18 patients underwent anatomic repair at a median of 10 months (range 2 weeks – 11 years) from PAB. At most recent follow-up after anatomic repair, one patient developed moderate AR and 4 patients ≥ moderate LV dysfunction. AR and LV dysfunction developed in 4/6 patients banded after 2 years of age, compared to 0/12 patients banded before 2 years of age (P = 0.005). Following anatomic repair, composite endpoint was reached in 4/7 repaired after 3 years of age compared to 0/11 repaired before 3 years (P = 0.01).
Conclusion: Early PAB strategy is associated with favorable LV and neo-aortic valve function after anatomic repair for ccTGA with an unprepared LV. Candidates for anatomic repair who require LV training should be referred early in infancy for consideration of appropriate timing of PAB.

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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.

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Cantrell's Pentalogy: a rare congenital anomaly

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Introduction: Pentalogy of Cantrell is a rare congenital defect which combines five anomalies: a supraombilical abdominal wall defect, a lower sternal cleft, deficiency of the anterior diaphragm and 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 LV systolic 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 supraombilical hernia, a lower sternal defect, a deficiency of the anterior diaphragm and diaphragmatic portion of pericardium and confirmed the complete form of Pentalogy of Cantrell. Cardiac catheterisation confirmed the echocardiographic findings with infrasystemic reactive pulmonary hypertension secondary to overcirculation. Cardiac magnetic resonance showed a thick pouch of myocardial tissue arising from the apex of the left ventricle and contracting during systole, confirming the diagnosis of LV diverticulum. The child underwent VSD patch closure and resection of the LV diverticulum, with an uncomplicated post-operative course. Surgical repair of the abdominal wall defect was undertaken in a second stage, to avoid excessive bleeding from the anticoagulation necessary for cardio-pulmonary bypass.
Conclusion: We report a rare patient with complete pentalogy of Cantrell associated with an LV diverticulum, who underwent uncomplicated full repair.

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Eisenmenger in infancy – is it triggered by combined pressure-volume pulmonary blood flow rather than by increased pulmonary venous pressure alone? Immediate and midterm normalized pulmonary artery pressures in a 6 year old child with cor triatriatum after repair. A case report

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Introduction: Eisenmenger disease describes a condition with fixed pulmonary hypertension. Mostly congenital heart malformations with increased pulmonary arterial pressure and blood flow (VSD, ASD, PDA) or elevated pulmonary venous pressure (mitral stenosis, cor triatriatum, obstructed pulmonary veins) are thought to be responsible for the irreversible remodeling of the pulmonary vasculature. If such a condition is left untreated for approximately 2 years, failure of normal regression of the intimal smooth muscles occurs. We report on a 6 year old child from Togo with severe pulmonary hypertension due to an untreated cor triatriatum.
Material: 6 year old boy from Togo. At rest slight tachypnea of 40–45/min, thoracic deformation (cardiac voussure), saturation in room air >96%.
Methods: Echocardiography with diagnosis of a cor triatriatum, severe pulmonary arterial hypertension (TI gradient 150 mm Hg, BP 100/45 mm Hg, gradient over membran of cor triatriatum 55/15 mm Hg). No atrial or ventricular septal defect. At mild exertion (walking to outpatient clinic) immediate desaturation to 80% in room air with fatigue.
Results: After surgical repair the patient showed immediate recovery from pulmonary hypertension: 1/3 pulmonary arterial pressure while coming off bypass circulation with Milrinon but without antihypertensive treatment (NO, Prostacyline). After 6weeks improved physical performance with no desaturation while walking. Echocardiography with no evidence for pulmonary hypertension.
Conclusion: Excessive high pressure-volume pulmonary blood flow is most harmful for the pulmonary vascular bed and leads to early fixed pulmonary hypertension. This case illustrates that increased pulmonary venous pressure alone related to obstructive lesions such as a cor triatriatum behave hemodynamically similar to severe mitral stenosis in adults. In contrast to the high pressure-volume state in large shunt lesions who develop usually over a period of 24 to 48 months a fixed pulmonary hypertension these patients obviously have a great potential to recover from pulmonary hypertension regardless their age.

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Going down, going slow – Esmolol as potent myocardial protector in rescue cardiac extracorporal membrane oxygenation (ECMO)

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Introduction: Cardiac failure or arrest post elective cardiac surgery in neonates and children are rare events. However their occurrence during a highly vulnerable period of myocardial recovery imply immediate expert support. Timing, efficiency of resuscitation and duration of cannulation for ECMO are crucial. Equally important is the subsequent cardiovascular management to optimize myocardial recovery. Beside volume unloading, optimal coronary perfusion has to be maintained to protect cardiomyocytes from oxidative stress. Beta blockers combine cardioprotective mechanisms such as improved myocardial relaxation, coronary perfusion and also antioxidative activity.
Methods: Patients (n = 6) requiring rescue ECMO post elective cardiac surgery. They were started on Esmolol infusion as soon as stabilized (full flow ECMO ≥150 ml/kg/min). Serial transthoracic echocardiography was performed to assess myocardial contractility.
Results: 6 patients (2 male, 4 female), age 2.2 ± 4.1y with single ventricle physiology (n = 3), complex cyanotic heart disease (n = 2), coronary anomaly (n = 1). All patients had myocardial stunning. ECMO 8.8 ± 1.9 days, maximum dose Esmolol 106.7 ± 50.1 µg/kg/min, maximum heart rate (HR) prior to Esmolol 168.3 ± 11.7 beats per minute (bpm), maximum heart rate during Esmolol 73.3 ± 8.2 bpm, fractional shortning (FS) prior to Esmolol 9.2 ± 4.9%, FS post Esmolol 33.3 ± 7.5%. Weaning of ECMO successful in 4 patients.
Conclusions: In this small pilot study without case control, all patients showed significant improved myocardial contractility. Esmolol appears to provide cardioprotection for pediatric patients post cardiac failure / arrest requiring ECMO. Its combined antioxidative effect may support recovery of myocytes by increased gluthation peroxidise and superoxide dismutase activity.

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Congenital central hypoventilation syndrome (Undine syndrome) with recurrent hypercapnia and hypoxemia 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 autonomous nervous system. The incidence is estimated to be at 1 of 200,000 livebirths. Due to reccurent hypercapnia 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 3883m 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 3883 m above sea level all US subjects showed only mild increase in PHT in regards to baseline while controls developped moderate to severe pulmonary hypertension (38 ± 7 mm Hg vs. 55 ± 17 mm Hg).
Conclusion: 1. Despite recurrent hypercapnia US patients show high normal vascular function. We speculate endothelial preconditioning (recurrent hypercapnia as stimulus). Until today recurrent hypercapnia 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.

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

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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 varing degrees of genital anomalies. 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 rigth 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, for risk of malignancy of 50%. In accordance with the familly's wish, it was decided to attribute the female gender and postpone the surgical procedure until the child can participate in the deciscion according to the Swiss national ethical committee guidelines. In conclusion, most 45,X/46,XY cases remain undiagnosed, but the phenotypes of these patients vary greatly. So treating each patient individually is the most important step in the clincal management.

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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. Most parents tend to disfavor postponing 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 (normality 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, regardless of the consensus statement of 2005 and the subsequent call for multidisciplinary management.

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

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Introduction: Osteogenesis imperfecta (OI) is a 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 pregnancies and neonates with severe forms of OI is a challenge for patients and caregivers.
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 Prevot nails. Intravenous bisphosphonate therapy with Neridronat was started at the age of 7 weeks. Neridronate, 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 heterogenity. Diagnosis is usually suspected clinically but must be confirmed by radiological, biochemical and molecular findings.

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Neonatal thyrotoxicosis -potentially life-threatening!

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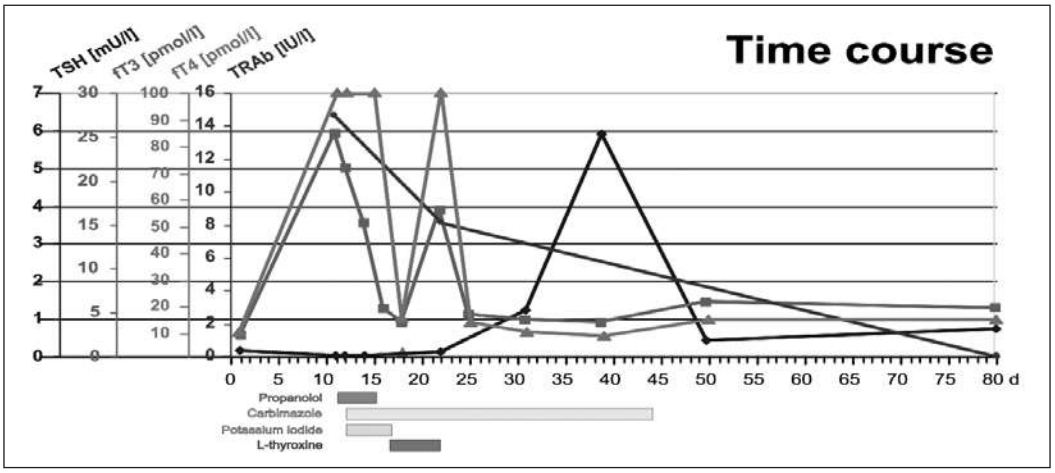
Background: Neonatal Graves'disease is a rare but potentially life-threatening condition in offspring of mothers with Graves' disease and elevated TRAb during pregnancy.
Case report: We report on a female term baby of a mother with highly active Graves'disease during pregnancy. The baby was presented 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.



Pneumology – Allergology – Miscellaneous

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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.

ED Presentation and Clinical Course Among Episodes RSV versus non-RSV

	RSV (n = 157)	non-RSV (n = 425)	P
Age, mean ± SD, months	4.2 ± 3.4	6.4 ± 2.9	<0.001
Age of <3 months, %	49	14	<0.001
Respiratory rate > normal for age, %	78	68	0.015
Oxygen saturation (room air), mean ± SD	94.9 ± 4.5	96.8 ± 3.7	<0.001
Hospitalization Ward/ICU, %	83	12	<0.001
Length of hospitalization, mean ± SD, days	5.1 ± 3.6	3.7 ± 2.8	0.01
Hospitalization in ICU, %	8	1	<0.001
Nasogastric tube, %	44	4	<0.001
Length of Nasogastric tube, mean ± SD, days	4.0 ± 3.4	3.6 ± 3.3	0.70
Length of Oxygentherapy, mean ± SD, days	3.1 ± 2.6	1.9 ± 2.4	0.006
Reconsultation after ED discharge, %	12	5	0.002

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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 under one 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 for odds ratio were analyzed 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 indicated that LOS of more than 4 days was more likely in children with age <6 months (odds ratio[OR] = 4.0; 95% confidence interval[CI]:2.0–7.9), RSV positive (OR = 2.6;95%CI:1.3–5.2), hospitalization in ICU (OR = 3.0;95%CI:1.0–8.9), need of nasogastric tube (NGT) (OR = 10.6;95%CI:5.4-21.2), presence of focal opacity in chest radiograph (OR = 6.4; 95%CI:1.5–27.4) and pC02 >6KPa (OR = 4.8;95%CI:1.3–17.2). Univariate linear regression analysis identified length of NGT (P <0.001) and length of oxygen therapy (P <0.001) as factors associated with longer LOS. In multivariate analysis the risk factors that remained significant were length of oxygen therapy, young age (<6 months) and need and length of NGT.
Conclusions: This study identified that younger age associated with NGT and oxygen therapy were the most important determinants of longer 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 tidal breathing test to assess ventilation inhomogeneity (VI) in cystic fibrosis (CF) patient. Two breathing protocols are currently used for measurement: Free tidal breathing or 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 (Exhalyzer 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 Sacin.
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, Scond increased significantly. No change was seen in Sacin. Changes of N2MBW indices were heterogeneous with increasing variability within tests and between subjects.
Conclusion: Fixed tidal breathing protocols impact severely upon 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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Hereditary angioedema with normal C1 inhibitor function: an important differencial diagnosis of anaphylaxis

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Introduction: Angioedema associated with urticaria is a frequent condition in children. Mostly idiopathic or peri-infectious, it can be due to an allergy to food or various drugs. Hereditary angioedema (HAE) represent a rare but challenging differential diagnosis of acute angioedema, particularly in children. Its presentation can be similar to other more frequent causes of angioedema due to histaminic release. HAE is associated with an either quantitative (Type I) or qualitative (type II) deficiency of the protein C1 esterase inhibitor (C1-INH). Recently HAE with normal C1-INH activity (HAEnC1-INH), occurring in woman and influenced by oestrogens has been described.
Results: We report of a 10-year-old boy who presented with subacute edema of the eyelids, the right hand, the left foot and the penis as well as dysphagia and epigastric pain. He also presented itchy urticarial lesions on both hands and feet for about 10 days. No triggering drug, food or infection could be identified. Six years prior to this episode, he experienced a similar attack of angioedema while taking ibuprofen for a viral upper airway infection. Family history revealed maternal episodes of angioedema in childhood. The sister of the mother had also described similar symptoms. No other family members were affected. Physical examination was remarkable for pale edema of the penis, the right hand and left foot, the uvula and the anterior peri-tonsillar pillars. Symptoms rapidly disappeared after injection of icatibant with complete regression after about 3–5 hours. Laboratory findings during acute episode showed normal serum tryptase, fraction 3 and 4 of the complement levels, CH50 and C1-INH function. Exploration of the bradykinin metabolism showed an increased spontaneous activity of kinin-producing kininogenases. None of the two known mutations (Thr328Lys/Arg) of factor XII (FXII) gene that can be associated with angioedema with normal C1 inhibitor function have been found.
Conclusion: A diagnosis of hereditary angioedema with normal C1 inhibitor funtion (HAEnC1-INH) was suspected in presence of a normal initial work-up including C1-INH activity and C4 level. The pathogenesis is thought to be mainly due to a gain of function of the kinin-producing kininogenases. Only a few pediatric cases have been published so far, all females. With this first pediatric male case of HAE with normal C1 inhibitor function we want to emphasize that angioedema with normal C1-INH might also occur in pediatric population, independent on gender and hormonal influence, representing an important differential diagnosis of anaphylaxis. No consensus for treatment, either prophylactic or during acute attacks has been published for HAEnC1-INH. Treatment is mainly based on the clinical experience of addressing other forms of HAE and isolated case reports.

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Decreased breath-by-breath variability of expired CO_2 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 CO_2 volume ($VeCO_2$) 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 CO_2 fraction vs. expired volume) were obtained by mainstream capnography and the the area under the CO_2 curve was used to calculate the $VeCO_2$. The ratio of the $VeCO_2$ over the expiratory volume ($VeCO_2$/Ve) was used as surrogate for the amount of the expired CO_2 per breath. The relative $VeCO_2$/Ve change, and the domain areas of the two- and three-dimensional embedding plots of $VeCO_2$/Ve with one-breath lag, were used as measures of $VeCO_2$/Ve variability.
Results: All indices of interest differed significantly between the two groups. BPD infants had lower relative $VeCO_2$/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 – 18.2] vs. 17.8 [11.0 – 22.9]; 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 VeCO2/Ve 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.

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 pneumonia* (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 (0–10); 0d (0–40), respectively). Median (range) length of stay was 13 (7–42) and 15d (8–140), respectively. Complications occurred in 3/23 children without NP (pneumothorax, bronchopleural fistula, pneumotocele) 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 were observed, between children with or without risks factors. CT scan might be questionable if just done to diagnose 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 betalactams 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 incriminated antibiotic. Basophils activation tests (BAT) were done according to manufacturer protocol (Buhlmann, Switzerland).
Results: We analyzed data 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 macula-papular rash during treatment with a BL.

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Hospitalized lung infection in children: a 6-years observational study in Geneva

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Introduction: Pulmonary infection is a major care problem, and one of the main causes of hospitalization, morbidity and mortality. We aimed to study the characteristics of patients hospitalized because of pulmonary infection, in the period preceding the implementation of 13-valent pneumococcal vaccine in Switzerland.
Method: In this observational and retrospective study, we included all children (below 16 years) hospitalized from January 2005 to December 2011 in Geneva University Hospital, with a diagnosis of pneumonia, pneumopathy, empyema or pulmonary abscess. Empyemas were confirmed, according to published criteria (Hardy W et al., Clin Infect Dis 1996). Collected data were: age, hospital length of stay, diagnosis, pathogen(s), pulmonary complication(s), and co-morbidity(ies).
Results: We included 382 children (mean (SD) age: 4.4 (4.1) years), undergoing 387 hospitalizations (mean (SD) duration: 10.7 (13.4) days). 48 children presented a co-morbidity, mainly asthma (n = 16, 33%) and cardiopathy (n = 16, 33%). Diagnoses were pneumonia (72%) including necrotizing pneumonia (1.5%), pneumonia with para-pneumonic effusion (9.6%), and empyema (16.3%) including confirmed empyema (12.4%), and lung abscess (2.1%). Microbiologic diagnosis were bacteria (64.2%), virus (33.7%) and fungus (0.5%) infection. Bacteria findings were *Streptoccocus Pneumoniae* (27.8%), *Mycoplasma Pneumoniae* (18.1%), *Haemophilus Influenzae* (8.1%), *Pseudomonas Aeruginosa* (6.4%), *Staphyloccocus* (3.6%), others (7.2%), and unknown bacteria (28.6%). Virus findings were Respiratory Syncitial Virus (50.4%), Influenza (6.9%), Paramyxovirus (5.3%), Adenovirus (3%), others (5.3%) and unknown virus (26.7%).
Conclusion: In hospitalized patients, we found a very high rate of pathogens agents. The knowledge of the pathogens and type of pulmonary infection will help us to improve the management of children, in terms of microbiological testing and antibiotic treatment. Those data, collected in the period preceding the 13-valent pneumococcal vaccine, will be further compared with the ones collected since its implementation, in order to study potential changes in incidence, pathogens or severity of pulmonary infections.

P 99

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 pink, foamy sputum 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: Preterms with BPD among others need a regular pulmonary follow-up to correctly advice daily activity on an individual basis.

P 100

Prognostic factors for the outcome of congenital omphalocele

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Background: Congenital omphaloceles [CO] are known to be a very variable condition regarding size (small omphalocele [sCO] vs. giant omphalocele [gCO]), associated malformations and prognosis. Predictive prognostic factors are largely unknown.
Methods: Analysis of retrospective data of all newborn patients with CO treated in our hospital between 2009 and 2012.
Results: 75% (6/8) of the subjects were diagnosed with a gCO. Two were born preterm (34 1/7 WG with sCO, 35 5/7 WG with gCO). In 50% of all patients associated malformations were found (averaging 1.125 malformations per patient) affecting the cardiovascular (n = 4), bronchopulmonal (n = 3), gastrointestinal (n = 1), urogenital (n = 1) and otorhinolaryngeal (n = 1) organ system. In all subjects surgical repair of the CO was performed. Six children survived the initial hospitalisation; two died during the initial hospitalisation aged 167 and 308 days, respectively. Of the non-surviving subjects both had gCO and were diagnosed with a cardiovascular and a bronchopulmonal associated malformation. Both patients showed malacia of the left main bronchus in flexible bronchoscopy and were mechanically ventilated throughout the initial hospitalisation. No surviving patient died after discharge.
Conclusion: Our results suggest the giant form of CO and the number of associated malformations (bronchomalacia in particular) to be negative prognostic factors in CO. Data analysis has not been completed; detailed results will be presented at the congress.

P 101

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 ΔF508/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, increasing abdominal pain and impairment of general condition in the further progress. He presented at a local hospital, without further diagnostic procedures or intervention. Upon urge of his mother he returned early on day seven.
Physical examination: Considerably reduced general condition, cardiopulmonary stable, subfebrile temperatures and signs of severe dehydration.
Laboratory results: Leukocytes 25.100/µl, CRP 41 mg/l, urea 32.9 mmol/l, creatinine 342 mmol/l, uric acid 1460 µmol/l, sodium 112 mmol/l, chloride 47 mmol/l, potassium 3.4 mmol/l, pH 7.51, HCO_3 37.8 mmol/l, BE 15.5 mmol/l.
Diagnosis: Pseudo-Bartter's syndrome (metabolic alkalosis with hyponatraemia, hypokalemia and hypochloraemia) with prerenal acute renal failure and dehydration in a patient with CF and salt wasting. In addition, non-bacterial pulmonary inflammatory syndrome as result of severe dehydration with prolonged decrease of pulmonary function.
Pathophysiology: As a result of high outside temperature and insufficient salt intake and based on the CF basic defect, development of a hyponatraemia with intensive vomiting 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 normalisation 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 consiliton. In patients with CF presenting gastrointestinal symptoms, pseudo-Bartter's syndrome should be included in the differential diagnosis and a BGA should be made.

P 102

Advantages of flexible bronchoscopy in management of foreign body aspiration in children

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Introduction: Inhalation of foreign bodies (FB) is a frequent and serious condition during childhood. The situation requires a rapid diagnosis based on anamnestic, clinical and radiological finding to allow rapid intervention. Although rigid bronchoscopy is the diagnostic and therapeutic method of choice, flexible bronchoscopy can now have its role in this management.
Methods: We included children having undergone bronchoscopy (flexible and/or rigid) for suspected FB inhalation in our institution, from January 2009 to December 2011. Data were retrospectively collected: age, gender, clinical presentation, radiological finding, final diagnosis, type and location of FB, management (flexible or rigid bronchoscopy or both) and outcome.
Results: 42 children, with a median age of 36,8 months (9 months–16 years), sex ratio: 1,62 were included for suspected FB inhalation. 31 flexible bronchoscopy, 9 combined flexible and rigid bronchoscopy and 2 rigid bronchoscopy were performed. Presence of a FB was confirmed in 14 children, median age: 27,1 months (10 months-13,6 years), sex ratio: 2,5. Main symptoms were cough (n = 40), history of choking (n = 26) and dyspnea (n = 20). If FB was confirmed, choking was found in 13/14 children. Physical examination was normal in 18 cases, most often in absence of FB. Main radiological findings were: inspiration/expiration changes (n = 11) and located air trapping (n = 8). Chest X-Ray was normal in 18 cases, most often if negative bronchoscopy (table 1). The combinaison of history, clinical signs and radiological signs are more specific than each one separately (PPV: 0,89, NPV: 0,82) In case of FB, 9 were removed by combined flexible and rigid bronchoscopy, 4 by flexible bronchoscopy alone and 1 by rigid bronchoscopy alone. Rigid bronchoscopy was negative in only one case. Complications are rare: inflammation (9), infection (5), fragmentation (5), granuloma (2), desaturation (3). No failure of extraction.
Conclusion: Foreign body was found in 33,33% of the suspected cases. Flexible bronchoscopy can have a real place in case of suspicion of foreign body aspiration in children: avoid negative rigid bronchoscopy and allow removal of the foreign body in some cases.

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

	CE + (n = 14)	CE – (n = 28)	P
Cough, %	100%	93%	0.439
Hystory of choking, %	93%	46%	0.003
Cyanosis, %	50%	21%	0.064
Stridor, %	14%	11%	0.547
Dyspnea, %	71%	36%	0.031
Presence of viral symptoms,%	21%	54%	0.047
Abnormal clinical signs, %	86%	43%	0.009
Abnormal chest radiographic findings, %	67%*	36%	0.073

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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 inhalated epinephrine and systemic glucocorticoids was not effective. After measurement of a very high procalcitonine level 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 croup in absence of clinical response to inhalated epinephrine and systemic glucocorticoids. In our opinion procalcitonin can be particulary helpful of a possible quickly severe evolution.

P 104

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 CISs 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 siblings. 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 bear in mind this impact and acknowledge the siblings as well as help parents deal with a sick child and his/her siblings in an equal manner.

P 105

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) (6 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 CIAs wanted to be considered as normal. While some CIAs 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 CIAs 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.

P 146

Hypotonia and weakness; don't forget the Pompe disease

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Introduction: Pompe disease (also called Glycogen storage disease type II) is an autosomal recessive metabolic disorder described in 1932 by the Dutch pathologist J.C.Pompe. This pathology is a lysosomal storage disease secondary to lysosomal acid alpha-glucosidase enzyme deficiency leading to lysosomial accumulation of glycogen which particularly affects the skeletal and respiratory muscles. The estimated incidence is about 1/138,000 for the infantile form. The build-up of glycogen causes progressive muscle weakness throughout the body and affects various body tissues, particularly the heart, skeletal muscles, liver and nervous system.
Case-Report: a 3 year old female patient presented with diffuse muscle weakness lasting for one year associated with difficulty to seat down and stand up. The familial history was negative. Clinical examination was remarkable for hypotonia and weakness of the limbs. The initial investigations indicated markedly increased serum creatine kinase at 1217 u/l without inflammatory markers and the chest X-ray was normal. A muscle biopsy was performed and microscopic analysis revealed a vacuolar myopathy with accumulation of glycogen. The electrocardiogram was remarkable for left ventricular hypertrophy and the echocardiography revealed mild hypertrophic cardiomyopathy, a rare finding at this age. Polygraphy revealed sleep disordered breathing leading to nocturnal hypoventilation with hypoxemia (median SaO_2 = 90%, minimal SaO_2: 81%) and permanent hypercapnia (median pCO_2: 7.04 kPa, maximal pCO2: 7.41 kPa) that indicating nocturnal noninvasive positive pressure ventilation. Genetic analyzis was positive for a deficiency of alpha –Glucosidase, confirming our suspicion of muscle disorder and allowing for the diagnosis of Pompe disease.
Conclusion: Glycogen storage disease type II is a rare and invalidant disease. Early detection and treatment is extremely important because untreated patients with the infantile form are at risk of death in the first two years of life secondary to cardio-respiratory failure. In addition to physical and occupational therapy, enzyme substitution with alglucosidase alfa is available and the drug has obtained European marketing authorization as an orphan drug for the treatment of patients with Pompe disease.

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Plastic Bronchitis in Monozygotic Twins caused by Bocavirus Infection: Coincidence or Proof of a Genetic Predisposition?

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Plastic bronchitis is an extremely rare disease characterized by the formation of tracheobronchial airway casts, which are composed of a fibrinous 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.

P 107

Thoracic asymmetry and limited mobilisation of right arm

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Case report: A 3 years old immunocompetent boy presented with 4 days fever and 1 day right thoracic asymmetry. Exam showed limited mobilisation of right arm and 1 cm supraclavicular adenopathy. Blood tests revealed leukocytosis (19 G/l), thrombocytosis and elevated CRP (273 mg/l). Thoracic MRI showed an extra- and intrathoracic abscess

extending to the pleura with empyema of the pulmonary middle-lobe and multiple adenopathies. IV antibiotherapy was given during 3 weeks. Collection's puncture detected an MSSA. There were neither traumatisms nor insect bites. No tuberculosis, cat-scratch disease or endocarditis were 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 cytopathologic 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 actinomyces, fusobacterium or parasites.The management request a combination of abscess drainage and prolonged antibiotherapy.
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.

P 108

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 marrow 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 a precipitous fall in at least two blood cell lines, fibrinogen and ESR despite persistently high CRP, serum transaminases, triglycerides and ferritin. Treatment includes high dose IV steroids and ciclosporin.
Conclusion: A sudden drop in the platelet count, particularly in combination with increase in serum ferritin levels, should raise a suspicion of impending MAS, a complication with a high mortality rate (up to 30%). As occurs in our case, MAS episode can be recurrent, thus all patients require closer monitoring.

P 109

Homeostasis and function of a potent regulatory T cell subset in wildtype and lymphopenic mice

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Introduction: Regulatory T cells (T_{reg}) 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 T_{reg} pool consists of different T_{reg} effector populations that are likely involved in different biological processes utilizing distinct regulatory pathways. To investigate this issue further, we have analysed wildtype (WT) and T cell lymphopenic mice for the presence and function of T_{reg} cells.
Methods: T_{reg} 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 α_E/β_7 integrin (CD103), functionally different T_{reg} subpopulations were identified that demonstrate a marked hierarchy in their in vitro and in vivo regulatory potential: $ICOS^{pos}CD103^{neg}$ (designated ICOS) and $ICOS^{pos}CD103^{pos}$ (double positive, DP) T_{reg} display a significantly higher degree of CD4 responder inhibition than $ICOS^{neg}CD103^{neg}$ (double negative, DN) T_{reg} and $ICOS^{neg}CD103^{pos}$ (CD103) T_{reg}. 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 T_{reg} subpopulations. T cell lymphopenia causes a significant thymus-independent over-representation of the potent inhibitory DP T_{reg} subset within the lymph nodes but not the spleen, a pattern strongly correlating with IL-7 availability and reflected by high IL-7 receptor α expression on DP T_{reg}.
Conclusion: T_{reg} function and homeostasis differ between discrete T_{reg} populations as defined by the expression of CD103 and ICOS, a fact that needs to be acknowledged when assessing T_{reg} biology in health and disease.

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β-catenin function is required for thymus organogenesis and maintenance

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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 third pharyngeal pouch become committed to a 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 and developmental stage 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, γ-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.

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A severe case of EBV associated encephalitis

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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 first week. Hospital admission occurred due to repetitive tonic-clonic seizures and depressed level of consciousness requiring intubation and admission to the PICU. Until confirmation of diagnosis she was empirically treated with intravenous antibacterial and antiviral drugs. Clinical seizures stopped on day 2 under phenobarbital treatment. MR scan on day 3 showed cortical swelling and signs of a vasogenic edema in the left temporal lobe. Clinical improvement allowed for extubation on day 4. On the same day positive EBV VCA IgM as well as negative ENBA IgG in blood samples confirmed EBV infection. PCR assay detected EBV DNA in blood and cerebral fluid, whereas it was negative for HSV DNA. Neurologic examination on day 5 revealed affective instability and memory problems. At 6-month follow up there were still neurocognitive deficits characterized by concentration and memory problems and anomic aphasia.
In retrospect the patient history was clearly suggestive of EBV infection. Especially the bilateral upper eye-lid swelling are very specific for EBV infection. The latter finding, also known as Hoagland sign, can be seen in up to 10% of patients with mononucleosis infectiosa.

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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 Contegra tube. Upon arrival he presented intermittently low-grade fever with hepatosplenomegaly, glomerular hematuria, a high level of blood inflammation, anti-neutrophil cytoplasmic antibodies (ANCA) and a Coombs positive 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 broad-range PCR in the blood were negative. PCR of the Contegra valve but not of the Contegra tube were positive for *Coxiella burnetii.* Serologies for phase I and phase II IgG and IgM were highly positive. There were neither liver lesions in abdominal ultrasound nor bone lesions in a total body MRI. Treatment was adjusted to hydroxychloroquin and doxycycline 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: Children with 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.

P 113

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 biopsy and specific circulating antibodies.
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 contagiosa with systemic erythromycin and a local antibiotic ointment 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. Treatment with high dose prednisone (2 mg/kg/d) was started and led to rapid initial improvement. 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 it may mimic more common skin conditions including bullous impetigo contagiosa, urticarial eczema or erythema multiforme. Prognosis is generally good with appropriate treatment and remission is usually achieved within one year.

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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 to be sterile 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/clavulanate (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 <P3, 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/clavulanate 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 blood for an interferon gamma release test (IGRA, 27.53 IU/ml with good mitogen stimulation), aspirated gastric and bronchial fluid (where no acid fast bacilli could be detected in the ziehl-neelsen stain). Pleurocentesis revealed an exsudate (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 pyrazinamid. 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 *S. pneumoniae* 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 typically 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.

P 115

A new primary immunodeficiency FILS-Syndrome with facial dysmorphism, immunodeficiency, livedo, and short stature is caused by Polymerase epsilon 1 mutation

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DNA polymerase epsilon plays an important role in synthesis of new DNA and is also implicated in a wide variety of cellular processes, including cell cycle progression and DNA repair. We describe a novel clinical entity in patients with facial dysmorphism, immunodeficiency, livedo and short stature ("FILS syndrome"). Of note, the patients did not show increased susceptibility to malignancies. In these patients, we have found a homozygous missense mutation in *POLE1,* encoding the catalytic subunit of DNA polymerase epsilon. The mutation results in an alternative splicing which dramatically reduces protein expression. Proliferation of the patients' lymphocytes and G1- to S-phase progression in the cell cycle *in vitro* was impaired. Depletion of DNA polymerase epsilon also impaired G1- to S-phase progression in B-lymphocytes, chondrocytes and osteoblasts. Our data show the impact of a deficiency of DNA polymerase epsilon catalytic subunit in a newly recognized, genetic human disorder.

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Subchronic infection of the sternum by Coxiella burnetii

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Introduction: Q fever is an acute or chronic infection caused by Coxiella burnetii, a highly infectious zoonotic intracellular bacterium, rarely diagnosed in children. Transmission occurs through inhalation, direct contact or consumption of unpasteurized milk. Not much evidence is available on treatment strategy in children. Thus, duration of antibiotic treatment and follow up is guided by serology. We report a case of a 4-year-old farm boy presenting with a localized subchronic Coxiella burnetii infection of the sternum.
Case Report: A 4-year-old farm boy consuming raw milk on regular basis, presented himself six weeks after a minor trauma with progressive yet painless swelling of the lower sternum. Neither clinical signs nor symptoms indicated localized or systemic infection. ESR and CRP values were normal. Suspecting an organized hematoma, we decided to puncture the swelling. To our surprise, suppurative fluid was aspirated. Chest radiography revealed some diffuse lysis of the sternal periosteum. While bacterial culture of the aspirate was negative, eubacterial PCR diagnostic revealed Coxiella burnetii. In addition, serology (IF) was positive (Phase I > Phase II) pinpointing subchronic infection. As a consequence, the patient was started on an antimicrobial treatment with TMP/SMX (Co-Trimoxazole).

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.

P 117

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 multiorgan 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 rush on day 1 after septorhinoplasty, 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.

P 118

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, antibiotherapy 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.

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Neuroborreliosis-associated cerebral vasculitis – an uncommon manifestation of Lyme disease

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Introduction: Lyme disease caused by Borrelia burgdorferi is the most common vector-borne illness in Europe. In about 10 to 15% of patients the peripheral or central nervous system is involved. We describe a rare manifestation of neuroborreliosis-associated cerebral vasculitis with cerebellar microinfarction and subtotal vascular occlusion of the vertebral and basilar arteries in a paediatric patient.
Case report: A nine year old boy was referred to our paediatric department presenting with chronic fatigue, headache, intermittent nausea, vomiting and abdominal pain for 2 months. He had a medical history of erythema migrans 2 years ago treated adaquately with amoxicillin for 2 weeks. At admission, physical examination revealed only an intermittent mild postural tremor of both hands and a mild nystagmus. A cerebral MRI angiography was performed, showing two fresh small cerebellar infarctions in the posterior inferior cerebellar artery area and diameter irregularities of the basilar artery, highly suspicious of an underlying vasculitis. Conventional cerebral angiography detected a subtotal occlusion of the basilar and bilateral vertebral arteries with retrograde bloodflow to the posterior cerebral circulation. Extended immunological, hematological and endocrinological laboratory evaluation revealed no abnormalities. Instead, *Borrelia burdorferi* serology was positive for IgM and IgG, with confirmation of four positive bands in Western blot. The cerebrospinal fluid showed a lymphocytosis with increased protein and decreased glucose levels along with an intrathecal production of *Borrelia burgdorferi* IgM antibodies. Due to these results we postulated an underlying neuroborreliosis and started to treat with intravenous ceftriaxon for 3 weeks. In addition, acetylsaliciylic acid was started to prevent new infarction and oral prednisolone to treat possible cerebral vascular inflammation. Clinical symptoms subsequently improved, and neurological examination returned to normal. A follow-up lumbar puncture three weeks later showed a reduction in pleocytosis and a normalization of liquor protein. The following MRI angiography two months later showed the absence of cerebellar diffusion restrictions, but an unchanged presentation of the basilar and bilateral vertebral arteries occlusion.
Conclusion: Lyme disease as underlying cause of cerebral vasculitis is a rare manifestation and only described by few authors. In our patient, even though a vascular biopsy was not performed due to the sensitive anatomic localization, the cerebral vascular findings leading to multiple cerebral infarction and arterial occlusion are highly suspicious of Lyme neuroborreliosis.

P 120

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 (bili199 mmol/l) with ABO 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 favour of spherocytosis. Over the first year, despite clinically well tolerated anemia, nine transfusions were required for Hb level <60 g/l.
Discussion: HS diagnosis may be difficult in newborns. Although transmission is mainly autosomal dominant, few cases are 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.

P 121

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 infection, malignancy, immunodeficiency or autoimmune process. 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, without known medical history, presented with fever without focus. Initial investigations showed isolated moderate thrombopenia and elevated CRP leading to introduction of antibiotics while waiting culture results. Few days later appeared livedo, hepatosplenomegaly with moderately elevated liver enzymes and pancytopenia, associated with persistence of fever and inflammatory syndrome, leading to extensive investigations that revealed elevated ferritine and triglycerides and lowered fibrinogen. Clinical presentation was complicated by repeated clonic seizures with favorable evolution under Levetiracetam, and respiratory insufficiency caused by pulmonary hemorrhage and requiring intubation. The bone marrow aspiration performed ten days after admission confirmed the suspicion of HLH and a treatment was immediately started with dexamethasone, etoposid and ciclosporine, with subsequent addition of anti-thymoglobulin because of clinical severity. The clinical and laboratory responses were excellent under treatment with almost complete remission. The genetic analyses returned positive for double heterozygotous 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.

P 122

Spherocytosis – no rule without exception

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Introduction: Hereditary spherocytosis (HS) is the most common hemolytic 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 departement 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 recticulocytosis 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 anemia, 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 suspicious for hereditary spherocytosis and the osmotic resistance of the parents was completely normal. However further fragility tests became positive together with ektacytrometry. Eosin-5-maleimidic test (EMA-test), membrane protein and gene analysis were not performed. Until now 9 packed red blood cell transfusions were needed. Hereditary elliptocytosis, pyropoikilocytosis, stomatocytosis and xerocytosis were excluded so far. The majority of patients with HS has an autosomal dominant inheritance. This is a case of a child with an unusual, but in the literature described, presentation of a membranous chronic haemolytic anaemia.

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Neurofibromatosis 1 (NF1) increases incidence of different types of pediatric cancers

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Introduction: Neurofibromatosis is a group of autosomal dominant genetic disorders, which are known to increase the frequency of some benign and malignant tumors among children and adults.
NF1 affects 1/3000 live births and relates to a mutation that affects neurofibromin, a protein implicated in the RAS signaling pathway, important determinant of cell growth and regulation. The overall risk of malignancy in NF1 is estimated at between 5 and 15 percent of affected individuals, a rate approximately 2.5 to fourfold higher than that of the general population. The predominant tumors associated with NF1 are plexiform neurofibromas, optic pathway gliomas and malignant peripheral nerve sheath tumours. We report here the case of two patients with NF1 who presented during the last year with malignant tumors.
Case 1: a 5-year old girl, known for a proximal limb weakness and multiple café-au-lait spots, presented with walk refusal and abdominal pain. The radiologic investigations showed an abdominal mass with histologic findings that led to a diagnosis of multimetastatic Stage IV Neuroblastoma. An unknown, probably pathogenic mutation of the neurofibromin was found in the germline DNA.
Case 2: a 15-year-old boy, known for NF1, with numerous subcutaneous neurofibromas, presented with a rapidly progressive painless left thigh mass (diameter 10 cm). Biopsy confirmed the diagnosis of Malignant Peripheral Nerve Sheath Tumor (MPNST) without radiologic evidence of metastatic disease.
Conclusion: As the disease associates various oncologic and non-oncologic complications, children with NF should be yearly evaluated within a multidisciplinary approach. At the oncologic level, special attention should be pay to any change in consistency, pain or growth pattern of an existing plexiform neurofibroma. Also signs of increased intracranial pressure, precocious puberty, ophthalmologic symptoms or any unexplained complication should motive investigation to exclude tumoral origin.

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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 doctors and nurses encounter 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 catheterization without any further sequelae. The second patient was a 2-year old girl who developed subcutaneous edema after flushing the PAC. Disconnection of the PAC was seen on x-ray and echocardiography, and the device was removed surgically.
Conclusion: Our two cases highlight the importance of immediate diagnostic work-up of PAC-associated problems. Standard operating procedures for PAC-associated complications like pain, clotted line or paravasation should be available for medical personnel who is in charge of these patients. 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.

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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 intermittent normal mean 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 crusts on the scalp as well as recurrent enoral candida. A thrombocytopenia 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 alloimmune 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 initial atypical dermatological presentation with blisters and crusts. With persistent thrombocytopenia and the appearance of lymphadenopathy, autoimmune manifestations, recurrent episodes of febrile infections, a decreased number of CD8+ T-cells and abnormal immunoglobuline isotypes, as well as new skin findings consistent with eczema, we decided to further investigate. We excluded Langerhans cell histiocytosis and autoimmune lymphoproliferative syndrome and did a peripheral blood film to check the platelet size. At this point the platelets were small. The genetic analysis of the WAS-Gene showed the mutation c.1280delC, implicating a classic WAS.
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. Clinicians should not exclude a diagnosis of WAS if the MPV is 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.

P 126

Can delay in diagnosing a germinoma result in transformation into a nongerminomatous 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 nongerminomatous 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 girl of 13 years 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 hypernatriemic dehydration, due to a diabetes insipidus (DI) accompanied by a panhypopituitarism including a growth arrest during the last 2 years and a decreased visual acuity due to chiasmic compression. Brain magnetic resonance imaging (MRI) revealed an enhanced mass in the suprasellar region. β-HCG was increased in both CSF and serum. A subtotal resection revealed the diagnosis of a mixed NGGCT with germinomatous and choriocarcinomatous components. Multimodal therapy according to COG protocol ACNS0122 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 so-called germ cell theory and several case reports. Five patients are reported in the literature with initial diagnosis of germinoma and relapse diagnosis of NGGCT. Four of them had undergone radiation or chemotherapy before the diagnosis of NGGCT, therefore a transformation due to therapy induced changes in the genomic structure can not be excluded. One of them showed a spontaneous transformation without prior therapy.
Conclusion: Hypothesizing that germinomas can spontaneously transform into NGGCTs over time, which worsens the prognosis, striving for early diagnosis is important. In our patient growth arrest could have been an early symptom of a germ cell tumour in the suprasellar region. The diagnosis of anorexia nervosa should not be made without prior CNS imaging. In patients with idiopathic DI or other symptoms of hypopituitarism MRI plus monitoring of AFP and β-HCG in serum and CSF plus tests of anterior and posterior pituitary function should be performed at regular intervals.

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Langherans cell histiocytosis: an unusual cause of torticollis in children

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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 an unusual cause of torticollis.
Case report: A previously healthy 10-years-old boy presented with a 4-weeks history of progressive pain and decreased mobility of the cervical spine with paresthesia and impaired function of the left arm. Myorelaxant and AINS treatment was tried unsuccessfully one month before. Standard X-ray of the cervical spine was performed 2 weeks after symptoms occured showing C3–C4 posterior subluxation. Two weeks later the child presented in the emergency room because of worsening of symptoms: on physical examination torticollis without fever was noted, a left proximal arm paresis was observed without hypoesthesia. MRI scan of cervical spine showed a large lytic expansive mass of the left part of the 4th cervical vertebra with compression of the left fifth nervous roots but without medullary mass effect. Differential diagnosis primarily included a malignant tumor such as Ewing sarcoma, lymphoma, osteosarcoma, and benign neoplasm such as osteoblastoma and Langherans cell histiocytosis (LCH). Surgical biopsy through posterior approach was performed, the histological exam revealed LCH. No other lesions were demonstrated in total body PET scan and in cerebral MRI scan. An inflammatory syndrome was noted (ESR 40 mm/sec, WBC 10.3 G/L) and urinary analysis excluded insipid diabetes. Induction treatment was rapidly introduced consisting in oral prednisone over 6 weeks and intravenous vinblastine once a week during 6 weeks according to HL2010 recommendation. Neurological symptoms completely regressed after 4 weeks of treatment.
Conclusion: Torticollis is a challenging diagnosis for paediatricians. Early diagnostic evaluation is mandatory to prevent neurological complications. Langerhans cell histiocytosis is a rare condition in childhood presenting in different forms ranging from a single bony disease to a multisystemic disease involving vital organs. LCH must be considered in differential diagnosis of torticollis if a lytic lesion is demonstrated in the cervical spine.

P 128

Administration of rituximab after hematopoietic stem cell transplantation can induce severe and prolonged hypogammaglobulinemia in children

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A 10 year-old boy received an allogeneic hematopoietic stem cell transplantation (HSCT) for post-hepatitis aplastic anemia, from an 9/10 HLA-matched unrelated donor. Engraftment occurred on day 24, and full donor chimerism was achieved on day 25. 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 auto-immune hemolytic anemia occurred, which did not respond to treatment with corticosteroids. Therefore, the patient received 4 consecutive weekly injections of rituximab (375 mg/m^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, the patient still suffered from severe 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 agammaglobulinemia 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 EBV-induced lymphoproliferative 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.

P 129

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 se-lection of T cells. This essential role is mainly prompted by cortical and medullary thymic epithelial cells (cTEC and mTEC), which are themselves subject to immuno-suppressive 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 microenviroment and a reduction in the transcription of TEC-specific chemokines that control the attraction of T-cell precursors to the thymus. These changes correlated in aggregate with the degree of peripheral lymphopenia.
Conclusion: Selective inhibition of mTOR function limits the expansion of TECs, affects their phenotype and hinders their function. The two individual mTOR complexes are non-redundant and their combined deficiency in the thymic epithelia result in a phenotype that is more striking when compared to single mutant mice. These data identify TEC as a direct target of mTOR inhibitors used in clinical immunosuppression.

P 130

Unusual cause of acute bruising in a previously healthy girl

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Introduction: Acute bruising is a relatively common condition in pediatric clinical practice. We present a rare cause of acquired bleeding diathesis in a previously healthy 7 years old girl.
Case report: The patient was referred to the emergency unit by her pediatrician for acute bruising. Her mother noticed several unexplained hematomas newly appeared two days before. There was no history of trauma, medical treatment, toxics ingestion or previous signs of hemorrhagic diathesis. She presented signs of viral infection a week before with several vomiting, abdominal pain and fatigue without fever. No bleeding disorder was noted in the familial history. The physical exam revealed various hematomas, predominantly on the legs and the back and a few isolated petechias without mucosal bleeding. No organomegaly or adenopathy was found. General condition was excellent and there were no clinical features of systemic lupus erythematosus or other auto-immune diseases. Complete blood count was normal; coagulation studies revealed prolonged Quick time (56%) and activated partial thromboplastin time (66 sec) with reduced clotting activity of factor II (12%) and factor IX (34%). Factor XI and XII were also slightly decreased. Fibrinogen, Platelet Function Analyzer (PFA) and Von Willebrand antigen and activity were normal. There was no hepatic dysfunction.
Because of normal parents coagulation assessment, acquired clotting factors deficiency was suspected. Search for lupus anticoagulant was positive; anti-cardiolipin and anti-beta-2-glycoprotein antibodies where negative. A week later blood tests showed arising of factor II and IX (43% and 67% respectively), clinical evolution was good without any treatment.
Conclusion: Hemorrhagic lupus anticoagulant syndrome (HLAS) secondary to autoimmune disease or viral infection is known in children as a rare cause of acquired bleeding diathesis. Both isolated hypoprothrombinemia and combined coagulation factors deficiency are described; in our case combined factor II and factor IX deficiency were mostly found. Because of risk of severe bleeding, HLAS should be considered in differential diagnosis of newly appeared bleeding symptoms in children.

P 131

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 neriin which inhibit Na-K-ATPase. This provokes increased intracellular calcium and hyperkaliemia 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.

P 132

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 nitrites 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 ($p < 0.0001$). According to a decision curve analysis, the model also offered a better strategy 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 DMSA scan. These results need further abroad validation.

P 133

Caught in a trap!

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Introduction: Transmesenteric 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. Event 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 diagnosed at the time of surgery. 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 hours-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 180/ 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 white blood cell count (16'000 G/L), an elevated C-Reactive Protein (130 mg/L), normochloremic hyponatremia (Na 129 mmol/L), and iv lactate 2.1 mmol/L. Plain abdominal X-Ray revealed small bowel distension in the left hemiabdomen. Abdominal ultrasound demonstrated abundant peritoneal 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 strangulation 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 Treve's Field congenital hernia in a child. Although rare, pediatricians should not forget incarcerated internal intestinal hernia through a mesenteric defect as a potential cause of small bowel obstruction. If suspected, immediate proper surgical exploration should be performed.

P 134

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 hypovolemia 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 stabilized, received intravenous Vitamin K 2 mg/day, volume and appropriate intravenous antibiotiques. He rapidly recovered over 48 hours and remained hospitalized for 6 days. Vitamin K was continued per os at 2 mg/day for 10 days. Blood and urinary cultures remained sterile and antibiotiques 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.

P 135

Ciguatera fish poisoning: 2 cases in Geneva

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Introduction: Although they do not exist in our country, marine toxins diseases may be imported as European children travel increasingly to tropical regions.
Case report: A family with two children was on holidays in Cuba. Several hours after consuming a soup containing fish and seafood, each member of the family began to complain of abdominal pain, vomiting and diarrhea. They also complained of dyspnea and headhache. During three days, they suffered from myalgia, exhaustion, palmar and plantar pruritus. A few days later, they showed dysesthesia like electrical discharges in the arms and legs when they come into contact with cold liquids. They arrived in Switzerland, 14 days after the initiation of their symptoms and they were still suffering from myalgia, arthralgia preferentially at night, palmar and plantar prurit, headache and paresthesia. Physical exam was normal; in particular, neurological, cardiac, abdominal and osteoarticulary systems were completely normal.
Discussion: History and physical exam were consistent with a classical ciguatera fish poisoning. A work up was therefore unnecessary and is usually normal. Treatment is symptomatic with paracetamol and anti-histaminics and the patient should avoid any food containing cafein, alcool, nuts or any fish, as they may reactivate neurologic symptoms. In severe cases, intravenous Mannitol can be use to reduce intraneuronal oedema, but this wasn't needed in our patient. Symptoms progressively disappeared over several few weeks in both children.
Ciguatera is a toxin produced by a microalga called *Gambierdiscus toxicus* and is eaten by fish in tropical regions. Ciguatera toxin-containing fish does not taste, smell, or appear unusual and cooking does not desactivate the toxin. The toxin opens a sodium channel, triggering membrane depolarization. This action produces a neuronal oedema and leads to a dysfonction of sensitive and motor nervous system but also of parasympathic and sympathic system. Various symptoms are described like gastrointestinal, cardiac, (bradycardia and hypotension) or neuronal.
It is expected that ciguatera will increase in the next years because of global warming.

P 136

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 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 hypoventilation, 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 added strong 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 combinations of markers (CRP >80 mg/l or PCT >2 mcg/l, 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, then bedside inflammatory markers, to rule-out the diagnosis, and if necessary, specific pneumococcal or viral PCR to rule it in.

P 145

Arsenic trioxide: first line treatment of relapse of acute promyelocytic leukemia of children?

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Introduction: Relapse of Acute Promyelocytic leukemia (APL) in children is rare and remains a challenge because a consensus about treatment is lacking. In adult therapy, Arsenic trioxide (ATO) is a very active agent in treatment of newly diagnosed or relapsed APL.
Clinical case: We present a case of a 6 years old girl addressed in our service for relapse of APL PML-RAR alpha positive diagnosed 3 years previously. We decided to treat with a combination of ATO and all-trans-retinoic acid (ATRA), following the adult schema "AML-BMF 2004". Treatment was begun with 10 days of oral ATRA (25 mg/m^2/day). Then, she received 5 days a week intravenous ATO (0.15 mg/kg/day) during 10 weeks for a total of 75 doses. After that, we prescribed again ATRA for 3 weeks followed by 5 weeks of same treatment with ATO. She received also two dose of intratechal cytarabine. ATO or ATRA was well tolerated. Remission was obtained after first cycle. Currently, 14 months after the end of treatment, she is still in complete remission.
Discussion: Use of ATO and ATRA is actually approved in USA and Europe for treatment of adult AML. In pediatric patients ATO is described alone or in combination with ATRA for a long period. At our knowledge; this schema including combination of short treatment ATO and ATRA without other intravenous conventional chemotherapy is described for the first time for treatment of relapsed AML of child.
One of main the benefit of ATO treatment is the limitation of side effect which is important in heavely pretreated leukemic children. Because people think about arsenic as a poison, prescribers may fear risk of acute intoxication and mortality or risk of chronic intoxication such as dermatitis QT prolonged and chronic polyneuropathy. Publications show the safety of ATO compared to conventional chemotherapy, principally because of shortness of exposure.
Due to recent use of ATO in children, long term follow up of side effect is needed.
Conclusion: Our experience confirms the efficacy of arsenic trioxide for treatment of child relapsed APL and must be considered as first line treatment. A prospective randomized trial is needed to confirm a long term remission with "limited" chemotherapy.

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YR 1

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, but 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 NS.
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 to 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/cm^2] 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 which they had 8.5 relapses (IQR 4–13).The mean cumulative dose of prednisone was 0.27 mg/kg/day (IQR 0.18–0.35). Half of the children had corticosteroid-sensible NS (n = 15) and the other half had corticosteroid-resistant NS (n = 7) or corticosteroid-dependant NS (n = 8) disease. Growth was negatively associated to the cumulative dose of prednisone (p = 0.001). Patient with high cumulative dose of prednisone had lower final height Z-score (–1.46 [SD], SD 0.84) than those with medium dose (–0.15, SD 0.95; p = 0.008) or low dose (+0.5, SD 0.47; p <0.001). Changes in rachis Z-score was also 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.
Conclusion: 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.

YR 2

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 FEV_1 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 is done during normal tidal breathing. Double-tracer gas constitutes 26.3% helium and 5% sulfur hexafluoride. Triplicate SBW and spirometry tests were performed in all children (n = 66) at baseline and after bronchodilation in asthmatic children (n = 31).
Results: Acinar ventilation heterogeneity (S_{DTG}) was significantly increased in asthma compared to controls. S_{DTG} was abnormal (≤-2 z-scores) in 11/31 asthmatic children, FEF_{25-75} in 3/31 and FEV1 in 0/31. After bronchodilaton SDTG, FEF_{25-75} and FEV_1 significantly changed: Average (95% CI) change given as percentage from baseline was 36 (15–56)%, 17 (9–25)% and 6 (3–9)%, 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.

YR 3

The Swiss Pediatric Sepsis Study – obstacles and opportunities in establishing a national pediatric cohort study in Switzerland

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Background: Sepsis remains one of the leading causes of infant and childhood mortality worldwide. Only large-scale multicentre 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 difficult 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 that cause a high susceptibility to sepsis using massive parallel 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%.
Significance: Establishing this study required huge efforts from involved investigators. Continuous CTU support (SwissPedNet) and dedicated research staff are needed to improve feasibility and quality of pediatric cohort studies. From a public health perspective, this project surveys pediatric sepsis in Switzerland. The design using next generation genomic technology allows to promote functional studies on host genomics and host-pathogen interaction, and to link with international sepsis collaborations. Finally, scientific collaboration between Swiss pediatric institutions is enhanced.

YR 4

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 Staphylocccus 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 clinical 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.
Methods: Bacterial cultures were obtained from 24 AD patients between 7 months and 18 years and 24 uninfected 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, *mec*A. 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 SCC*mec* 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 chemostaxis 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* ($p = 0.0327$), which encodes for an enterotoxin known to act as 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 virulence 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.

YR 5

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 bone marrow transplantation. In case no matched bone marrow donor is available, the only alternative treatment option is gene therapy of 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 viral 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.

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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 (50 upper limb fractures (group 1) and 50 lower limb fractures (group 2)) and 50 healthy controls (group 3) 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 immunoassays.
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 <78 nmol/L), whereas 6% and 34% of healthy controls were respectively vitamin D deficient and insufficient. There were no significant differences for serum 25(OH) D levels, L2-L4 BMD Z-score and L2-L4 BMC Z-score variables ($p = 0.216$) between the three groups nor for the calcaneal BMD Z score variables ($p = 0.278$) between healthy controls and lower limb fractures victims. Investigations on the influences of serum 25(OH)D on BMD and BMC showed no correlation between serum 25(OH)D and L2-L4 BMD Z-scores ($r = –0.15$; $p = 0.135$), whereas low but significant inverse correlations were, surprisingly, detected between serum 25(OH)D and calcaneal BMD Z-scores ($r = –0.21$; $p = 0.034$) and between serum 25(OH)D andL2-L4 BMC Z-scores ($r = –0.22$; $p = 0.029$).
Conclusion: A significant proportion of Swiss Caucasian teenagers independent of limb fracture status in our study were vitamin D insufficient. However, this study failed to show an influence of low vitamin D status on bone mineral density and/or content of the lumbar spine, and heel.

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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

currently contra-indicated because of immunosuppression. This study aims were to evaluate the safety, immunogenicity (humoral and cellular), and efficacy of VZV vaccine when given after LT.
Study design: Interventional prospective national cohort study.
Methods: All children followed at the national pediatric LT center and >1 year after LT were eligible. A baseline blood sample evaluated VZV-specific cellular (CD4+ T-cell) and humoral (IgG) immunity. It identified patients non-seroprotected (IgG <50 [IU/L]) to whom varicella vaccine was administered (Priorix®; 2 doses, 2 months apart). A blood sample 2 months after the last vaccine dose evaluated vaccine responses. A third dose was given to patients non-seroprotected after 2 doses. Blood sample 1 year after immunization measured cellular immunity and persistence of VZV-specific IgG. Vaccine safety was assessed by standardized side effect cards and phone calls.
Results: We included 77 patients (38 boys, 39 girls) at a median age of 7.8 (interquartile range (IQR) 3.9–11.9): half of the patients (39/77) were not seroprotected against VZV. We immunized 36 patients who were 3.1 years (IQR 1.3–9.0) after LT. All patients reached seroprotective VZV-specific IgG titer 8.1 weeks (IQR 4.6–53.9) after 1 to 3 dose(s) of VZV vaccine (p <0.001), and 97% were still seroprotected at follow-up (median 1.7 year after immunization, IQR 0.4–3.4). Cellular immunity also increased significatively after immunization (p = 0.0119). Local and systemic side effects were present in 55% and 65% of patients, respectively. No serious adverse event was reported, nor any LT rejection episode. No breakthrough VZV disease was observed (median follow-up 4.1 years, IQR 3.6–4.5).
Conclusion: Although currently contra-indicated, our study shows that VZV vaccine side effect profile after LT is similar to the reports in healthy children. Hence, VZV immunization after LT is needed, immunogenic, efficient and safe.
Acknowledgments: We thank all the children included and their parents, as well as the many pediatricians involved in Switzerland.

YR 8

Asymptomatic oropharyngeal carriage rate of *K. kingae* does not correlate with the incidence of invasive osteoarticular infections

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Purpose: The aim of this study was to investigate the changes of oropharyngeal K. kingae carriage rate during the first four years of live, 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 6 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 7.6% 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 due to this germ. Therefore further investigations are needed to elucidate which other factors play a role in the pathogenesis of invasive infections.

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The "blue infant", a case report of methemoglobinemia

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Methemoglobinemia is a rare condition due to an imbalance consisting of either increased methemoglobin (MetHb) production or decreased methemoglobin reduction. The congenital form is characterized by a diminished enzymatic reduction of methemoglobin (hemoglobin with iron in the ferric state) to functional hemoglobin (hemoglobin with iron in the ferrous state). Affected patients appear cyanotic but are generally asymptomatic. Acquired methemoglobinemia typically results from ingestion of specific drugs or agents, such as nitrites, leading to an increased production of methemoglobin. A thorough history and an early clinical recognition are critical, as clinically important symptoms can rapidly develop at a relatively low MetHb level. If left untreated, methemoglobinemia can lead to cardiopulmonary impairment, severe neurologic effects and even death.
A previously well 7-months-old infant was admitted to the Emergency Department with central cyanosis of sudden onset. She underwent clinical, laboratory and radiological evaluation. She had no fever, anemia, nor any history of cardiac disease; a chest radiography was normal. Physical examination revealed a child in good general condition, well-nourished, alert and playing with refractory central cyanosis.
Oxygen saturation by pulse oxymetry was 77% at room air and rose to 85% with a FiO_2 of 100%. Blood gas analysis and a MetHb blood level recorded at 37% (norm less than 1.5%) confirmed our clinical suspicion. For practical considerations the patient was transferred to the nearest University Center. She was successfully treated with one dose of intravenous Methylene blue and kept for observation for 24 hours. In this case the most likely cause was traced to her food intake: caregivers had given the child prior thawed raw fennel and broccoli stored overnight in the fridge, thus allowing for the production of nitrite compounds.
We aimed to describe this case of methemoglobinemia in order to raise awareness among practitioners of this diagnosis and share our review of this condition.

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Bordetella holmesii bacteremia in a child with nephroblastoma

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Introduction: *Bordetella holmesii* is a recent addition to the *Bordetella* spp. It has been occasionally reported to cause bacteremia -mostly in patient with asplenia-, other invasive infections, and pertussis-like symptoms. No Swiss case has been reported to date.
Case-report: A 3.5 year-old boy treated by cyclophosphamide and doxorubicin for bilateral nephroblastoma, and on trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis, presented with febrile neutropenia (CRP 20 [mg/l], PCT 0.15 [µg/l]). He initially responded to ceftazidime and was discharged on day 3 (d3). *Bordetella holmesii* was identified in his blood after 6 days of culture; hence, the patient was started on ceftriaxone on d6. Antibiomicrobial susceptibility testing revealed a resistance to ceftriaxone, and treatment was switched to intra-venous TMP-SMX on d9. As the patient remained febrile on d13, imipenem replaced TMP-SMX in order to have a bactericidal effect for a 14-days course. The patient, afebrile and well, was discharged on d22. 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, *B. holmesii* is often misdiagnosed as *B. pertussis* since the PCR routinely used to diagnose *Bordetella* is not species-specific. Treatment can be tricky: *B. holmesii* strains are often resistant to ceftriaxone, sometimes resistant to TMP-SMX, and usually less susceptible to macrolides then *B. pertussis.* Carbapenem and fluoroquinolones are often reported as the most effective antibiotics against *B. holmesii.*
Conclusion: *Bordetella holmesii* is a recently identified organism that pediatrician should be aware of since it can cause invasive disease, and is often difficult to diagnose and treat.

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Effectiveness of an exercise intervention on health-related quality of life and well-being in parents from hospitalized children with severe illness: 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 (Bf-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 favour 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 Bf-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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Epigenetics 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 involves a process 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 Dnmt3a, 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, while T cell development is unchanged, without 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.

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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 (TEC) differentiation as 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 hypomorhpic 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 slightly mitigated 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 generation of a T cell repertoire that reveals its autoreactivity over time by causing severe colitis.

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Epithelial cytoprotection sustains ectopic expression of tissue-restricted antigens in the 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 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 ($mTEC^{high}$). Since the thymus epithelium is a target of donor T-cell alloimmunity we hypothesized that thymic aGVHD interfered with the $mTEC^{high}$ capacity to sustain TRA diversity.
Methods: Ectopic expression of TRAs was tested in a murine allogeneic transplantation model.
Results: We found that reductions in $mTEC^{high}$ compartment sizes were universal manifestations of thymic aGVHD in murine models of haploidentical and fully MHC-disparate transplantation. Contraction of the total $mTEC^{high}$ pool corresponded to a progressive decrease in the subset which expresses *autoimmune regulator* (Aire), a key regulator of TRA expression. When testing entire residual $mTEC^{high}$ cell pools we found that aGVHD altered expression of ubiquitous genes (Ub) and TRAs, however, at different frequencies. The most substantially repressed TRAs were enriched for genes specific for known target tissues of chronic GVHD. Fibroblast-growth-factor-7 rescued $mTEC^{high}$ numbers and fewer TRAs were repressed.
Conclusions: Our data may provide a mechanism for how autoimmunity develops in the context of aGVHD. Moreover, approaches for epithelial cytoprotection 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 immunoglobulines (type1) or by self-polymerisation or binding to other proteins (type2). 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 present 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 an aunt and two cousins which were not followed up further. Several investigations including laboratory tests had already been performed: Extended serological and immunological laboratory testings for infective or autoimmune hepatitis were negative. Coeruloplasmin and copper were within the reference range. Abdominal ultrasound showed

no pathologic findings. Gastroscopy showed no oesophageal varices. Since no pathology could be histologically determined in liver biopsy, genetic testing for Morbus Wilson was conducted without identification of a known mutation. In our department ASAT was still found to be elevated with 194 U/l (ref. range <40 U/l). Since the patient had been asymptomatic the presence of macro-ASAT was considered. After treatment of the patient's plasma with polyethylene glycol to precipitate immunoglobulines ASAT concentration was reduced to 8 U/l whereas ASAT activity in controls (plasma samples of patients with elevated liver enzymes without known associated pathology) decreased minimally (169 to 144 U/L, 106 to 92 U/L, 131 to 101 U/L).
Conclusion: In healthy subjects with isolated elevation of one serum enzyme it is important to consider the presence of macroenzymes. Polyethylen glycol precipitation is a fast and inexpensive screening test for macroenzymes that can spare the patient invasive and costly diagnostic tests.

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Influenza Vaccination in Pregnant Woman: 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.

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