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1-1

Regional differences in fever management by Swiss pediatricians: The results of a cross-sectional survey

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Introduction: In symptomatic fever management by pediatricians, there is often a gap between evidence-based guidelines and everyday clinical practice. We were interested to see whether the 3 main linguistic regions of Switzerland differ in the management of fever.
Methods: A pilot-tested, close-ended questionnaire was sent by electronic mail to 900 Swiss pediatricians. The survey was not commercially sponsored.
Results: The questionnaire was answered by 322 (36%) pediatricians: 214 answered the German, 78 the French and 30 the Italian version of the questionnaire. The female to male ratio and the time since qualification were not statistically different in the 3 groups of respondents. French- and Italian-speaking pediatricians identify a lower (P <0.001) temperature threshold for initiating a treatment and more frequently (P <0.001) reduce the threshold for a treatment in children with history of febrile seizures. A reduced general appearance leads more frequently to a lower threshold for a treatment among German-speaking than among French- (P <0.001) and Italian- (P <0.001) speaking pediatricians. Among 1.5 and 5 year-old children the preference for the rectal route is more pronounced (P <0.001) in the German- than in the French-speaking region. Respondents of the French-speaking region more frequently (P <0.001) prescribe ibuprofen and an alternating regimen with 2 drugs than German-speaking respondents. Finally, the stated occurrence of exaggerated fear of fever was higher (P <0.001) among German- and Italian-speaking pediatricians.
Conclusions: The present comparison proves the existence of significant regional differences in symptomatic fever management and in the perceived frequency of exaggerated fear of fever.

1-2

Suspecting sepsis and initiating treatment in a pediatric emergency department. How can we reduce the door to antibiotic time?

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Background: Administration of broad-spectrum antibiotic treatment within 1 hour of diagnosis and aggressive early fluid resuscitation are recommendations of the Surviving Sepsis Campaign to improve morbidity and mortality in pediatric patients with severe sepsis and septic shock. The aim of this study was to analyse adherence to these recommendations in our emergency department before and after introduction of standardized training of the emergency department staff.
Methods: All patients (between 4 weeks and 18 years of age) admitted to the emergency department of a tertiary children hospital with sepsis, severe sepsis or septic shock were identified retrospectively by structured chart review over a 5 year period from 01/2007 – 12/2011. Patients with malignant diseases were excluded. Halfway through the observation period, a standardized training program was introduced and repeated every 3 months with case based skill training. The targeted audience were staff nurses and physicians at the emergency department. Clinical presentation, performed diagnostic tests as well as staffing were assessed, and the time from admission to initiation of appropriate treatment was calculated. Mean time before (T1) and after (T2) introduction of the standardized training was analysed.
Results: 42 patients, 23 females and 19 males with a mean age of 7.1 years (range 30 days to 18 years) were included in the study. All patients had systemic inflammatory response syndrome (SIRS) on admission. In addition bacteria were detected in normally sterile body fluids. 16 patients needed intensive care, 3 patients died. Neisseria meningitidis was the most frequent pathogen identified (N = 10). Median time until administration of broad-spectrum antibiotic treatment was reduced from 160 minutes (inter quartile range [IQR] 1858 for T1, N = 22) to 112 minutes (IQR 223 for T2, N = 20). Also with respect to the early aggressive fluid resuscitation an improvement was observed.
Conclusion: Standardized training in sepsis management at a regular basis of the staff in our emergency department over a 2.5 year period resulted in a considerable reduction in the time between admission and administration of antibiotics and fluid resuscitation in patients with clinical signs of sepsis. Further improvement is needed to comply with the early-goal directed therapy recommended by the Surviving Sepsis Campaign.

1-3

Comparison of pediatric emergency departments in Switzerland

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Introduction: The emergency department is an essential component of the medical service in any hospital. Due to historical reasons pediatric emergency departments (PED) are structured and organised differently in every hospital in Switzerland. Information on these differences is lacking.
Methods: In 2011 a structured interview was conducted in 13 PED throughout the country. Focus was laid on infrastructure and organisational processes.
Results: Fourteen catchment areas with 30 PED were identified. For each catchment area the ratio PED/child range from 1/16'000 (Ticino) to 1/150'000 (Innerschweiz). There are 5 university hospitals in Switzerland; four of which see around 30'000 children/year (Basel, Genève, Lausanne, Zürich), the fifth one around 19'000 children/year (Bern). The number of children seen per year in the other PED ranges from a few thousand to 12'000 in Luzern, Sion and St. Gallen. Due to the absence of pediatric emergency specialists in many centers, most PED are supervised by "general" pediatricians having many other tasks. All centers have a triage system, with the majority using the Australian triage system (ATS). In all but one centre parental telephone counselling is done by the staff of the emergency department, resulting in interruptions in patient care. Infrastructure varies enormously, with a ratio of emergency rooms per consulting child ranging from 1/800 in Chur to 1/4660 in Basel. Most serious traumas are managed in the adult shock room, resulting in structural and organisational challenges.
Conclusion: Within the 13 pediatric emergency departments visited in Switzerland, heterogeneity was observed in number of patients seen, manpower, infrastructure and standard of care, with each centre doing its best with the means provided. Improvement could be achieved by forming pediatric emergency specialist, and unifying organisational processes as well as infrastructures.

1-4

Interdisciplinarity and organizational structure of Pediatric Emergency Departments in Switzerland

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Introduction: For the last years large children's hospitals in Switzerland mainly organize their emergency care in interdisciplinary pediatric centers. Actual data on principal structures and systems of these centers and of smaller pediatric emergency care systems are presented.
Methods: In 2011 all heads of pediatric emergency departments (ED, n = 36) were asked to answer a questionnaire about their institution concerning: level of autonomy, interdisciplinarity, type of organization, personnel, as well as strategies for triage, treatment strategies, integration of external pediatricians in the ED and telephone triage and advice service.
Results: 20 of 31 hospitals do have an interdisciplinary emergency department (65%). 5 of these 20 do have their own chief of staff (all university hospitals). In 7 pediatric emergency departments, interdisciplinarity is set at the level of senior physicians, in 7 at the level of residents. 26 hospitals have a systematic triage, mostly (21) based on the Australasian Triage Scale. All university hospitals run an ambulatory/fast track system where patients with less severe illnesses are treated separately, while 9 non-universitary children's hospitals do run such a system. In 6 hospitals external pediatricians participate in these ambulatories. Most pediatric emergency departments provide telephone advice for patients (29 of 31). In 21 hospitals this advice is free of charge, 8 hospitals provide a pediatrician based telephone advice service with charge. Average staff in large pediatrics hospitals is equipped as follows: 0.17 senior physicians, 0.53 residents and 1.41 nurses per 1000 patients.
Conclusions: Compared to other European countries Switzerland has a well developed and often interdisciplinary pediatric emergency care system. Manpower requirements are substantial. More and more pediatricians and pediatric surgeons specialize in this field. Crucial point for quality of medical care and for patients' and parents' satisfaction is the organization of the ED. This study was supported by PEMS (Pediatric Emergency Medicine Switzerland).

1-5

Triage evaluation of all patients in the year 2010 at the emergency department of the children's hospital Zurich

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Introduction: In 2003 the Australasian Triage Score (ATS) system was introduced at our interdisciplinary emergency department (ED) at the University Children's Hospital in Zurich. We are reporting our data and experience with the ATS for all admissions in 2010.
Methods: Electronic charts of all admitted patients were retrospectively analysed. The first triage category (cat.) given by the triage nurse at the reception was recorded, as well as a change in the cat. during the patients' stay in the ED. We further measured the time between the first and the second triage assessment, and if patient assessment by a physician occurred within the time frames as defined by the ATS system.
Results: Of all 31462 consultations in 2010, 94 scored cat. 1, 908 cat. 2, 6658 cat. 3, 18'838 cat. 4, and 4964 cat. 5. The first triage assessment was identical to the second in 98.6% of cat. 1, in 96.8% of cat. 2, in 94.2% of cat. 3, in 91.9% of cat. 4, and in 86% of cat. 5 patients. The time between the first and the second triage assessment was less than 10 min in 51.8% of cat. 2, less than 30 min. in 86.5% of cat. 3, less then 60 min. in 95.8% of cat. 4, and less than 120 min. in 99.3% of cat. 5 patients. Patient assessment by a physician occurred immediately in 32.9% of cat. 1, within 10 min in 55.1% of cat. 2, within 30 min. in 67.4% of cat. 3, within 60 min in 68.3% of cat. 4, and within 120 min. in 93.5% of cat. 5 patients.
Conclusion: The consistency of cat. allocation between the first and second triage assessment is high over all and proportionally higher in the lower cat. It would appear that in lower cat. patients the assessment by physician did not occur within the defined time frames. However, our patient-flow rules say that cat. 1 or 2 patients are assessed by a nurse and a doctor prior to data entry in our electronic patient information system; this could explain the apparent delay in these groups of patients. In 32,6% of cat. 3 patients assessment does not occur within the requested time frame, while in 86,5% of cat. 3 patients the second triage assessment is done within these 30 min. We are reassured to see that 99,3% of all patients are seen for a second triage assessment within 2 hours from admission. It is our intention to further evaluate if the outcome of cat. 3, 4 and 5 patients was impaired by the time delay in the physician's assessment, and to analyse the causes for this delay. This will lead to the development of strategies aimed at improvement of our workflow.

1-6

Minor head injury

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Minor head injuries in childhood are a serious health problem contributing to ~10% of all pediatric admissions. Definition and terminology of traumatic brain injury, contusion or concussion are uncertain. Knowledge of appropriate management can be improved in healthcare providers and also in the public, which may lead to more specific patient care and better prevention of second injuries. In up to 70% of patients with minor head injuries CT imaging was performed despite the fact that less than 3% of them had intracranial findings requiring neurosurgical intervention. Long-term sequelae (hypothyroidism, growth hormone deficiency) are underestimated and can be seen in more than 50% of patients. Minor head injuries in young athletes are a growing issue in the medical literature and a matter of practical interest for patients, parents, coaches and practitioners of sports medicine. A second impact before full recovery from the first may have deleterious consequences and should be avoided by strict rules for "return to play". Recent research suggests that repetitive minor hits may cause delayed brain damage (Dementia pugilistica or punch-drunk syndrome), and a link to Alzheimer's disease is described by amyloid beta plaques in those brains.
A genetic predisposition (apolipoprotein) is discussed. We aim to present different recommendations on which patients can be safely discharged home with proper instructions, have to be admitted or require a cranial CT. Furthermore, we present new findings and a concise rule for "return to play" in the care of young athletes.

2-1

Higher multiple births in Switzerland: neonatal outcome and evolution over the last twenty years

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Introduction: The dramatic increase in the incidence of higher-order multiple births (HOMB) since the mid-seventies is well documented in the literature. These infants are born prematurely and have a higher mortality and morbidity rate compared with those of singletons. In Switzerland, two national epidemiological surveys were performed in 1985–88 and 1995–98 respectively. We decided to perform a third national study in order to determine the actual incidence of HOMB in Switzerland, evaluate the neonatal morbidity and mortality, and analyse the change observed over the last two decades.
Methods: In this retrospective study, data about HOMB from 1.1.2005 until 31.12.2008 were obtained from all Swiss obstetrics and neonatal departments and processed anonymously. Compared with the Swiss Federal Statistical Office, 95% of all triplet births and 100% of all quadruplet and quintuplet births were included in the present survey. The results were compared with data from the first two Swiss national surveys.
Results: The incidence of HOMB was 35.3/100,000 live births for triplets, 0.7/100,000 for quadruplets and 0.3/100,000 for quintuplets. All newborns were premature with a median gestational age of $32^{1}/_{7}$ weeks for triplets, $29\ ^{2}/_{7}$ weeks for quadruplets and $28\ ^{4}/_{7}$ weeks for quintuplets. 94% of triplets and all quadruplets and quintuplets survived the neonatal period. Compared with the two previous surveys, the incidence of quadruplet and quintuplet births has fallen, whereas that of triplets has risen by 40%. The perinatal mortality of triplets has decreased but the neonatal morbidity, mainly respiratory distress, has remained constant.
Conclusion: Although perinatal mortality has decreased, neonatal morbidity is still high in HOMB without improvement over the last two decades. The ongoing increase of HOMB incidence indicates that reproductive medicine in Switzerland is not yet sufficiently controlled and monitored.

2-2

Population Based Trends in Mortality, Morbidity and Treatment for Very Preterm- and Very Low Birth Weight Infants Over 12 Years

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Background: Over the last two decades, improvements in medical care have been associated with a significant increase and better outcome of very preterm (VP, <32 completed gestational weeks) and very low birth weight infants (VLBW, <1500 g). Only a few publications analyse changes of their short-term outcome in a geographically defined area over more than 10 years. We therefore aimed to investigate the net change of VP- and VLBW infants leaving the hospital without major complications.
Methods: Our population-based observational cohort study used the Minimal Neonatal Data Set, a database maintained by the Swiss Society of Neonatology including information of all VP- and VLBW infants. Perinatal characteristics, mortality and morbidity rates and the survival free of major complications were analysed and their temporal trends evaluated.
Results: In 1996, 2000, 2004, and 2008, a total number of 3090 infants were enrolled in the Network Database. At the same time the rate of VP- and VLBW neonates increased significantly from 0.87% to 1.10% ($p < 0.001$). The overall mortality remained stable by 13%, but the survival free of major complications increased from 66.9% to 71.7% ($p < 0.01$). The percentage of infants getting a full course of antenatal corticosteroids increased from 67.7% in 1996 to 91.4% in 2008 ($p < 0.001$). Surfactant was given more frequently (24.8% in 1996 compared to 40.1% in 2008, $p < 0.001$) and the frequency of mechanical ventilation remained stable by about 43%. However, the use of CPAP therapy increased considerably from 43% to 73.2% ($p < 0.001$). Some of the typical neonatal pathologies like bronchopulmonary dysplasia, necrotising enterocolitis and intraventricular haemorrhage decreased significantly ($p \leq 0.02$) whereas others like patent ductus arteriosus and respiratory distress syndrome increased ($p < 0.001$).
Conclusions: Over the 12-year observation period, the number of VP- and VLBW infants increased significantly. An unchanged overall mortality rate and an increase of survivors free of major complication resulted in a considerable net gain in infants with potentially good outcome.

2-3

Neurodevelopmental Outcome in Extremely Premature Infants born in Switzerland between 2000 and 2008 – Preliminary Data of the Swiss Neonatal Network.

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Introduction: So far, national outcome data on extremely premature infants in Switzerland were not available, and discussions on the care of these patients were based on earlier studies from other countries. This national study assessed neurodevelopment in Swiss infants born between 2000 and 2008 at 24 0/7 to 27 6/7 weeks gestational age.
Methods: Neurodevelopment was assessed at 2 years using the BSID II. Moderate neurodevelopmental disability (ND) was defined as a mental (MDI) or psychomotor (PDI) development index of 55-70, or mild cerebral palsy (GMFCS level 2). Severe ND was defined as a MDI or PDI <55, cerebral palsy (GMFCS level ≥3), deafness or blindness. Multivariate logistic regression was performed.
Results: Among the 1147 extremely preterms born during the study period 303 (26%) died. Follow-up information was available in 684 (81%) survivors. 440 (64%) showed normal development, 166 (24%) moderate ND, and 78 (12%) severe ND. Severe ND was significantly ($p < 0.05$) associated with earlier year of birth, major intracerebral lesions, bronchopulmonary dysplasia, grade 3 retinopathy of prematurity, and lower socioeconomic status. In contrast, birth weight, gestational age and sex showed only trendwise associations with severe ND.
Conclusion: Based on these preliminary analyses, we now are ready to establish representative Swiss national data on the outcome of extremely premature infants. These will offer guidance to obstetricians, neonatologists, neurologists and parents based on Swiss data.

2-4

Is it safe to reduce the use of diagnostic tests in newborns at risk of developing early-onset sepsis?

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Background: Early-onset neonatal sepsis (EOS) is associated with high mortality and morbidity. Therefore, antibiotics are started promptly in infants with signs of EOS. In asymptomatic newborns with risk factors for EOS, national and international recommendations advocate the use of diagnostic tests (complete blood count and acute phase reactants) to decide whether antibiotics should be administered. However, the low positive predictive value of diagnostic tests results in a large number of unnecessary antibiotic treatments. For that reason, we developed a new protocol for newborns with risk factors for EOS, where diagnostic tests were replaced by repeated clinical examination.
Objective: The objective of our study was to evaluate the safety of a protocol based on repeated clinical examination to screen infants with risk factors for EOS.
Methods: Data from 6073 infants born at ≥35 weeks of gestation at our institution between December 2006 and September 2009 (Period 1) were compared to data from 4968 infants born between October 2009 and September 2011 (Period 2). During Period 1, a complete blood count and measurement of C-reactive protein were performed in infants with risk factors for EOS according to the 2002 guidelines of the Swiss Society of Neonatology. During Period 2, a complete blood count was performed only in infants exposed to maternal chorioamnionitis. During period 2, infants with risk factors for EOS were examined by pediatric residents every 8 hours during the first 24 hours, in addition to the surveillance of vital signs performed by midwives during Period 1.
Results: In infants treated with antibiotics for suspected EOS, the mean time between birth and the first dose of antibiotics was 18.6 hours and 11.4 hours, in Period 1 and Period 2 ($P < 0.01$). The number of patients treated with antibiotics in Period 1 and Period 2 was 2.2 and 1.6 per 100 live births, and their mean duration of hospitalization was 10.2 and 8.0 days.
Conclusion: Reduction in the use of diagnostic tests such as complete blood count and C-reactive protein does not cause a delay in initiation of antibiotic treatment in newborns with suspected EOS but may decrease the number of infants who receive unnecessary antibiotic treatment.

2-5

Burden of chronic exposure to difficult ethical decisions on caregivers in Swiss NICUs

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Introduction: This study aimed at exploring the degree of burden due to chronic exposure to difficult medical, nursing and ethical issues and decisions on the health care providers (HQP) working in Swiss level III neonatal intensive care units (NICUs).
Methods: 224 Questionnaires were sent to neonatal physicians and nurses of all level III neonatal intensive care units in Switzerland. Demographical information, attitudes and behaviours towards ethical decisions, and the impact of those decisions on HCP's health and private life were collected and analysed.
Results: The overall response rate was 50% with 52 neonatal physicians and 60 nurses (27 men, 85 women) taking part in this survey. Altogether, 78% stated that the ethical dilemmas and decision-making represent a burden to them. 87% experience this burden as momentary. Moreover and in nearly 40% of answers, this burden affects private life; in another 48% it was found to occasionally impact on private life. 25% of physicians and 10% nurses suffer from exhaustion. Most of the respondents find relief from stress through their hobbies (70%) and discussions with family members and friends (74%). The most used coping strategies are debriefings after ethical discussions, team discussions and support from hospital pastoral care. Professional moderation of debriefings was only rarely available (10%).
Conclusion: Chronic exposure to stressful situations represents a burden for the majority of HCP working in NICU environment. Exhaustion is far more frequent than physical and psychosomatic symptoms. Hobbies and social contacts are important coping strategies. Given the potential of chronic burden to not only affect health of caregiver but also to shape the attitudes of caregivers in daily neonatal intensive care medicine, the importance of team debriefings and support under professional guidance cannot be stressed enough.

2-6

Natal / neonatal teeth – a real problem?

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Introduction: Etiology and development in the long term of natal / neonatal teeth are not well known. A longitudinal survey aimed at clarifying some controversial points.
Method: Prospective, longitudinal survey of 80 neonates with natal / neonatal teeth. They were followed up for 1 to 11 years (median 6 years) depending on parents' co-operation.
Results: ***Supernumerary teeth?*** No, all teeth involved were prematurely erupted deciduous teeth.
Danger of aspiration of loose teeth? No documented cases, neither in the literature nor in this survey. Thus there is no reason for systematic removal of loose teeth. Root formation, just about to start at the time of birth, provides little stability for teeth erupting at this stage. In this survey, 7 (9%) of the natal / neonatal teeth were very loose and therefore removed in the first 2 to 3 months because of impaired feeding.
Breastfeeding? On enquiry, only 2 mothers mentioned pain related to the baby's teeth while breastfeeding. With regular suckling, the tongue lies on top of the lower alveolar ridge. Thus there is no direct contact between tooth and nipple. However, five out of 80 babies (6%) developed a traumatic ulcer on the lower surface of the tip of the tongue which healed spontaneously after slight polishing of the teeth.
Survival time of natal / neonatal teeth? In 50% of the 30 children followed up long enough, the natal / neonatal teeth stayed on to the regular time of exfoliation. Neonatal teeth in which root formation was more advanced at the time of eruption, fared rather better than natal teeth.
Consequences for the permanent dentition? Space for lower permanent front teeth in the children surveyed remained within the range found in the overall population.
Conclusion: The results of our study contradict frequent statements from the literature: Natal / neonatal teeth are not in danger of being aspirated and do not really impede breastfeeding. Such teeth, unless extremely loose, have a fair chance of surviving up to the time of regular shedding. Space for permanent lower front teeth is not a specific problem in these children.

3-1

Incidental findings of mass lesions on neuroimages in children

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Introduction: Increasing use of neuroimaging in children has led to more incidental findings of CNS mass lesions, the management of which is uncertain. The aims of this study are to describe these mass lesions and their evolution, as well as to discuss the management options and to determine the prevalence of incidental CNS mass lesions at our hospital.
Methods: A retrospective study was undertaken in children with primary CNS tumors who were younger than 18 years old and were admitted to the University Children's Hospital of Zurich between January 1995 and December 2010.
Results: In 19 (5.7%) of 335 patients with newly diagnosed CNS tumors, the diagnosis of a CNS mass lesion was an incidental finding. Reasons for obtaining neuroimages in these 19 patients were head trauma (in 6 patients); research protocols (in 3); nasal/orbital malformations (in 2); endocrinological and psychiatric evaluations (in 2); and vertebral bone anomaly without neurological signs, absence seizures, congenital ataxia, recurrent vomiting, developmental delay, and "check-up" at the explicit request of the parents (in 1 patient each). Seven patients underwent immediate surgery for low-grade glioma (4 patients) and craniopharyngioma, ependymoma, and choroid plexus papilloma (1 patient each); and 12 were treated conservatively or were observed. Ten of 12 conservatively treated patients remained stable (median follow-up time 1.8 years) and the other 2 underwent delayed surgery because of tumor progression (medulloblastoma in one patient and fibrillary astrocytoma in the other).
Conclusion: Clinicians are increasingly challenged by the discovery of incidental CNS mass lesions. A subgroup of such lesions (with typical imaging patterns such as tectal glioma and dysembryoplastic neuroepithelial tumor) can be monitored conservatively, clinically, and radiographically. Future prospective studies are needed to define optimal management strategies based on larger collections of natural histories, as well as to assess the true prevalence of incidental CNS mass lesions.

3-2

The development of atopic dermatitis according to age of onset and the association with early life exposures

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Background: Environmental factors may affect the development of atopic dermatitis and this was described to be already effective during pregnancy and in early life. An important early postnatal exposure is nutrition and its association with allergic disease remains unclear.
Objective: To determine prospectively whether early postnatal exposures, such as the introduction to complementary food in the first year of life, are associated with the development of atopic dermatitis, taking into account the reverse causality.
Methods: 1041 children who participated in a birth cohort study, the Protection against Allergy-Study in Rural Environments were included in this study. Atopic dermatitis was defined by doctor diagnosis reported by the parents up to 4 years of age by questionnaires and/or with positive Scorad score from 1 year of age and according to the age of onset, within or after the first year of life. Feeding practices were reported by parents in monthly diaries between the 3rd and 12th month of life.
Results: The diversity of introduction of complementary food in the first year of life was associated with a reduction of the risk of having atopic dermatitis with onset after the first year of life (adjusted odds ratio for atopic dermatitis with each additional major food items introduced, 0.76; 95%CI, 0.65–0.88). The introduction of yogurt in the first year of life reduced also the risk for atopic dermatitis (adjusted odds ratio, 0.41; 95%CI, 0.23–0.73).
Conclusion: As early life exposure, the introduction of yogurt and the diversity of food introduced in the first year of life might have a protective effect against atopic dermatitis.

3-3

Prospective Clinical Trial analysing Efficacy and Safety of Evening Pimrose Oil (Epogam® 1000, Ze 358) in Patients with Atopic Dermatitis

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Introduction: In patients with atopic dermatitis (AD) there is an imbalance in fatty acid metabolism related to a deficiency in the delta-6-desaturase, an enzyme responsible for the conversion of linoleic acid (LA) to gamma-linolenic acid (GLA). Evening primrose oil (EPO) is extracted from seeds of this plant which contains high amounts of GLA (approximately 80 mg per 1 g of EPO). The aim of the study was to investigate whether an increase in blood levels of GLA and DGLA correlates with the clinical improvement of AD (measured as a reduction in SCORAD) in patients treated with EPO.
Methods: This prospective, multi-centre, pilot trial was performed in 5 clinical sites. 23 children and adults, with clinical symptoms of AD, aged between 2 to 45 years, were enrolled. According to subject's age, 4–6 capsules of EPO (corresponding to 320–480 mg GLA) were administered daily during 12 weeks.
Results: In the ITT population (n = 21), a statistically significant increase in plasma GLA and DGLA and a decrease of total SCORAD as well as most individual elements of SCORAD over time was observed after treatment with EPO. In the PP group (n = 14), there was a significant inverse correlation between increase in plasma GLA and the reduction of SCORAD (R = 0.68, p = 0.008). 80 to 90% of patients with an increase in blood GLA or DGLA experienced a significant clinical response. No serious adverse events occurred; EPO was well tolerated in children and adults.
Conclusion: EPO is an effective treatment of AD resulting in a significant increase in GLA and DGLA which is highly correlated with a clinical response as measured by a reduction of SCORAD.

3-4

First-Day Step-Down to Oral Outpatient Treatment versus Continued Standard Treatment in Children with Cancer and Low-Risk Fever in Neutropenia. A Randomized Controlled Trial within the Multicenter SPOG 2003 FN Study

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Background: In children with malignancies, the standard treatment of fever in chemotherapy-induced neutropenia (FN) includes emergency hospitalization and empirical intravenous antimicrobial therapy. This study determined if first-day step-down to oral outpatient treatment is not inferior to continued standard in-hospital treatment regarding safety and efficacy in children with low-risk FN.
Procedure: In a randomized controlled non-blinded multicenter study, pediatric patients with low-risk FN after non-myeloablative chemotherapy were reassessed after 8 to 22 hours of inpatient intravenous antimicrobial therapy. Eligible patients were randomized to first-day step-down to experimental (outpatient, oral amoxicillin plus ciprofloxacin) versus continued standard treatment. Exact non-inferiority tests were used for safety (no serious medical complication; non-inferiority margin of difference, 3.5%) and efficacy (resolution of infection without recurrence, no modification of antimicrobial therapy, no adverse event; 10%)
Results: In 93 (26%) of 355 potentially eligible FN episodes low-risk criteria were fulfilled. 62 were randomized, 28 to experimental (1 lost to follow-up) and 34 to standard treatment. In intention-to-treat analyses, non-inferiority was not proven for safety (27 of 27 [100%] versus 33 of 34 [97%; 1 death] episodes; 95% upper confidence border, 6.7%; $P = 0.11$), but non-inferiority was proven for efficacy (23 of 27 [85%] versus 26 of 34 [76%] episodes; 95% upper confidence border, 9.4%;

P = 0.045). Conclusions: In children with low-risk FN, the efficacy of first-day step-down to oral antimicrobial therapy in an outpatient setting was non-inferior to continued hospitalization and intravenous antimicrobial therapy. The safety of this procedure however, was not assessable with sufficient power.

3-5

Psychological Distress in Adolescent Survivors of Childhood Cancer

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Background: Adolescent survivors of childhood cancer may be particularly at risk for developing psychological distress. However, to our knowledge no study assessed psychological outcomes in this age group. Therefore we aimed to 1) evaluate psychological distress in adolescent childhood cancer survivors and siblings, 2) determine the severity of distress and 3) determine potential risk factors associated with poor psychological outcomes in survivors.
Methods: We sent a questionnaire to all childhood cancer survivors aged <16 when diagnosed, who had survived ≥5 years and aged 16–20 years at study. We sent a similar questionnaire to siblings. Psychological distress was measured with the Brief Symptom Inventory-18 (BSI-18) assessing somatization, depression, anxiety and a global severity index (GSI). Survivors and siblings at risk for distress were identified by transforming raw scores into T-scores (case rule T≥57). To characterize distressed survivors, we computed univariable and multivariable logistic regressions.
Results: We evaluated the BSI-18 in 407 survivors and 102 siblings (response rate 67% and 36% respectively). Most survivors (86%) and siblings (89%) reported no symptoms of psychological distress. Distressed survivors had significantly higher scores in somatization (p = 0.027) and GSI (p = 0.016) than distressed siblings. Psychological distress was associated with female sex (OR 1.6-6.1), self-reported late effects (OR 4.1–6.9) and low perceived parents' support (OR 7.2–12.5).
Conclusion: Results suggest that most survivors did not report psychological distress. However, a subgroup of survivors reported distress in the clinical range. Therefore, it is essential to screen survivors for psychological distress, provide systematic psychological follow-up, and support them during the challenging period of adolescence.

3-6

Acute Poisoning in Children – Looking at Iron Poisoning: What should be done?

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Introduction: In 2011, 35,568 poisoning consultations were carried out by the Swiss Toxicological Information Centre. 80% of the cases were accidental poisoning and most toxic exposures occurred with pharmaceuticals (36%). Looking at the calls received with toxic exposure, children were involved in 52% of the cases. In home environment, poisoning most often occurs in small children. At the Ostschweizer Kinderspital in St. Gallen we treated 294 pediatric poisoning cases in the past 5 years. Two cases involved accidental ingestion of iron tablets. Iron deficiency is the most common cause of nutritional anemia in humans, thus the use of iron products for prophylaxis and treatment is very common not only in children but also in adults, i.e. during pregnancy. New coloured and flavoured tablets and fluid formulations were created in order to improve treatment compliance. Unfortunately these formulations are likely to represent a higher risk of poisoning in children.
Case Presentation: We report on two preschool children with acute iron poisoning with doses up to 60 mg/kg body weight that needed special treatment but different approach and follow up. One of these cases is laboratory-chemically, radiologically and endoscopically well documented during a period of 4 weeks after poisoning.
Conclusion: Primary prevention is the best modality for decreasing morbidity and mortality of all poisonings including iron. Preschool children need to be actively protected. After iron poisoning, gastrointestinal-decontamination (endoscopic removal of tablets and/or whole bowel irrigation) has to be performed as soon as possible. Early chelation therapy in moderate to severe poisoning reduces complications and mortality. Most patients with iron poisoning respond well to conservative therapy and the majority of them have a good outcome and excellent long-term prognosis. Acute liver failure, coagulopathy, shock and severe acidosis are poor prognostic indicators.

4-1

Newborn screening for cystic fibrosis in Switzerland – Evaluation after one year

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Background: Newborn screening (NBS) for cystic fibrosis (CF) was introduced in Switzerland on January 1st 2011 as a pilot study for two years. It comprises measurement of immunoreactive trypsinogen (IRT) followed by searching for the 7 most common DNA mutations in Switzerland.
Methods: To evaluate the NBS, we measured the initial IRT tests, recall rate, number of children referred to a CF centre and number of confirmed diagnoses. Then, we calculated referral rate, current positive predictive value (PPV) and incidence.
Results: Within one year, 85'588 IRT tests from 83'198 live births were performed; 0.76% of them (648/85'588) were positive, and DNA screening was performed. In 440 children, a 2nd IRT test was necessary. In total, 85 children were screened positive and referred to a CF center for further investigations. In 28 children (33%), the diagnosis of CF could be confirmed, and an additional child was clinically diagnosed having meconium ileus (MI) with a normal IRT. 54 children (64%) had a negative sweat test or genetic testing, and in three children, the diagnosis was not yet made (not yet fully investigated). The recall rate for the 2nd IRT test was 0.51% (440/85'588), the referral rate to a CF centre was 13.1% (85/648) and the PPV was 34.1% (28/82). The provisional incidence rate was 1:2869 (29/83'198)
Conclusions: There were no major obstacles in the implementation of the NBS for CF in Switzerland. The recall rate of 0.51% was lower than expected. One third of patients referred for sweat tests were diagnosed with CF. The incidence rate of 1:2869 has to be interpreted with caution, as the exact birth rate and the definite diagnosis of all children was not yet available at the time of writing this abstract. In children with MI, CF should always be confirmed or excluded by sweat test or DNA analysis.

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4-2

Newborn screening for cystic fibrosis in Switzerland – Confirmation of a tentative CF diagnosis by CFTR gene analysis

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Introduction: Cystic fibrosis (CF) is the second most common life threatening autosomal recessive disorder among Caucasians, with an incidence of around 1 in 2500 births. As newborn screening (NBS) for CF improves outcomes, it is increasingly being implemented worldwide and, on 01.01.11, has also been started in Switzerland. CF NBS is, however, a screen, not a diagnostic test, and a positive screening result must be confirmed by direct diagnostics such as sweat testing and/or genetic analyses.
Methods: From 01.01.11 to 27.01.12 EDTA blood or buccal cell samples from 35 newborns with positive NBS or, if negative, with meconium ileus (MI) were sent to the Division of Human Genetics at the University Hospital in Bern for CFTR analysis. In a first step we tested for the 32 most common CFTR mutations using the CF-OLA Kit (Abbott). In cases where the test failed to detect two mutations we performed screening of the entire coding sequence (including exon/intron boundaries) by SSCP analysis and sequencing and searched for large deletions/duplications by MLPA (MRC Holland).
Results: In 28 out of the 35 samples (80%) we identified two CFTR mutations confirming the diagnosis of a classic CF in 23 (82%) newborns, 14 of them being F508del homozygous. Five infants were found to carry one missense (4) and/or one alternative splice mutation (3) corresponding to IRT values of 55-66 and borderline sweat tests and predicting therefore a milder disease course. Two babies were identified as heterozygotes and in five infants no CFTR mutation was detectable. Beside the most common mutation F508del, found in 71% of the CF chromosomes, 15 individual mutations were identified one of them (G486) being not yet described. The diagnostic interval decreased from a mean time span of 198 days before NBS to 38 days since NBS.
Conclusions: The genetic diagnosis was in all cases in accordance with the NBS and/or with the sweat test results. Genetic testing allows confirmation of NBS findings, early diagnosis in newborns with MI as well as determination of carrier state in family members for further family planning.

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4-3

Newborn screening for cystic fibrosis in Switzerland - Comparison of Nanoduct versus Macroduct sweat test in the diagnosis of CF

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Background: Newborn screening (NBS) for cystic fibrosis (CF), based on immunoreactive trypsinogen (IRT) and 7 most common CFTR mutations, was introduced in Switzerland on January 1st 2011. In the pilot phase, we compared the performance of two sweat test methods for diagnosing CF in the NBS.
Methods: All children with a positive screening result were referred to a CF center for confirmatory (diagnostic) testing with: a) the Nanoduct sweat test (conductivity); and b) the Macroduct test (chloride). If sweat test results were positive, borderline or inconclusive, an extensive DNA analysis was performed.
Results: Within one year, 85 children were screened positive and further investigations in a CF center were needed. In 28 children the diagnosis of CF could be confirmed (by genetic testing), 54 children had negative investigations for CF, and 3 children were not yet fully investigated. In 76 children, all details of the investigations were available and these were included in our analysis. The 76 children were seen in a CF center at a median age of 26 days. The Macroduct was attempted in 64 children, the Nanoduct in 71 children. A reliable test result was available in 66% (42/64) for the Macroduct and 79% (56/71) for the Nanoduct. In 37 children both sweat tests could be performed, while in 19 only the Nanoduct and in 5 only the Macroduct was feasible. In 8 children none of the two sweat tests gave a reliable result, and confirmation or exclusion of CF was based on extensive DNA analysis alone.
Conclusions: In this pilot study, the Nanoduct sweat test showed a better feasibility for use in newborns compared to the Macroduct test, mainly because it needs a lower sweat volume. Analysis of a larger dataset will allow to compare sensitivity and specificity of the two tests for the final CF diagnosis.

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4-4

Newborn screening for cystic fibrosis in Switzerland – Consequences after analysis of 4 months pilot study

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Background: Newborn screening for cystic fibrosis (CF), based on immunoreactive trypsinogen (IRT) and 7 most common CFTR mutations, was introduced in Switzerland on January 1st, 2011. The suggested IRT value for the 99th percentile from the literature was 60 ng/ml. In a test run in December 2010, the corresponding IRT value for the 99th percentile turned out to be lower (45 ng/ml). One aim of this pilot study was to find out if this cut-off is too low and resulting in unnecessary 2nd IRT measurements if no CFTR mutations were found.
Methods: We evaluated the IRT cut-off, recall rate, the number of children referred to a CF centre, and compared it to IRT values of the confirmed diagnosis. All children referred to a CF centre had an additional IRT measurement when sweat testing was performed.
Results: In the first 4 months, 27'297 IRT tests were performed, 0.92% of them (251/27'297) were above 45 ng/ml, and DNA screening was performed. In 211 children, a 2nd IRT measurement was necessary (recall rate 0.77%). 40 children were referred to a CF centre (referral rate 15.9%) and the positive predictive value was 20% (8/40). No child with CF had an IRT value <60 ng/ml. All 15 children with initial IRT between 45 and 60 ng/ml and no CFTR mutations had a normal 2nd IRT test. After changing the IRT cut-off, the recall rate decreased by 45%: In the further 8 months, only 229 children needed an 2nd IRT test and 46 were referred to a CF centre for sweat testing, and only 5 out of them had twice an elevated IRT value but no CFTR mutation.
Conclusions: The change of the IRT cut-off from 45 to 50 ng/ml (99.3th percentile) resulted in less recalls without losing diagnostic accuracy.

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4-5

Newborn screening for cystic fibrosis in Switzerland – Feedback from parents

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Background: In January 2011, Switzerland started a pilot study on new-born screening (NBS) for cystic fibrosis (CF) as part of the Guthrie test. For final implementation of the screening, it is important to know what affected families think about it. We therefore assessed: 1) if the information given to parents about the screening was satisfying; 2) the parents' feelings during the screening process; 3) the parents' overall approval of the screening.
Methods: All children who screened positive in the Guthrie test were referred for investigations to the nearest CF centre. The CF centre gave a phone call to the families, inviting them to a visit with sweat test. After the visit, parents were given an anonymous questionnaire for criticising different aspects of the screening procedure.
Results: By January 2012, 85 children had a suspicious screening result and were referred to a CF centre. Of those, 29 were diagnosed with CF. The questionnaire was distributed to 80 families and returned by 43 (54%). Response rates varied between centres (20–89%) but did not differ by final CF diagnosis ($p = 0.985$). The information received in the maternity ward was satisfying for 70% of families (28/43). The additional information received in the CF centre was satisfying for 91% (39/43). After the telephone call from the CF centre, most parents (34, 79%) felt troubled or anxious. After the visit in the CF centre, only 12 families (28%) remained anxious: 4/29 families without a CF diagnosis (14%) and 8/14 families with a CF diagnosis (57%; $p = 0.003$). The large majority of parents (91%, 39/43) was glad that their child had been screened, only 2 (5%) were not (independently of the final CF diagnosis, $p = 0.345$).
Conclusion: Although many parents felt anxious after the initial phone call, most became calm after the visit in the CF centre. It is therefore important to keep this time span as short as possible. The large majority of families, independent of the final CF diagnosis, were glad that the screening tests had been performed.

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4-6

How do patterns of wheeze change over the first 14 years of life?

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Background: The clinical patterns of wheeze in children change with age. Few studies have shown these changes in sufficient detail and over a wide age range. Our aim was to describe reported symptom patterns in children with wheeze from age 1 to 14 years, with a focus on indicators of wheeze severity and triggers of attacks.
Methods: In a population-based respiratory cohort study in Leicestershire, UK, we assessed prevalence of parent-reported wheeze and associated symptoms at the ages of 1, 2, 4, 6, 9 and 14 years respectively. Using a validated questionnaire, we asked for indicators of severity in the preceding 12 months (number of wheezing attacks, shortness of breath, sleep disturbance and activity disturbance due to wheeze), wheeze not associated with colds, wheeze associated with colds and triggers of wheeze (exercise, food and contact with aeroallergens).
Results: The prevalence of reported wheeze decreased from 36% (1446/4035) at age 1 to 16% (471/3003) at age 6 years and remained stable thereafter. In children with wheeze the proportion reporting frequent attacks (≥4) changed little from age 1 (35%) to 14 years (32%). From age 1 to age 14 years, the following characteristics become more frequent with age: reported shortness of breath (increasing from 54% at age 1 to 85% at age 14), wheeze apart from colds (32% to 61%), exercise-induced attacks (26% to 71%) and aeroallergen-induced symptoms (6% to 50%). Activity disturbance, sleep disturbance, wheeze associated with colds and food-induced attacks changed less over time.
Conclusion: We found significant age-related changes in wheezing patterns from infancy to adolescence. Some of the questions typically used for assessing asthma severity might be mainly useful for school-age children. Such age-related differences in reporting of asthma symptoms need to be taken into account when designing questionnaires and planning studies.
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5-1

Fourteen years of regional experience with respiratory syncytial virus in hospitalized children at the University Children's Hospital Bern, Switzerland

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Background: Respiratory syncytial virus (RSV) is the most important viral etiology of lower respiratory tract infections in children younger than 5 years, and is prevalent all over the world. RSV epidemics occur in intervals of varying predictability, influenced by local climate conditions. In temperate climates with yearly RSV epidemics, few areas have noted a regular biannual cycling of the intensity of RSV seasons. We report on 14 consecutive RSV seasons in a representative area of Switzerland and describe epidemiological and clinical characteristics of our patient cohort.
Patients and Methods: Single center observational study of retrospectively (1997-2000) and prospectively collected data (2000–2011) on all pediatric patient hospitalized for RSV infection ≥24 hours since 1 July 1997. Both differences in individual and epidemiological disease characteristics between minor and major seasons, as well as trends over the course of time are analyzed by descriptive and regression analysis.
Results: Over the course of 14 consecutive RSV epidemics 2243 patients with RSV infection were hospitalized at our institution. Major and minor seasons differed significantly by the number of patients hospitalized (median number of admissions 222 [interquartile range (IQR) 206.5–242] vs. 106 [IQR 81.5–113]; p <0.001). Additionally, patients hospitalized during major RSV epidemics were significantly younger (median age 4.5 months [IQR 1.7–11.7] vs. 5.6 months [IQR 2.2–12.8]; p = 0.006) and had a higher likelihood of being transferred to the pediatric intensive care unit (Odds ratio 1.75). Over the course of time a significant increase of the number of patients hospitalized every RSV season was observed, accompanied by an increased likelihood of having supplemental oxygen administered. In parallel, a reduction in length of hospital stay, duration of supplemental oxygen administration, length of PICU stay, and duration of mechanical ventilation was noted.
Conclusions: At our location the RSV-associated disease burden is reliably predictable and shows a distinct biannual cycling of magnitude of epidemics and disease severity in hospitalized infants and children.

5-2

Impact of prenatal diagnosis of congenital heart disease on neonatal outcome in a regional case controlled study (Canton of Vaud, Switzerland)

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Introduction: This study reports on the outcome of a fetal cardiac screening program in the Swiss canton of Vaud from 1.5.2003 to 31.12.2008
Methods: 40'567 births were registered in Eurocat registry, 572 cases of congenital cardiac pathology (CCP) were reported. Cardiac abnormalities were sorted in four separate categories based on the severity of the CCP.
Results: 128 of the 572 CCP could be attributed to the 4 defined groups considered major cardiac congenital malformations. Prenatally diagnosed in this population were 83/126 detection rate 67%. Group I (32 cases), all CCP for which only palliative care is available, 28 were detected antenatally (28/32, 87.5%), resulting in TOP in 24 (85.7%), 3 were diagnosed at birth. Of the 7 live birth 4 died (comfort care), 3 went on to be operated. Group 2 (6 cases) severe heart disease requiring immediate postnatal. Of the 4 detected prenatally, 2 had associated chromosomal anomaly and underwent TOP. The 2 other prenatally diagnosed and 1 non- diagnosed underwent arterial switch, and another non-diagnosed TGA died within 2 hours after birth during transport. Group 3 requiring immediate postnatal care but deferred surgical or interventional correction like conotruncal anomalies, AVSD) 52 cases were included in the Eurocat register, of these 36/52 were detected prenatally (69.2%). 34/52 had a chromosomal anomaly.There were 22 TOP (21 chromosomal abnormal), 28 born alive, 2 stillbirths. Of the 28 born alive, 26 had a surgical correction, 1 died shortly after birth (pulmonary atresia type of Fallot) and 1 (with VACTERL) received palliative care and died subsequently. Group 4: The group consisted of 38 cases of pathologies needing a follow-up such as Ebstein's disease, large perimembranous VSDs, coarctation, aortic stenosis. Prenatal diagnosis 15/38, TOP in 10 cases (associated with chromosomal/ syndromal anomalies or other malformation). 28 were born alive.
Conclusion: This study shows that the percentage of prenatal diagnosed cases of congenital heart disease increases over the years, probably as a result of increasing experience, improving technology and intensive teaching. The study shows that in the most severe group of congenital heart disease the percentage of interruption of pregnancy reaches 86% in the prenatal diagnosed group. TOP were associated with severe heart diseases or heart disease combined with chromosom/syndromal/other anomalies.

5-3

The Swiss Growth Registry: aims, methods and first results

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Introduction: Recombinant human growth hormone (rhGH) has been introduced in 1985. Since then, its use has multiplied. Large population-based studies on long-term safety are sparse. Therefore, the Swiss Growth Registry (SGR) was founded in 2010. It aims to include all persons treated with GH during childhood in Switzerland, to describe underlying diagnoses in response to GH treatment and to determine long-term outcomes.
Methods: Patients are identified patients via paediatric and adult endocrinologists and other specialists prescribing rhGH (including paediatric nephrologists and oncologists). We extract data directly from original patient records. The SGR database contains demographic information, treatment data, clinical status at follow-up and late outcomes (e.g. final height).
Results: By Dec 31st, 2011, we identified 1692 patients with rhGH treatment during childhood. Out of these, 57% are male (N = 971) and 43% female (N = 921). Mean age is 19.2 years ± 6.7SD (1.2–42.2). Indications for rhGH treatment were classified according European Society for Paediatric Endocrinology (ESPE) guidelines. We completed data collection for patients over 18 years (N = 776). In these, indications for rhGH treatment were: growth hormone deficiency in 42% (N = 325), Turner syndrome in 20% (N = 152), cancer in 13% (N = 98), deficiencies of anterior pituitary hormones in 7% (N = 55), primary growth failure in 7% (N = 52), chronic renal failure in 6% (N = 48), idiopathic short stature in 3% (N = 27) and other indications in 2% (N = 19). In total, only 2% (N = 17) of these patients are reported to have died.
Conclusion: We identified a larger number of rhGH treated patients (N = 1692) than anticipated, and patient registration is still ongoing. The range of underlying diagnoses is broad. During the next years, the database will be completed and studies on long-term safety of rhGH use will be performed using data from Swiss mortality statistics and cancer registries.
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5-4

Neonatal Arterial Ischemic Stroke in Switzerland

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Aim: To describe the characteristics and epidemiology of neonatal arterial ischemic stroke (AIS) in Switzerland.
Method: Data on clinical manifestation, neuroimaging, risk factors (RF's), and treatment procedure were gathered prospectively for all neonates diagnosed with AIS and born in Switzerland between 2000 and 2007. A re-evaluation of available neuroimaging studies was performed by two experienced investigators. Clinical follow-up assessments were performed. Predictors of poor outcome (including symptoms, infarct characteristics, RF's and treatment) were determined.

Results: Seventy-nine neonates (53 boys, 26 girls) have been reported. The incidence of neonatal AIS in Switzerland was 14 per 100'000. Seizures were the most common symptoms (91%). RF's including maternal conditions, birth complications, neonatal comorbidities and prothrombotic states were found in 77%. Eighty percent had unilateral lesions (80% left-sided) and 20% had bilateral lesions. The anterior circulation (mainly the medial cerebral artery) was mostly involved (85%). At follow-up (mean 6 months) 41% showed hemiplegia and 26% received anticonvulsant medication. Respiratory symptoms at presentation (OR 5.580, 95% CI 1.104–28.203, p = 0.038), muscle tone abnormalities at presentation (OR 2.032, 95% CI 1.001–8.588, p = 0.050) and the presence of neonatal comorbidities (OR 2.932, 95% CI 1.001–8.588, p = 0.050) were significant predictors of poor outcome in an univariate regression analysis. No variable remained significant in a multivariate analysis.
Interpretation: Neonatal AIS often present with seizures but can be pauci-symptomatic. Missing significance for an outcome predictor is most likely due to the multi-factorial ethiology and pathophysiology of neonatal stroke. As a result larger scale multicenter case-control studies are mandatory.

5-5

The Swiss national registry of primary immunodeficiency diseases

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Introduction: To date >250 primary immunodeficiencies (PID) with more than 180 genetic causes are known. Most are rare diseases that are often diagnosed late or not at all with ensuing organ damage or death. The overall prevalence for PIDs is estimated to be 1:1000, and 1: 10.000 for severe PIDs. In Switzerland we therefore expect 7000 patients with PID. In a first publication in 1988 only 313 patients were documented. This was the incentive to start a Swiss National Registry for PID. The aims of this registry are to enrol as many Swiss PID patients as possible, to determine the prevalence of different PIDs and to search for geographic differences or family clustering. To build up a Swiss National Registry for PID, a nationwide network would be helpful.
Methods: In 2008 we started to register Swiss patients in the online registry of the European Society of Immunodeficiency (ESID). Today there are 89 documenting centres in Europe that have registered over 13.000 subjects since 2004. The registry has been used as a platform for many translational/basic research studies because it offers a wide range of well-defined patient collectives and it has turned out to be a useful tool to connect different centres.
Results: Today all 5 university centres, 3 level A Hospitals (Aarau, Lucerne and Sankt Gallen) and 1 centre in Bellinzona participate. Most of these started to register, and 177 patients with PID are already registered. Distribution of different PIDs, age distribution and the diagnostic delay for the different diseases are similar to the statistical data of the European cohort. Half of the registered Swiss patients (89/177) suffer from antibody deficiencies, more prevalent in adults (80%), and 47% (79/177) of them need regular immunoglobulin-substitution.
Conclusions: When all centres have registered their patients by the end of 2012, the first nationwide statistical analysis will be possible. As other national PID registries the Swiss National Registry can provide a basis for both national and international investigations and activities that aim to raise physicians' awareness of PID, allow better knowledge on clinical evolution or complications, and may have an impact on therapy costs.

5-6

Suggested Guidelines for Diagnosis and Treatment of Urea Cycle Disorders – a Consensus of European Countries

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Introduction: Urea cycle disorders (UCDs) are inborn errors of metabolism affecting ammonia detoxification and arginine synthesis. UCDs result from defects of the Krebs-Henseleit cycle (five core enzymes, one activating enzyme and one mitochondrial citrulline/ornithine antiporter) with an estimated overall incidence of 1:8.000. Patients present with hyperammonemia either shortly after birth (~50%) or at any age in postnatal life, leading to death or to severe neurological handicap in many survivors. Despite the existence of an effective treatment of acute hyperammonemia and of permanent cure of the metabolic condition with liver transplantation, the highly non-specific clinical presentation, dominated by episodes of decreased consciousness ranging from lethargy to deep coma, and the insufficient awareness of health care professionals because of disease rarity, leads to under-recognition or delayed diagnosis, resulting in much poorer outcomes than possible. The suggested guidelines aim at providing a trans-European consensus for guiding practitioners and for giving a solid foundation to awareness campaigns.
Methods: To achieve their goals the guidelines have been developed using a Delphi methodology by having professionals on UCDs across seven European countries to gather all the existing evidence, scoring it according to the SIGN evidence level system and drawing a series of statements supported by an associated level of evidence. The guidelines have been revised by external specialist consultants, unrelated authorities in the field of UCDs and practicing pediatricians in training.
Results: Although the evidence degree did not exceed level C (evidence from non-analytical studies like case reports and series), it was sufficient to set a sound and clear picture for guiding practice on both acute and chronic presentations, addressing diagnosis, management, monitoring, outcomes, and psychosocial and ethical issues. It also identified knowledge voids that must be filled by future research.
Conclusion: We believe that these guidelines will help to harmonize practice, setting common standards and spreading good practices, having a positive impact on the outcomes of UCD patients.

6-1

Prevention of vitamin K deficiency bleeding with three oral mixed micellar phylloquinone doses: results of a 6-year (2005–2011) surveillance in Switzerland

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Introduction: In 2003, the Swiss national guidelines to prevent vitamin K deficiency bleeding (VKDB) were adapted. As it had been shown that two oral doses (hour 4, day 4) of mixed micellar vitamin K preparation had failed to abolish VKDB (1995–2001 study, 18 late VKDB cases, incidence 3.79/10^5), a third dose (week 4) was introduced in the hope it would permit complete eradication of
VKDB. This report summarizes the results of a prospective 6-year surveillance to study the new guidelines influence on the incidence of VKDB.
Subjects and methods: With the help of the Swiss Paediatric Surveillance Unit, using an internationally accepted definition of VKDB, data were prospectively collected in all Swiss hospitals with pediatric units from July 1, 2005 until June 30, 2011.
Results: Out of a population of 457942 live birth, there were 5 confirmed VKDB, respectively 1 and 4 cases of early and late VKDB (incidence 0.87/10^5, 95% CI 0.24–2.24). Compared with the 1995–2001 data, there were significantly less late VKDB (Fisher, P = 0.004). All were fully breast fed, 4 had an unknown cholestatic liver disease at the time of bleeding, 4 had received no prophylactic VK because of parental refusal and 1 had received only day 1/4 VK doses as the 3rd had been omitted. By definition, only the last case represents a prophylactic failure (0.22/10^5, 95% CI 0.01–1.22). No case represents however a true prophylactic failure (VKDB after adequate prophylaxis and without predisposing factor). If patients who had received no or incomplete VK prophylaxis were excluded, the incidence of late VKDB was 0.00/10^5 (95% CI 0.00–0.81). If patients with cholestatic liver disease and inappropriate vitamin K prophylaxis were excluded, the incidence of late VKDB was 0.00/10^5(95% CI 0.00–0.81).
Conclusions: With the three mixed micellar VK oral doses regimen (hour 4, day 4 week 4), the incidence of VKDB has become very rare but has not disappeared. The main risk factor for VKDB is VK prophylaxis refusal by parents and/or an unknown cholestatic liver disease. To further prevent VKDB in Switzerland, parents have to be better informed of oral VK prophylaxis refusal risks and infantile cholestatic diseases have to be diagnosed early.

6-2

Spectrum Bias of Rapid Antigen Diagnostic Test for Group A β-Haemolytic Streptococcal Pharyngitis in a tertiary paediatric emergency department

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Objective: To determine the performance of rapid antigen diagnostic test (RADT) for group A β-haemolytic streptococcal (GABHS) pharyngitis among children who presented a sore throat in a paediatric emergency department by severity clinical scoring system of pharyngitis.
Methods: We conducted a prospective longitudinal study between January 2010 and July 2011. We included all children aged 3-18 years who presented a sore throat and did not receive any antibiotic during the previous seven days. For all children, two pharyngeal swabs were taken for rapid antigen detection test (RADT) and throat culture. We evaluated performance of RADT to compare with culture (Gold standard) calculating sensitivity (Se) with 95% confidence interval (95%CI). We evaluated pharyngitis severity using McIsaac Score.

Results: We included 2089 patients. The overall sensitivity of the RADT test is 81–95%CI (78-84). RADT sensitivity increased with McIsaac Score. Sensitivity of RADT is 50–95%CI (24-76) among children with score 0–1, 58–95%CI (43–72) among those with score 2, 77–95%CI (70-83) among those with score 3, 80–95%CI (76-85) among those with score 4 and 93–95CI (90-97) among those with score 5.
Conclusion: Performance of RADT is not a fixed value. Performance of RADT varies with severity clinical score of pharyngitis. Performance of RADT is poor when the clinical score is low and it is high when clinical score is elevated. The existence of a spectrum bias of RADT must be known to the physicians because it must be taken into account in the interpretation and indication of diagnostic test.

6-3

Inflammatory markers combined with pneumococcal urinary antigen predict pneumococcal etiology in children with community-acquired pneumonia

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Background and aims: Lower respiratory tract infections are still a common cause of antibiotic overuse in children. At the emergency room, our objective was to evaluate parameters that could predict a pneumococcal etiology of community-acquired pneumonia in children (P-CAP).
Methods: Children hospitalized for pneumonia following the WHO definition were enrolled in a prospective study. The following parameters were determined: antibodies against pneumococcal surface proteins (anti-Ply, PhtD, PhtE, LytB and PcpA), viral serology, naso-pharyngeal culture and PCR for 13 respiratory viruses, blood pneumococcal PCR, urinary pneumococcal antigen, procalcitonin and C-reactive protein. Presumed P-CAP was defined as a positive blood culture or PCR, or as a pneumococcal surface protein seroresponse (≥2-fold increase).
Results: 75 patients were included and 37 (49%) met the criteria of P-CAP. PCT and CRP were strongly associated with P-CAP with OR of 23 for PCT and 19 for CRP in multivariate analysis. The sensitivity was 94.4 % for PCT (cut off: 1.5 ng/mL) and 91.9% for CRP (cut off: 100 mg/L). The combination of elevated inflammatory markers with a positive pneumococcal urinary antigen or with the absence of a viral etiology greatly improved the post test probability: 79/83% for high PCT/CRP combined with a positive urinary test and 88% for high PCT/CRP combined with virus negativity.
Conclusion: Elevated PCT and CRP in combination with a positive pneumococcal urinary antigen are reliable predictors of pneumococcal pneumonia. The use of these tests could improve the management of pneumonia in children at the emergency room.

6-4

Children Hospitalized for Severe Pneumonia: why so frequent delayed care in Switzerland too?

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Introduction: Delayed diagnosis of community acquired pneumonia (CAP) potentially leads to increased mortality (developing countries) or mobidity (developed countries). The lack of consensus about clinical diagnosis criteria and biological markers for CAP further increases the diagnostic challenge.
Objectives: To explore clinically relevant factors that potentially delay CAP diagnosis leading to an increased morbidity in a busy Pediatric Emergency Department (PED) (35'000 visits/year) in Switzerland, where each admitted child is triaged (ATS: Australian Triage Scale) to determine the immediate level of severity of the disease.
Methods: A retrospective case series (November 2011 to January 2012) of all CAP hospitalized children <5 years. CAP was clinically defined (WHO criteria + an abnormal chest radiograph); children with bronchiolitis and/or chronic underlying disease were excluded. Analysed variables were determined by medical record and parental report.
Results: 20 patients included (median age 32 months), 3 with a large pleural effusion, all immunised (Prevenar® 7 or 13). 10/20 had been examined at the PED within 48 h before hospital admission; 8/10 ATS score were retrospectively incorrect; all these 10 patients showed anamnestic and clinical signs (general: high grade fever, pallor, or respiratory: dyspnea, tachypnea, grunting, chest pain accompanying cough) compatible with a CAP, clearly mentionned by mothers and/or written in the medical report. Inital diagnosis were otitis media (4/10, AB prescribed) and viral infection (6/10).
Conclusions: 1. Half of children hospitalized with a CAP could have been diagnosed at the time of a previous consultation, when already presenting CAP diagnosis criteria, most of them mentionned by the mother; 2. Unnecessary diagnostic delays were potentially caused by unused anamnestic and clinical data, uncorrect triage and the laying of ENT diagnoses masking the CAP; 3. The result is a possible increased risk of severe and complicated pneumonia; 4. These observations support a prospective study to confirm or invalidate these questioning data.

6-5

Necrotizing pneumonia in children: Characteristics and outcomes, a two- year survey

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Introduction: Very few studies focused on necrotizing pneumonia (NP), a rare complication of pneumococcal (~7%) or staphylococcal (<2%) lung infection. We aimed to describe characteristics, management and outcome of children with NP.
Methods: We included all children hospitalized in our institution, from January 2010 to December 2011, with NP diagnosis assessed by computed tomography (CT). Data were retrospectively collected: age, gender, underlying disease, clinical presentation, pathogens, biological and radiological findings, management (pleural tap, chest tube, antibiotherapy, oxygenotherapy and duration of hospitalization) and outcome.
Results: Sixteen children with a median age of 3.89 y (0.5–10) were included. 8/16 were previously vaccinated with Prevenar7®. Main symptoms were fever (n = 15), cough (12), rhinitis (5), abdominal pain (4) and chest pain (4). Leucocyte count was >10 G/l in 12/16 children and 6 had a left-shift. C-reactive protein value was 185 mg/l (72–447 mg/l). CT was performed because of clinical worsening (n = 3), pleural effusion increasing (7), radiological finding (2), other reasons (4). Concomitant pleural empyema was diagnosed in 12/16 children, requiring pleural tap (n = 3), chest tube (11) for a duration of 6 days (3-110), and thoracoscopy (9). Pathogens were identified in 13/16 children: *streptococcus pneumonia* (n = 11), *staphylococcus aureus* (2) and others (3), including 2 co-infections. Intravenous antibiotherapy was given for a duration of 10 d (4-64): amoxicilline (n = 3), amoxicilline-clavulanate (5) and ceftriaxone (7). Total hospital stay was 10 d (5-120). 15/16 were further treated by oral antibiotics for a duration of 28 d (7-35). 3/16 patients had complicated outcome: right superior lobectomy for persistent pneumothorax and pulmonary collapse, prolonged chest tube for broncho-pleural fistula, and prolonged hospitalization for multiples chest tubes and post operative secondary infection. After 1 month, chest X-ray was still abnormal in all patients. To date, 10 patients were evaluated at 6 months, and 7 had normalized X-ray.
Conclusion: Aggressive management allows short hospitalization stay and full clinical recovery. Regarding the long term effect, pulmonary function test should be performed to evaluate potential sequela of lung lost.

6-6

Predictive values of indirect detection of Kingella kingae osteoarticular infections in young children by PCR assays on throat's swab: toward a novel diagnostic method

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Background: *K. kingae* is currently considered as the major bacterial cause of OAI in children less than 48 months. However, diagnosis of *K. kingae* OAI remains challenging because clinical and biologic signs at admission may remain within the normal range of values, and because this fastidious microorganism is difficult to isolate on solid medium. Although pathogenesis of *K. kingae* invasive infections remains unclear, there is evidence that *K. kingae* first colonizes the oropharynx before penetrating the bloodstream and invading distant organs. We hypothesized that *K. kingae* should be present in oropharyngeal flora in children with *K. kingae* OAI and should be detectable by a PCR assay targeting *K. kingae's* RTX toxin gene on oropharayngeal swabs. Thus, the purpose of this study was to investigate if an oropharyngeal swab PCR assay could predict osteoarticular infections (OAI) due to *K. kingae* in young children.
Methods: One hundred eleven consecutive children aged 6 to 48 months, presenting atraumatic osteoarticular complaints were prospectively enrolled. All had a clinical evaluation, radiological investigations, and blood samples. Oropharayngeal specimens were tested with a PCR assay specific for *K. kingae*.

Results: Among 111 children, 39 met the OAI case definition. Among these 39 OAI cases, 27 (69.2%) had *K. kingae* OAI, two (5.3%) had other organisms, and ten (25.6%) had no microbiologic diagnosis. All 27 oropharyngeal swabs from *K. kingae* case patients, and eight (7.9%) swabs from 74 other patients, were positive. The sensitivity, specificity, positive predictive value, and negative predictive value of the oropharayngeal swab PCR assay for *K. kingae* were 100%, 89.2%, 77.1%, and 100%, respectively.

Conclusions: Detection of *K. kingae* DNA in the oropharayngeal swab of children with clinical findings of OAI is highly predictive of *K. kingae* mediated OAI. If these findings are replicated in other settings, detection of *K. kingae* by PCR assays could become a helpful diagnostic tool for this disease and then radically improve recognition of OAI.

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P 2

High Birth Weight: a Major Risk Factor for Developmental Dysplasia of the Hip

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The aim of this retrospective study was to investigate the influence of birth weight on the incidence of developmental dysplasia of the hip (DDH).
Material and Methods: Between 1993 and 2003, ultrasonography (US) of the hips was performed in 7417 consecutive newborns at 34–42 weeks' gestation using the Graf method during the first week of life. US showed pathological findings in 168 hips (2.3%). According to Graf's classification there were 63 type IIc, 56 type D, 46 type IIIa and 3 type IV hips (all classified There were 139 girls (82.7%) and 29 boys (17.3%). Except for one boy (type IIIa) all were successfully treated by conservative orthopaedic methods. Overweight, which was defined as large for gestational age (GA) in association with breech presentation was the highest morbidity factor requiring treatment (15.6%), followed by normal weight and breech presentation (7.6%), and large for GA newborns at term (5%). The lowest percentage of newborns in need of subsequent orthopaedic treatment was in 66 small for GA with breech presentation (1.5%). There was no association with developmental dysplasia of the hip (DDH) in 230 small for GA newborns at term, and in 174 twins. The results suggest that high birth weight is a major factor in the etiology of DDH, especially when combined with other already well known risk factors.

P 3

Executive functions of children born very preterm – deficit or delay?

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Introduction: Children born very preterm or at very low birth weight (VPT/VLBW) are known to perform lower than their term-born counterparts in tests of executive functions (EF), such as inhibition, working memory (WM), and shifting. Still, it is unknown whether a) VPT/VLBW children differ in their developmental pattern of EF when compared to controls, and b) whether they perform poorer than controls across all ages or catch up in performance with increasing age.
Methods: Seventy-two VPT/VLBW children with no/minimal neonatal cerebral brain lesions and no/minimal history of neurodevelopmental impairments and fifty term-born controls of three age groups were recruited (7–8 years; 9–10 years; 11–12 years). All children completed tasks of inhibition, WM, and shifting.
Results: Across the ages of 7 to 12 years, the same developmental pattern was found in both VPT/VLBW children and controls, with large gain in shifting, medium gain in WM, and low gain in inhibition. Analyses of age groups revealed that younger VPT/VLBW children (7–8 years) performed significantly lower in shifting and tendentially lower in inhibition and WM when compared to controls, whereas older VPT/VLBW children (11–12 years) approached the control's level of performance across all three EF.
Conclusion: VPT/VLBW children showed a catch-up in performance of EF to the level reached by controls by the age of 11 to 12 years. Poor performance in inhibition, WM, and shifting of young VPT/VLBW children with no/minimal brain lesions and no/minimal history of neurodevelopmental impairments reflects a delay rather than a deficit.

P 4

Optimizing radiographic control of gastric feeding tube placement in neonates

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Objectives: This study should examine, whether injection of air via gastric feeding tube improves stomach visibility on radiographs and thereby improves definition of gastric feeding tube positions in neonates. The reproducibility of defining tube positions on radiographs using this method and the safety of this method should be determined.
Methods: In neonates undergoing radiography we injected 5–10 ml of air via lying gastric feeding tube prior to taking the radiograph. In an observer-interventional study design the usefulness of this procedure was analysed by comparing radiographs taken with and without this intervention. Prevalence of correct and incorrect gastric tube positions, as well as possible interacting factors were analysed.
Results: In 8 of 153 radiographs (5%) with air filling no classification of exact gastric tube position was possible, compared to 78 of 381 radiographs (21%) taken without this intervention. This leads to a significant reduction of indefinable gastric tube positions (p-value <0.001). Inter- and intra-rater agreements with the intervention were both 96%. Furthermore, low gastric feeding tube position was associated with a higher amount of bloody gastric aspirates.
Conclusion: This new standardised procedure improves the visibility of the gas bubble of the stomach on radiographs and thereby significantly improves the definition of exact gastric feeding tube position in neonates. This method shows good reproducibility, is safe and easy to perform. It helps to achieve optimal assessment of gastric feeding tube positions and therefore may prevent harm caused by malposition of the feeding tube.

P 5

Bilateral thalamic lesions in a preterm female, incidental finding on routine cerebral ultrasound at first day of life

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Introduction/Background: Bilateral thalamic lesions in newborns are usually due to cerebral sinovenous thrombosis (CSVT) or are associated with an hypoxic ischemic event during pregnancy or delivery. Mostly they are detected in newborns presenting with neurological abnormalities such as feeding difficulties, seizures or presence of muscular hypertonia. Outcome seems to be rather poor. In a small number of asymptomatic newborns thalamic lesions are detected incidentally on routine cerebral ultrasound.
Case presentation: A 20 year old mother with a spontaneous twin pregnancy was hospitalised at 33 weeks of gestation because of severe growth retardation in twin B. An emergency caesarean section was performed in the 34 2/7 week of pregnancy because of fetal bradycardia in twin B. One female (twin A) and one male infant were delivered with normal primary adaptation. The Apgar of twin A was 7/8/9, arterial cord pH was 7.40, lactate was normal. Birth weight was 2240 g (P25–50). A routine cerebral ultrasound on day 1 revealed bilateral hyperechogenicities of the thalami without intraventricular hemorrhage. An extensive Doppler examination did not show any signs of CSVT. On day 6, cerebral magnetic resonance imaging with MR-venography was performed, showing bilateral hemorrhages of the medial thalami and a hypoplastic left sinus transversus. History was negative for known or suspected maternal, perinatal or neonatal risk factors for CSVT. Examination of the placenta of twin A was unremarkable. The baby girl had an uneventful neonatal course and was discharged at the age of 15 days. Neurologic examination in the neonatal period and at a corrected age of 2.5 months were normal.

Conclusion: In the preterm infant, CSVT should be considered in bilateral thalamic lesions with or without intraventricular hemorrhage and otherwise uncomplicated neonatal course. Even though neuroimaging in our patient could not confirm the diagnosis, a small thrombosis not detected on cerebral MRI seems to be the most obvious cause.

P 6

Cauliflower in a preterm brain

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Introduction: We describe a preterm boy born at 28 weeks of gestation who developed respiratory distress on the third day of life. No further symptoms were detected at that stage. Despite immediate intubation and intensive cardiovascular support, the baby died within five hours due to multiorgan failure.
Results: The cerebral ultrasound showed multiple cauliflower-like intraparenchymatous necrotic lesions in the white matter. The grey matter was normal. Blood – and cerebrospinal fluid cultures were positive for Bacillus cereus within 13 hours of obtaining the cultures.
Conclusion: Bacillus cereus are gram positive spore forming rods that produce toxins. In preterm infants, they may cause devastating systemic infection including meningoencephalitis, often with a fatal course. The diagnosis is made by the culture of blood and cerebrbrospinal fluid, but also by the typical and unique cauliflower-like pattern on cerebral ultrasound.

P 7

Neonatal distress syndrome due to congenital vocal cords paralysis

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Introduction: Obstruction of the upper respiratory tract is a rare but potentially serious cause of respiratory distress of the newborn at birth. Congenital paralysis of the vocal cords is a typical example.
Case report: A full-term newborn presents at birth with respiratory distress, central cyanosis and stridor. Diagnosis of idiopathic congenital left vocal cord paralysis and right cord paresis was made by direct laryngoscopy. Patient was treated by CPAP, which could be stopped after 6 months. Feeding difficulties with gastroesophageal reflux (GER) were main complications of this case, treated by nasogastric tube and antireflux medication. At 4 years of age, the patient is asymptomatic at rest, but stridor remains on effort and in case of respiratory tract infection. Patient's growth and cognitive development are normal.
Discussion: Vocal cord paralysis is the third most common laryngeal abnormality producing stridor. It may be congenital, mostly idiopathic, or acquired, for example by birth trauma. It is often unilateral, rarely bilateral and in this case associated with other neurological problems. It may be associated with dysphagia, bronchoaspiration, and failure to thrive. Endoscopy is essential for evaluation, diagnosis and follow-up. As prognosis is usually good, with spontaneous recovery of vocal cord function, conservative treatment is sufficient in most cases. In severe cases, CPAP may avoid intubation. Digestive complications as poor feeding and GER must be treated specifically.
Conclusion: Vocal cord paralysis should be considered in a case of respiratory distress syndrome with stridor at birth. Diagnosis should be rapidly done by direct laryngoscopy to initiate appropriate treatment and avoid complications. Conservative treatment with or without CPAP is sufficient in most of the cases.

P 8

Recombinant factor VII: a therapeutic option for refractory hemorrhagic pulmonary edema in preterm infants?

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Introduction: Hemorrhagic pulmonary edema affects approximately 5% of very low birth weight infants and has been associated with surfactant administration, patent ductus arteriosus and left ventricular dysfunction. It is thought to result from capillary stress failure associated with lung overdistension, inadequate protective surface tension, and fragility of the pulmonary capillary wall.
Case report: This preterm male infant (gestational age 28 4/7 weeks) was intubated in the delivery room and surfactant was administered at the age of 15 minutes because of marked respiratory distress. After initial stabilization on conventional mechanical ventilation, he was switched to high frequency oscillatory ventilation on day 2 of life because of increasing oxygenation difficulties. Twenty-four hours later, he developed hemorrhagic pulmonary edema. A hemodynamically significant ductus arteriosus was closed with three doses of ibuprofen and thrombocytopenia was corrected with a platelet transfusion. Despite these interventions, his respiratory condition continued to deteriorate. An additional dose of surfactant was administered but had no effect. When tracheal aspirates were still grossly bloody on day 10 of life, recombinant factor VII (rF7) was given and continued for 5 days. Within 24 hours, oxygenation improved and ventilator pressures could be reduced. Three days later, he was successfully extubated to nasal CPAP
Discussion: Severe hemorrhagic pulmonary edema is associated with a high mortality rates in extremely preterm infants. If patients cannot be stabilized with conventional management, rF7 may be an effective additional treatment option that should be discussed early.

P 9

Rapid onset of rhG-CSF therapy in Neonatal Allo-Immune Neutropenia (NAIN) due to Anti-HNA-2a antibodies does not shorten neutropenia duration. A report in two siblings

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Introduction: Incidence of Neonatal Allo-Immune Neutropenia is rare (<1 % of neonates). More common differential diagnosis include sepsis or diminished production due to intra-uterine growth restriction.
Case description: Patient 1 presented with a deep inguinal skin infection at 4 days of life. Despite adequate antibiotic treatment for the isolated s. aureus and clinical improvement, work-up showed persistent neutropenia (min. ANC: 150 /µl). While suspecting NAIN, G-CSF was started at day of life 14. After 2 days of treatment, ANC rose to 14 200/ µl. Daily doses were reduced to twice weekly and finally ceased after 10 weeks altogether. 2 years later, patient 2 was born at 35 1/7 weeks of gestation. In view of the family history, a complete blood count was done for screening where ANC was 90 /µl. She was therefore admitted and a G-CSF treatment (5 µg/ kg daily) was initiated on day 2 of life. Despite rapid start, neutropenia persisted for 15 days. After 3 weeks, G-CSF injections were reduced to twice weekly and finally stopped at 6 weeks of age. Further investigations (Universitätsklinikum Giessen und Marburg, Prof. G. Bein) confirmed maternal Allo-antibodies against CD 177, confirming the diagnosis of NAIN due to Anti NHA-2a antibodies.
Conclusion: Despite onset of G-CSF treatment at day two of life, neutropenia in NAIN may persist for up to 14 days without any clinical symptoms. Whether this delayed response is due to prematurity or is just consistent to previous reports remains unanswered.

P 10

EXIT procedure for massive cervical lymphangioma

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Introduction: The EXIT procedure (ex utero intrapartum treatment) was originally developed to reverse temporary tracheal occlusion in patients who had undergone fetal surgery for severe congenital diaphragmatic hernia. In patients with potentially life-threatening upper airway obstruction, the EXIT procedure allows to secure the airway while maintaining fetal-placental perfusion.
Case report: At 22 weeks of gestation, prenatal ultrasound examination revealed a cystic neck mass consistent with either a cervical lymphangioma or a teratoma in an otherwise normal fetus. The structure continued to increase in size over the following weeks and was later associated with polyhydramnios suggesting impairment of fetal swallowing. At 37 5/7 weeks, after meticulous interdisciplinary planning, an EXIT procedure was performed. Following delivery of the head and the left arm, direct laryngoscopy allowed visualization of the larynx, and successful nasotracheal intubation with a 3.5 ETT was performed by the pediatric anesthesiologist. The ETT was secured with a suture to the nasal septum and a trial of ventilation was successful. The infant was fully delivered and, after the cord was camped and cut (seven minutes after uterine incision), handed over to the neonatologists. Maternal blood loss was approximately 1000 ml and her postoperative course was uneventful. At the age of 8 and 23 days, the sclerosing agent OK 432 (picibanil) was injected into the lymphatic cysts but failed to decrease the size of the neck mass and the infant remained intubated. Four weeks later, a debulking procedure and tracheostomy were performed and the infant was successfully weaned from mechanical ventilation. To facilitate home care, a gastrostomy tube was placed at the age of 3 months and the patient was discharged home one week later.
Conclusion: The EXIT procedure may facilitate safe transition from intrauterine to extrauterine life in patients with large neck masses that could otherwise lead to life-threatening upper airway obstruction immediately after conventional delivery.

P 11

A premature born girl and her inflammasome: why neonatologists and pediatricians must know CINCA?

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Background: Chronic infantile neurologic cutaneous articular (CINCA) syndrome is a rare chronic inflammatory disease characterized by neonatal-onset, central nervous system involvement, chronic arthritis and rash. Autosomal dominant mutation in the gene which encodes the cryopyrin protein of the inflammasome in macrophages and neutrophils can be found.
Case report: A premature born girl (35 4/7 weeks gestational age, 2650 g body weight) was admitted to our NICU with an urticaria-like rash starting 7 hours after birth. Because of high CRP (101 mg/l) and Interleukin(IL)-6 (528 ng/l) neonatal infection was suspected and antibiotic therapy started. Despite therapy high inflammatory markers (leucocytosis, thrombocytosis, increased CRP, low albumin) and rash persisted. Clinically, the newborn was never septic and the blood culture negative, consecutively the antibiotic therapy was stopped. On day six the newborn developed arthritis of the right knee and several fingers and toes. This leaded us to the strong suspicion of a CINCA syndrome which was genetically confirmed with a heterozygous mutation c.1698C>G (p.Phe566Leu) of NLRP3 (also known as cryopyrin). The lumbar puncture showed mononuclear pleocytosis and elevated protein levels. An ultrasound of the brain was normal. Furthermore the newborn was irritable, with poor weight gain and progressive severe anaemia (Hb nadir 76 g/l). After starting therapy with Anakinra (an IL-1receptor antagonist) subcutaneously on day 35, the inflammatory markers normalized, urticaria-like rash disappeared, arthritis improved and weight gain was appropriate.
Conclusion: Neonatologists and pediatricians should be aware of because CINCA might lead to severe deforming arthropathy, mental retardation, loss of peripheral vision, hearing loss, systemic amyloidosis, even death. An ongoing study in infants 1 month to 4 years old tests if this debilitating consequences can be omitted with early therapy. Normally the drugs, Anakinra or Canakinumab (monoclonal anti-IL-1-antibody with a longer half life) are well tolerated; no serious adverse events have been reported so far. Therapy needs to be given lifelong.

P 12

Cow's milk protein allergy in a premature baby: pitfalls in therapy

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Introduction: Colitis caused by cow's milk protein allergy represent a frequent diagnosis and therapeutic challenge for premature babies. An initial trial with extensive hydrolyzed protein milk or maternal milk with strict maternal diet (without milk proteins) is the usual therapy. In such case, hidden sources of cow's milk protein should be searched and excluded.
Case report: Premature girls born at $34^{2/7}$ weeks of gestation, low birth weight with an uneventful neonatal evolution. Initially breastfeeded with standard supplementation of maternal milk with FM 85 after 2 days of life (dietary supplement for low birth weight infants). After 8 days of life, she presented hematochezia and low grade anemia in an otherwise well-looking baby. Despite the introduction of a strict maternal diet without cow's milk protein and soy protein, there was a continuous worsening of the anemia (minimal Hb 87 g/L at 17 days of life) and an increasing hematochezia. X-rays showed intestinal pneumatosis at 17 days of life suggestive of Necrotising Enterocolitis (NEC). After a clinical exclusion of NEC (including temporary fasting and antibiotics), feeding was reintroduced on 19th day of life using an extensively hydrolyzed milk (Pregomin AS®). The result was the disappearance of the symptoms after a few days.
Conclusion: The lack of clinical response to the treatment despite strict eviction of cow's milk proteins in the maternal diet was explained by the supplementation of maternal milk with FM85 that contains lactoserum with only partially hydrolyzed milk protein (20 g of protein per 100g of FM 85). When cow's milk protein allergy is suspected in a breastfed baby, enrichment with FM85 should be stopped.

P 13

Floppy infant: Diagnostic challenge of a term neonate with pyruvate dehydrogenase complex deficiency (PDHCD)

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Aim/Introduction: This case report illustrates the clinical course of a diagnostically challenging term neonate being admitted with tachypnoea, generalised hypotonia, feeding difficulties. The aim is to provide a diagnostic algorithm, starting at the symptom "floppy infant" and leading to the diagnosis of pyruvate dehydrogenase complex deficiency (PDHCD). Genetic background, therapeutic options and aspects of prognosis are discussed.
Background: PDHCD is a rare nuclear encoded mitochondriopathy presenting as neurodegenerative disorder. Malfunction of citric acid cycle results in lowered intracellular ATP production. The clinical course depends on the residual activity of PDHCD. Genetic causes are heterogeneous and definitive prognosis is uncertain.
Results: On admission the baby was floppy and in impaired general condition. Family history, pregnancy and delivery were unremarkable. Initial laboratory results showed lactic acidosis. Biochemical analysis evidenced elevated levels of lactate, pyruvate and alanine. Cranial ultrasound demonstrated hypoplasia of the corpus callosum and indicated migration disorder. The synopsis of clinical, radiological and laboratory results lead to suspicion of PDHCD, which was confirmed by fibroblast culture and DNA- sequencing (E1 alpha).
Conclusion: Floppy infant in neonatal period is a diagnostic challenge requiring a logical diagnostic algorithm starting from more likely reasons tracing to rare diseases. A multidisciplinary team of specialists for inborn metabolic disorders, neuropaediatricians, geneticists, neonatologists and paediatricians is helpful in order to diagnose PDHCD. Given the severity of disease, ethical considerations are vital once diagnosis is established.

P 14

Coarctatio aortae in a neonate: dramatic presentation and positive outcome

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A newborn at term at the age of 2 days presented clinical and laboratory signs suggestive of neonatal infection. He was treated with antibiotics and discharged at the end of therapy in good health with good saturations, palpable femoral pulses and adequate capillary refill time. At the age of 10 days the baby was readmitted at the paediatric ward in dismal general condition, he was pale and sweating, had adequate femoral pulses, good saturations also at the lower extremities, had no respiratory distress or fever. His condition deteriorated quickly with progressive centralisation, diminished O_2 saturation (70–50%) at the lower extremities, femoral pulses no more palpable, but normal blood pressure at the arms, severe metabolic acidosis. Shocktherapy with oxygen, volume repletion and Dopamine infusion through an umbilical line as well as Prostaglandin PGE1 infusion were promptly started. Antibiotic therapy was also initiated. During this procedure the baby presented a cardio-respiratory arrest which recovered within one minute under intubation and ventilation, brief cardiac massage and Adrenalin. The clinical suspicion of a ductal dependent congenital hearth defect was confirmed by an echocardiography, which showed a massive dilated and hypertrophic right ventricle with compression of the septum and the left ventricle and a severe pulmonary hypertension. At this point the presumed diagnosis was coarctatio aortae. The clinical conditions improved slowly; after stabilisation the baby was transferred to a paediatric cardiosurgical centre. The diagnosis was confirmed and the baby underwent a surgical repair. He had an uneventful postoperative course and a favourable long term outcome.
Conclusion: A neonate who presents in shock within the first 3 weeks of life is highly likely to have congenital hearth disease, which should be considered ductal-dependent until proved otherwise. A Prostaglandin therapy has to be started immediately. In second line a septicaemia should be considered and treated. Coarctatio aortae occurs in 7 to 10% of ill newborn with congenital hearth disease. The diagnosis in utero is very difficult. In a severe coarctatio, which presents in the first few weeks of life the classical symptoms (a systolic gradient with week femoral pulses or/and a differential cyanosis) are often not detectable until the ductus is patent; closing of the ductus generally results in a cardio-vascular collapse. Neonates with left hearth obstructive lesions frequent present with profound metabolic acidosis and shock, but can be resuscitated effectively without persistent organ system impairment as the rule rather than the exception.

P 15

Failed neonatal resuscitation: the importance of post-mortem examinations

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Introduction: Unsuccessful resuscitation of a newborn infant in the delivery room is a very rare event. It is a devastating experience not only for the parents but also the resuscitation team, particularly when the reasons for resuscitation failure remain obscure.
Case report: This baby girl was born at 34 4/7 weeks of gestation by spontaneous vaginal delivery following premature rupture of membranes to a 37-year-old G7/P1. A left-sided congenital diaphragmatic hernia had been diagnosed antenatally, but based on a

favourable head-to-lung ratio severe pulmonary hypoplasia was felt to be unlikely. After delivery, there was no spontaneous respiratory effort and a heart rate of 80 bpm. Bag-mask ventilation led to recognizable chest excursions but the infant remained bradycardic. At three minutes of life, she was intubated without apparent difficulties. However, when attempts at ventilation through the endotracheal tube (ETT) produced no chest excursions, the ETT was removed and bag-mask ventilation was resumed. Adequate movement of the chest was again observed but the heart rate continued to deteriorate and chest compressions were started and epinephrine was administered. Additional attempts at intubation and ventilation through the ETT were unsuccessful. Tracheal agenesis with an esophago-tracheal or esophago-bronchial fistula was therefore suspected and an ETT was advertently placed into the esophagus. This time, bagging resulted in chest excursions consistent with the hypothesis. Unfortunately, the infant's heart rate continued to deteriorate and resuscitative efforts were discontinued after 45 minutes. On post-mortem chest X-ray, the stomach projected over the left lower chest but there was no lung aeration. Autopsy revealed bilateral agenesis of the diaphragms with bilateral intrathoracic herniation of the liver, as well as severe bilateral pulmonary hypoplasia.
Conclusions: Agenesis of the diaphragms with bilateral herniation of the liver can be missed on prenatal ultrasound examination due to similar echogenicity of liver and fluid-filled fetal lung. Post-mortem examinations (conventional radiography, magnetic resonance imaging and, of course, autopsy) may reveal unsuspected pathologies and thus provide much needed explanations.

P 16

Neonatal skull fracture and subdural hematoma after maternal aspirin treatment: casual association?

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Case report: Baby, born by caesarean section, with Kristeller's maneuver. Due to lupus anticoagulant Ab and a history of fetal loss, the mother was treated with aspirin during pregnancy. The newborn developed convulsions (day 2), fever (day 5), anemia and a massive increase of bilirubinemia. A CT-scan showed a subarachnoid and subdural hemorrhage predominant in the left cerebellar cisternal and a fracture at the middle occiput. PFA was abnormal. Evolution was good.
Discussion: The Kristeller's maneuver creates pressure on the bottom of the uterus to accelerate expulsion at birth. It may present several risks for the mother and the newborn, such as i.e. hematoma and hemorrhage. Inherited or acquired thrombophilia occurs in 50–65% of women with a history of unexplained fetal loss. Low-dose aspirin is the treatment of choice for prevention of venous thromboembolism and preeclampsia in pregnant women. Nevertheless, aspirin crosses the placenta and exerts antiplatelet effects in the fetus and newborn. Even if the risk is low, prenatal aspirin has been reported to be associated with the increased incidence of hemorrhage in the newborn infant.
Conclusion: Aspirin crosses the placenta and exerts antiplatelet effects in the fetus and newborn. Although only a few cases of minor bleeding tendencies have been reported, one should keep in mind that in combination with traumatic deliveries or in the presence of other haemostatic defects, the aspirin-induced platelet dysfunction may have a clinical relevance. Kristeller's maneuver should therefore be reserved for strictly indicated cases only. We suppose that the occiput fracture in this case report was caused by the Kristeller's maneuver, and – in combination with the aspirin-treatment of the mother – an intracranial bleeding was induced. We report the first case of an intracranial bleeding provoked by Kristeller's maneuver in combination with an aspirin treatment.

Poster SGP/SSP – Nephrology – Endocrinology – Diabetology

P 17

Assessment of glomerular filtration rate in children: from the new revised Schwartz formula to a new generalized formula

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The most widely used formula for estimating glomerular filtration rate (eGFR) in children is the Schwartz formula. It was revised in 2009 using iohexol clearances with measured GFR (mGFR) ranging between 15 and 75 ml/min x 1.73 m^2. Our study aimed to provide additional data to assess the accuracy of the Schwartz formula by using another gold standard method for mGFR, i.e. inulin clearance (iGFR); and to evaluate the accuracy of the Schwartz formula for children with less renal impairment. We compared 551 iGFR with the eGFR. The correlation between iGFR and eGFR was assessed using the Lin's concordance correlation coefficient. A circular binary segmentation method and a regression analysis were also performed, in order to find the best relationship between iGFR and eGFR. These approaches permitted to derive a new quadratic formula for eGFR. Both formulas were compared in terms of bias, precision and accuracy. Our results show that the Schwartz formula is applicable until a GFR of 103 ml/min x 1.73 m^2 and is significantly less accurate for a GFR ≥103 ml/min x 1.73 m^2. For an accuracy of 20% and 10%, the quadratic formula was significantly better than the Schwartz formula for all patients (P 0.04) and for patients with an iGFR ≥103 ml/min x 1.73 m^2 (P 0.02), respectively. In conclusion, the quadratic formula could replace the Schwartz formula which is only accurate for children with moderate chronic renal failure but not for those with less renal impairment or hyperfiltration.

P 18

Long term outcome after prenatal diagnosis of CAKUT

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Background: Congenital anomalies of the kidney and urinary tract (CAKUT) were commonly prenatal diagnosed. This retrospective study describes the long term outcome, potential risk factors and comparison of prenatal and postnatal diagnosis.
Patients and methods: 115 children with CAKUT (87 boys, 28 girls, born 1995–2000, treated at the Children's Hospital Zurich) were included. Prenatal data included ultrasound based diagnosis, pregnancy duration, amniotic fluid, complications, fetal interventions and extrarenal abnormalities. Following our local guidelines, patients were divided into 2 groups: 1) "Low risk" with unilateral (unil.) nephro-/uropathy or bilateral (bil.) isolated pelvic dilatation with normal amniotic fluid: US one week after birth and prophylactic antibiotics, if pelvic dilatation >10 mm, calixdilatation or hydroureter. 2) "High risk" with bil. pelvic dilatation and renal abnormalities, oligohydramnion, suspicion of posterior urethral valves (PUV) or other abnormalities: US within the first 2 days and prophylactic antibiotics immediately after birth, interventions according interdisciplinary approach. Follow up data included renal function (GFR calculated by Schwartz) and blood pressure. Study endpoints were normalisation of US, operation or death.
Results: Prenatally, isolated pelvic dilatation was most often diagnosed (81, 28 bil). Further diagnosis were hydroureteronephrosis (8, 2 bil.), cysts (14, 3 bil., 5 multicystic dysplastic kidney (MCDKD)), unil. malformation (3 double system (DS), 2 agenesies), abnormal kidney size (4), isolated megavesica (1), bil. hyperechogenicity (1) and abdominal tumor (1). Postnatally, 6 newborns had normal, 109 abnormal US: Mild pelvic dilatation of 5–10 mm (27, 15 bil.), ureteropelvic junction obstruction (30, 9 bil.), MCDKD (13), megaureter (11), isolated vesicoureteral reflux (8, all bil.), PUV (6), DS (4), autosomal dominant polycystic kidney disease (3), left agenesia (2), ureterocele and DS (2), cortical cyst (1), proximal ureterstenosis (1) and sinus urogenitalis (1). During long term follow up (median 13.3 months, range 0.1–185) 27 patients showed normalisation of the US

(median 12.8 months, range 0.1–108), 32 children received operation (median 5.2 months, range 01.–130), only 1 boy died. 34 patients showed reduced GFR, 17 of them had operations and 18 bil. abnormalities.
Conclusion: The most common prenatal diagnosis is isolated, unil. pelvic dilatation associated with good prognosis and often spontaneous remission. Bil. nephropathy, especially combined with malformations of the urinary tract, correlates with a higher risk of severe nephropathy.

P 19

Renal Function Follow-up Evaluation Using Cystatin C in Neonates Prenatally Diagnosed for Congenital Anomalies of the Kidney and Urinary Tract

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Objectives and study: Congenital abnormalities of the kidney and urinary tract (CAKUT) account for 20% of all significant anomalies detected on prenatal ultrasound. Despite this frequent occurrence, no reliable method to measure renal function (RF) is validated in neonates. Cystatin C (CysC) has been proposed to be an accurate renal marker for the neonatal period. The *aims* of this study were to assess long term RF prospectively from birth in neonates prenatally diagnosed with CAKUT.
Methods: 21 pts with severe kidney malformations (KM) had since birth renal function follow-up. Median follow-up is 235 (137-739) days. KM are repartee as follow: 12 pelvic dilatations >10 mm; 5 hypo-dysplastic or ectopic kidney (2 withTCF2 mutation); 3 urethral valves; 1 uretherocele; 1 megabladder. One of pts was start on dialyses and exclude from analyses. Factors influencing CysC were analyzed performing a linear mixed model to take account of the repeated measures.
Results: In our 20 pts, CysC decreases rapidly in the first month (M) (16.2%) p <0.001), slower between 1 M and 1 year (y) (3.9% per month, p <0.001) and stabilizes after 1 y (0.2% per month, p = 0.83). CysC was significantly increased in pts with bilateral KM compared to pts with unilateral KM (p = 0.02) and in TCF2 pts (p = 0.002). The decrease of the CysC over time was less pronounced in pts with bilateral KM (p = 0.04) and in TCF2 pts (p <0.001), these pts therefore presenting a worse prognosis in RF.
Conclusion: Renal function follow-up in pts diagnosed with CAKUT, using CysC showed a worse prognosis over time in pts with bilateral kidney malformation or TCF2 mutation.

P 20

Development of Nephrocalcinosis in Preterm Infants

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Introduction: Metabolic bone disease requiring calcium and phosphate substitution, is common in preterm infants below 32 weeks of gestation. An additional problem related to prematurity is Nephrocalcinosis (NC), the incidence of which ranges from 7% to 64%. The aim of this study was to determine the factors influencing the development of NC in preterm infants below 32 weeks of gestation.
Methods: The infants were divided into two groups, below 28 weeks and 28 to 32 weeks of gestation. The effects of birth weight, gestational age, nutrition, duration of TPN, use of antibiotics, especially gentamycin, caffeine, indomethacin, postnatal steroids, diuretics, calcium and phosphate substitution were assessed. Need for mechanical ventilation and the diagnosis of moderate to severe BPD were noted. 77 infants were recruited, 49 were between 28 to 32 weeks, 28 were below 28 weeks. Excretion of calcium, phosphate, citrate and oxalate were measured in spot urine samples at the age of 4, 8 and 12weeks. At the same time, ultrasound of the kidneys was performed.
Results: The incidence of NC in our patient population was 41.6% (32/77) with no difference in the two groups. Moderate NC was present in 21% (16/77) of the cases also with no difference in the two groups. Calcium excretion expressed as calcium:creatinine ratio was clearly higher in the subjects with NC. No significant correlation was noted with the factors mentioned above.
Conclusion: NC is common in preterm infants below 32 weeks of gestation. In accordance with the literature, the development of NC correlated with an increased urinary excretion of Calcium. There appeared to be no specific risk factors for the development of NC.

P 21

Neonatal hemolytic uremic syndrome due to Shiga-toxin-producing *Escherichia coli*

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Background: Hemolytic uremic syndrome (HUS) is a leading cause of acute renal failure in childhood. The majority of cases are preceded by an episode of diarrhea mostly due to Shiga-toxin-producing *Escherichia coli* (STEC). Metabolic diseases (cobalamin C disorder), defective regulation of the alternative complement pathway and congenital ADAMTS13 deficiency (Upshaw-Schulman syndrome) are possible causes for atypical HUS in the neonatal period. STEC can also rarely lead to neonatal HUS.
Case report: A newborn male, presenting with biliary vomiting two days after birth without diarrhea, showed on day six of life a sudden increase of total bilirubin (374 µmol/l). Laboratory findings showed hemolytic anemia with fragmentocytes (Hb 111 g/l), thrombocytopenia (39 $*10^9$/l) and acute renal failure (creatinine 101 µmol/l, urea 16 mmol/l). 24 hours later he developed epileptic seizures with good response to antiepileptic therapy (Phenobarbital and Topiramate). A cerebral ultrasound was normal. Family history was negative for renal diseases and none of the parents had shown gastrointestinal symptoms during the previous 2 weeks. Since the newborn recovered quickly with normalization of the hematological and renal parameters within 48 hours and normal neurological condition, plasma exchange or the monoclonal antibody against terminal complement protein C5 Eculizumab were not considered. Testing for causes of atypical HUS (metabolic, complement factors and ADAMTS13 activity) remained negative. Fecal analysis of both the newborn and his mother disclosed STEC, indistinguishable by microarray analysis, and pulsed-field gel electrophoresis, and harboring stx2B. Shiga-toxin Stx2B is of low virulence, not normally causing HUS. We postulate that the mother is a healthy carrier, who transmitted the bacteria by fecal-oral route to the newborn during delivery. In a newborn's steril bowel this microorganism can exceedingly proliferate thus leading to HUS.
Conclusion: HUS due to STEC expressing a toxin type of even low virulence can occur immediately after birth by mother-to-child fecal-oral transmission.

P 22

Severe hemorrhagic bullous skin lesions in Henoch Schoenlein purpura: a report of three cases

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Background: Henoch Schoenlein Purpura (HSP) is the most common acute systemic vasculitis in childhood, affecting skin, joints, gastrointestinal tract and kidneys. Severe hemorrhagic bullous skin lesions, which may create a diagnostic and therapeutic dilemma, have been rarely described in at most 2% of cases. Prognosis of HSP is generally excellent and long term sequelae are exclusively related to renal involvement.
Patients: Since 2004 we have observed three cases (all boys, age 16, 12 and 17 years at presentation) of otherwise typical presentations of HSP with remarkably impressive hemorrhagic bullous skin lesions primarily on the lower extremities. One patient presented with nephritic-nephrotic symptoms during the acute phase of the disease and subsequent persistent marked proteinuria. The other two patients did not have major manifestations in other organs or long-term sequelae.
Discussion: As with kidney involvement skin lesions of acute HSP may vary extremely in severity, which can lead to great uncertainty regarding diagnosis and treatment. Even apparently necrotic skin lesions seem to heal without scaring and severity of skin lesions do not seem to predict morbidity from other organs. There is no evidence of any benefit from steroids in the treatment of such severe forms of skin eruption in HSP. Reducing mobility seems to be the only way to prevent further spread of such lesions.
Conclusion: In case of a good general condition and other symptoms typical for HSP, even most severe vasculitic bullous eruptions on the skin should not lead to unnecessary investigations or treatment trials.

P 23

Bilateral central lung arterial thrombosis in a child with steroid sensitive idiopathic nephrotic syndrome

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Introduction: Children with idiopathic nephrotic syndrome (INS) are at increased risk of thromboembolic complications. Contributing factors include a high red blood cell count, hypovolaemia, drugs (steroids,diuretics,) and primary and secondary hypercoagulability.
Case report: We report a 7-year old boy with recurrent steroid-sensitive INS. When he experienced his 6th relapse, steroid therapy was deliberately withhold by his homeopathic therapist for 3 weeks leading to a severe nephrotic state with heavy proteinuria (protein/creatinine 742 g/mol), anasarca (massive edema) and increase of body weight from 24 to 32 kg. Standard oral prednisone therapy was commenced resulting in polyuria and remission (urine protein-free) within 10 days. Four days later he presented with orthopnea and dyspnea and marked weight loss (23 kg). D-dimer concentration was elevated (3298 ng/ml; n <500) and CT of the lungs demonstrated bilateral central lung arterial thrombosis. Extensive investigations revealed no further thrombosis or thromboembolic events; echocardiography was normal. Therapeutic anticoagulation was begun: Heparin intravenously for 2 days, followed by subcutaneous dalteparin. Within two days, the clinical symptoms resolved. A follow-up CT of the lungs one month later showed normal central vessels. Thus, prophylactic anticoagulation with subcutaneous enoxaparin was continued for 4 months. In addition, a primary thrombophilia was revealed (decreased free protein S concentration: 64%). The INS was treated with a 12-week course of oral cyclophosphamide, and the patient is in remission since.
Conclusion: Patients with INS are at risk of thromboembolic complications, in particular during a severe relapse, but also at the beginning of remission with marked changes in body fluid composition and coagulation factors. When patients with INS present with respiratory distress, pulmonary thromboembolism must be ruled out with CT of the lungs as method of choice. Patients with INS should be screened for primary hypercoagulability. The role of prophylactic anticoagulation in INS should be discussed based on the individual risk profile.

P 24

Idiopathic infantile hypercalcaemia and vitamin D prophylaxis – a new genetic disease

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Introduction: We present the case of a six months old boy who initially was diagnosed to have idiopathic hypercalcaemia of infancy in whom we detected at the age of six years two mutations in the CYP24A1 gene, leading to a deficiency of the 25-hydroxyvitamin D 24-hydroxylase enzyme accounting for an increased sensitivity to vitamin D. To our knowledge he is the first patient in Switzerland in whom the mutation could be found.
Case presentation: A six year old boy is followed in our outpatient clinic since his sixth month of life. Initially he presented with severe muscular hypotonia and developmental retardation. Diagnostic work-up revealed hypercalcaemia as well as nephrocalcinosis, parathyroid hormone was suppressed, 1.25-(OH)2-D3 in the upper normal range. After discontinuing daily vitamin D supplementation and introducing calcium reduced formula milk serum calcium decreased into the upper normal range. Nephrocalcinosis persisted, symptomatic nephrolithiasis occurred for the first time at the age of three years. Further extended diagnostic analyses did not contribute to a diagnosis. Recently genetic testing in our patient revealed two mutations in the CYP24A1 gene, which encodes the enzyme 24-hydroxylase that initiates the degradation of the 1.25-(OH)2-D3. A deficiency in 24-hydroxylase therefore leads to high concentrations of 1.25-(OH)2-D3 which in turn leads to an increase of the calcium and phosphate resorption triggered by vitamin D supplementation.
Conclusion: In infants with idiopathic hypercalcaemia, the presence of CYP24A1 mutations has to be considered and discontinuation of vitamin D supplementation may then be mandatory.

P 25

Pseudohypoaldosteronism: A rare cause of failure to thrive in infancy

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Introduction: Pseudohypoaldosteronism (PHA) secondary to urinary tract infection, i.e. pyelonephritis, may lead to a severe clinical picture with failure to thrive, dehydration and electrolyte dysbalance (hyponatraemia, hyperkalaemia). Differential diagnoses are congenital adrenal hyperplasia, adrenal hyopoplasia, primary aldosterone deficiency and gastrointestinal electrolyte losses. Transient PHA is a rare clinical entity, presenting in infants with pyelonephritis and/or underlying obstructive uropathy.
Case report: A 4-month-old Swiss boy was referred to our hospital because of failure to thrive. For the last 4 weeks he had suffered from pallor, mild diarrhea and less appetite, had drank more frequently smaller portions, but had neither fever nor signs of infection. He hadn't gained weight with fall from the 25th to the 3rd percentile. His past medical history was unremarkable except for a mild unilateral pyeloureteric junction obstruction (pyelon dilatation: 10 mm), already diagnosed prenatally. As vesicoureteric reflux had been excluded by cystography, no antibiotic prophylaxis was administered. At presentation, blood analysis showed hyponatraemia (121 mmol/l) and hyperkalaemia (5.2 mmol/l), but normal pH (7.41) and renal function (creatinine 19 umol/l). Blood count showed leucocytosis (18.2 G/L), CRP was normal (1 mg/l). Stool culture was negative. Urine examination revealed leucocyturia, positive nitrite and inappropriately high sodium (26 mmol/l); urine culture finally grew *E. coli* (10^6 CFU/ml). Intravenous therapy with ceftriaxone and amoxicilline, sodium substitution (3 mmol/kg per day) and fluid replacement was started. Assuming a PHA secondary to pyelonephritis, hormones were measured: Serum cortisol and ACTH were normal, but aldosterone (>10'000 ng/l) and renin (47130 mU/l) were highly elevated supporting the hypothesis. After 7 days the boy was discharged in good general condition on oral sodium substitution. Within 2 weeks, he had regained weight (10th percentile) while still on extra sodium (2.5 mmol/kg per d). One month later, serum aldosterone had returned to normal (487 ng/l).
Conclusion: The case of a young male infant with unexplained failure to thrive and salt-wasting finally led to the diagnosis of transient PHA. A review of the literature shows that almost all patients 1) were male infants <7 months of age, 2) had an underlying obstructive uropathy and 3) a febrile or afebrile pyelonephritis (*E. coli* or other bacteria). Tubular unresponsiveness to aldosterone with natriuresis is caused by combined action of cytokines in obstructive uropathy and bacterial endotoxins.

P 26

Late onset Group B streptococcal urinary tract infection with hyponatraemia and failure to thrive

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Introduction: Severe hyponatraemia with dehydration is a manifestation of a salt-losing crisis in neonates with congenital adrenal hyperplasia. We report a case of an infant with hyponatraemia with severe failure to thrive due to a renal cause with transient pseudohypoaldosteronism.
Case report: A 7 weeks old infant presented with severe failure to thrive (3250 g, P<3, SDS -2.4; birth weight: 3370 g), hyponatraemia (115 mmol/l) and potassium in the upper limit of norm (5.5 mmol/l). Skin showed erythematous non-folicular pustules indicating a miliaria rubra. The infant was afebrile and blood examination showed no signs of infection (leucocytes 12.7 G/l, CRP <0.6 mg/l). Catheter urine revealed macroscopic pyuria, an infection with Group B beta-hemolytic streptococci could be verified during the course. Blood cultures remained negative. Underlying causes for failure to thrive and electrolyte dysbalance like cystic fibrosis, renal waste of sodium (sodium in urine initial not measurable), thyroid disease or congenital adrenal hyperplasia could be ruled out. Additional laboratory investigation proved a pseudohypoaldosteronism with raised activity of plasma renin (847.0 mU/l, norm: 5–47) and high aldosterone (1631.2 ng/l, norm: 29–162). Initially hyponatraemia was corrected until within normal range and adequate treatment for urinary infection was started. With continued sodium substitution (maximum 3.6 mmol/kg/d) the child clinically improved. In the following months the girl showed catch-up growth, the levels of plasma renin activity and aldosterone normalised gradually and sodium substitution could be stopped at 5 month. Micturating cystourethrography showed a high-grade bilateral vesicoureteral reflux, the DMSA scintigraphy could not detect any cortical lesions. At last follow up with 12 month the girls weight was 9100 g (P50) and she showed normal psychomotoric development.
Conclusion: (Afebrile) urinary tract infection should be considered in infants presenting with hyponatraemia and failure to thrive. Salt-losing crisis are not always of adrenal origin. Due to inflammation and production of cytokines bacterial infection in combination with (obstructive) uropathy result in secondary pseudohypoaldosteronism. Urine diagnosis is crucial. Prompt clinical improvement occurred with antibiotic therapy and oral salt supplements. Miliaria rubra reinforces the diagnosis.

P 27

Aldosterone/Renin Ratio as a Key Player in the Diagnosis of Primary Hypoaldosteronism – a Case Report

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Introduction: Hypoaldosteronism is a rare inborn disorder due to a synthesis defect of aldosterone. It is relevant in newborns and infants as it leads untreated to life-threatening electrolyte imbalance.
Case presentation: A one month old female infant was transferred from a peripheral hospital with vomiting, dehydration, failure to thrive and electrolyte imbalance with Na 128 mmol/l (134–144), K 6.2 mmol/l (3.5–5.0). Pylorus stenosis, adrenogenital syndrome, complete adrenal insufficiency, renal malformations and insufficiency were excluded. Plasma renin concentration (PRC) checked on day 15 was highly elevated with 4935 mU/L (2.8–39.9) and plasma aldosterone concentration (PAC) was in the mid-range for newborns with 2314 pmol/l (27.7–4995). Because of the normal PAC hypoaldosteronism was not further considered. Conspicuous was the very low PAC/PRC ratio (0.46, normal 1- 105), indicating an insufficient increase of PAC in response to the high renin stimulation and suggesting hypoaldosteronism. Therefore, we started an oral substitution with fluodrocortisone and salt immediately. Under this therapy the general condition of the infant improved rapidly and the electrolytes remained within normal range.
Discussion and conclusions: In newborns and infants with consistent hyponatriaemia and hyperkaliaemia hypoaldosteronism should be promptly considered, since in this age group the salt-water homeostasis depends almost entirely on mineralocorticoids and their deficiency leads to life-threatening electrolyte imbalance. Diagnosis can be difficult due to the fact that PAC may appear in the normal range. In these cases the PAC to PRC ratio, which is an accepted screening tool for hyperaldosteronism, can be useful. PAC to PRC ratio <1 indicates an inappropriate low PA for the stimulus. Therefore, this ratio is suggestive for primary hypoaldosteronism as it was already shown in adults. Based on our experience of four newborns and infants with this rare disease, this ratio seems to be a reliable diagnostic parameter in this age group as well.

P 28

Molecular analysis of the 21-hydroxylase encoding gene CYP21A2 in patients with congenital adrenal hyperplasia

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Introduction: Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder originating from a defect in one of the enzymes involved in cortisol biosynthesis. CAH affects about 1:10'000 newborns with a carrier frequency of 1:50. A deficiency of the 21-hydroxylase is the most common cause of CAH. It is encoded by the CYP21A2 gene and depending on the mutation causes a classic CAH form with virilization and salt wasting or a milder non-classical form.
Method: For the molecular analysis of CYP21A2 we perform an MLPA analysis (MCR Holland) and sequence the entire gene. CYP21A2 is located close to a non-functional pseudogen on chromosome 6 and gene conversion between the two is the major cause of CYP21A2 mutations.
Results: We developed a strategy to sequence the entire CYP21A2 gene plus the surrounding regions. Here, we illustrate in an overview the four fragments that were amplified and list the primers used for amplification and sequencing of CYP21A2. Furthermore, we present several cases of CAH patients or carriers with mutations in the CYP21A2 gene and show their sequence or their MLPA results.
Conclusion: Over 150 different mutations have been described for the CYP21A2 gene so far. For this reason it is important that we not only search for the most abundant mutations but instead investigate the whole gene area for deletions/duplications and sequence the entire gene for point mutations. With this approach we assure that we also detect rare mutations.

P 29

Concomitant Blepharophimosis-Ptosis-Epicanthus Inversus Syndrome (BPES) and Congenital Adrenal Hyperplasia (CAH) in a young girl

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Introduction: The Blepharophimosis-Ptosis-Epicanthus Inversus Syndrome (BPES) is a rare autosomal dominant eyelid malformation associated to mutations in the *FOXL2* gene on chromosome 3q23. Type I includes the eye-malformations characteristics and premature ovarian failure, which is not found in type II. Congenital adrenal hyperplasia (CAH), associated to mutations in the *CYP21* gene on chromosome 6, is one of most common autosomal recessive disorders characterized either by salt wasting syndrome or simple virilization. A 3.2 years old girl with known BPES was referred to our unit because of an enlarged clitoris.
Case report: The only child of unrelated algerian parents presented at 3.2 years with an hypertrophic clitoris (20x4 mm, N: 12–15 mm) but no other signs of virilisation. Accelerated growth (+10.4 cm/y (+2.03SD)), slightly advanced bone age (3.75y) and typical signs associated with the BPES were noted. Blood test showed a normal serum Na 137 mmol/L (N: 135–145 mmol/l) and high morning 17-OH-Progesterone (59.8 nmol/L, N <3 nmol/L) with normal basal cortisol (419 nmol/L, N: <630 nmol/L). Adrenocorticotropin stimulation-test confirmed the diagnosis of CAH (17-OH-P max 141 nmol/L). Genetic testing demonstrated an inherited heterozygous compound form with a genetic conversion in the exons 1, 2 and 3 and a mutation V281L (1685G->T) in exon7 of the *CYP21* gene, consistent with CAH (simple virilization). A missense heterozygous mutation (c.650C>G, p.Ser217Cys) in the single exon of *FOXL2* gene was further identified. Hydrocortisone treatment was introduced, leading to normalization of growth velocity and stabilization of the clitoris size.
Conclusion: To our knowledge, we present the first description of concomitant BPES and CAH. Due to the high frequency of the *CYP21* mutations, this association is probably incidental. Pubertal development must be followed closely in our patient.

P 30

Not a coincidence: Diabetes mellitus in patients with renal, genital and other abnormalities (MODY 5)

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Background: HNF1β is a transcription factor involved in the development of pancreas, kidney, gut, liver, lung, neural tube, and internal genital structures. A defect in HNF1β causes structural and functional renal abnormalities as well as diabetes mellitus due to pancreas malformations (Renal Cyst and Diabetes Syndrome, MODY 5).
Case reports: Case 1 is a 10 year old girl with history of bilateral mulitcystic renal dysplasia sent for endocrine consult for familial early-normal pubertal development. Urinalysis revealed the coincidental finding of large glucosuria. Random Glucose was 11.4 mmol/l, HbA1c 9.2%, diagnostic for diabetes mellitus. Diabetes-specific auto-antibodies were negative, family history positive for atypical type 2 diabetes (T2DM) in 2 prior generations. Two months after diagnosis of diabetes and start of insulin treatment, the patient developed acute pancreatitis and cholangitis. MRI and Endosonography revealed an enlarged pancreatic head, inhomogeneous with multiple small cysts, partially compressing pancreatic and bile ducts, and agenesis of pancreas tail. Gene sequencing confirmed the suspected diagnosis of HNF1 β mutation (point mutation IVS1-1G>A). Case 2 is a 17yo girl with primary amenorrhea, initially diagnosed to have Mayer-Rokitansky-Küster-Hauser syndrome with hypoplastic vagina and aplastic uterus. Kidney function and anatomy were normal but for a single cyst in the right kidney. Urinalysis revealed large glucosuria, random glucose was 12.9 mmol/l, HbA1c 6.9%, diagnostic for diabetes mellitus. Diabetes-specific auto-antibodies were negative, family history positive for T2DM in both obese parents. Genetic analysis revealed a large deletion on chromosome 17q12 containing, among others, *HNF1B* gene.
Conclusions: – A cheap and simple measure like a urine dip stick may reveal unexpected diagnoses. – Hyperglycemia/ glucosuria should be sought in patients with otherwise unexplained structural or functional kidney abnormalities, as HNF1β mutations account for 14% of renal abnormalities, around half of which also cause diabetes mellitus. – The combination of diabetes mellitus and kidney or genitourinary abnormalities should raise suspicion for *HNF1β* mutation (MODY 5) – even with negative family history, as 32% arise de novo. – The etiology of diabetes mellitus in MODY 5 is caused by pancreas a- or hypoplasia, therefore treatment consists of insulin, oral hypoglycemic agents are mostly ineffective.

P 31

Five years follow-up of a patient with severe congenital hyperinsulinism

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Introduction: Congenital hyperinsulinism is associated with recurrent hypoglycaemia due to inappropriate insulin secretion by the pancreatic islet β cells. We present a newborn patient with severe hyperinsulinaemic hypoglycaemia and his five years follow-up.

Case report: A macrosomic (4640 gr (>P90)) female newborn was delivered at term after uneventful pregnancy by caesarean section because of pathological CTG with an Apgar score of 6/9/9. She developed severe hypoglycaemias (minimal <0.1 mmol/L; Norm (N) >2.5) immediately after birth, needing exogenous glucose infusion (>18 mg/kg/min). Laboratory workup during hypoglycaemia showed unsuppressed insulin (45.4 mU/L; N <2.8) in the absence of ketone bodies confirming the diagnosis of congenital hyperinsulinism. Initial treatment with diazoxide was ineffective and continuous subcutaneous octreotid administration by pump was initiated leading to rapid reduction of supplemental glucose intake. Genetic analysis (Odense University Hospital, Denmark) showed two genetic variations (probable polymorphism) c.753G>T (->G251G) and c.3989-62G>C on gene *ABCC8*. A 18F-DOPA PET-scan performed at 1½ years of age couldn't accurately differentiate between focal and diffuse type of congenital hyperinsulinism. The evolution was excellent with normalization of BMI at 2½ years of age and normal neurodevelopment. Octreotid treatment could be stopped at 5 years of age. Fasting insulin six months later was within normal range (10.7 mU/L; N 2.8–13.5), as well as glycaemia and C-peptide (0.8 µg/L; N 0.54–1.57).
Conclusion: Adequate and rapid initial treatment is essential to prevent deleterious neurodevelopmental outcome often associated with severe neonatal hypoglycaemia. Our patient showed successful and persistent response to octreotid permitting to avoid surgery. The evolution suggests a «transient» phenotype of congenital hyperinsulinism associated with two previously not described genetic variations on the *ABCC8* gene.

P 32

Always be suspicious! – Hypoglycemia caused by exogenous insulin intoxication

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Background: Hypoglycemia in infancy beyond the first few days of life is likely a sign of congenital endocrine disorder or inborn error of metabolism. The most common cause is congenital hyperinsulinism. Intoxication with exogenous insulin may mimic hyperinsulinism.
Case report: A two month old former preterm baby girl was admitted to the children's hospital emergency department by her parents for sudden loss of consciousness with seizures. Vital signs were and remained normal but for some brief apnoeic spells with decreased oxygen saturation. The remainder of the clinical examination was unremarkable. Laboratory evaluation revealed hypoglycemia of 0.6 mmol/l in the absence of ketonuria and with normal electrolytes. Critical labs were taken and iv glucose was administered. Glucose requirements reached a peak of 18 mg/kg/min with spontaneous decrease within 24 hours. Surprisingly, consciousness did not return until 24 hours after normalisation of plasma glucose. EEG and brain MRI, were normal. Critical lab results revealed largely elevated insulin (6550 pmol/l) with undetectable C-peptide, diagnostic for intoxication with exogenous insulin. In addition, urine tox screen was positive for benzodiazepines, explaining the prolonged impairment of consciousness. Patient history was remarkable for two prior admissions for unexplained loss of consciousness. However, blood glucose had been normal during those prior episodes. Tox screening had not been performed previously. After separation of the child from her parents, glucose values remained normal on enteral feeds ad libitum. Neurological examination was remarkable for lack of visual fixation – possibly a neurological sequel of severe hypoglycemia.
Conclusions: Exogenous insulin is an important differential diagnosis in hypoketotic hypoglycemia. Inappropriately low C-peptide in the presence of elevated insulin levels will differentiate between exogenous and endogenous insulin. As in our patient, polyintoxication may be present. We therefore recommend toxicological screening in any case of unexplained impairment of consciousness – even in very young patients.

P 33

A rare case of encephalopathy in a teenage boy

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We describe the case of an adolescent male with a rare cause of encephalopathy that require several hospitalizations before receiving the right diagnosis and consequently the adequate therapy. He presented many episodes of generalized tonic-clonic seizures followed by aggressiveness and extreme psychomotor excitement. In one case he was complaining of intense sensation of cold and showed hypotermia (TA 34.1°C). Biochemical and radiological exams (X-ray, cerebral CT and MRI) were all normal but cerebrospinal fluid reveled a hyperproteinorrachia with increased albumin and Ig G. The urine toxoscreen was negative. The blood culture and the search for common causes of infective encephalitis by serological and PCR based-analysis on the blood and cerebrospinal fluid were negative. EEG showed an asymmetry in basal activity with slow waves referred at posterior part of the right cerebral hemisphere. The endocrine assessment revealed the presence of a primitive hypothyroidism: TSH 21.390 mIU/L (NV 0.4–4.0), FT4 7.1 pmol/l (NV 7.5–21.1), FT3 4.7 pmol/l (NV 3.8–6.0) with autoimmunity (thyroperoxidase antibodies 10640 IU/ml (NV <60.0), thyroglobulin antibodies 55.5 U/ml, (NV <33). Furthermore the research of thyroid antibodies in CSF was positive (thyroperoxidase antibodies 80.10 (NV negative). The other markers of autoimmunity (antinuclear antibody, anti-DNA antibodies, anti transglutaminase antibody, acetylcholine antibody, antineutrophil cytoplasmic antibody, antifosfolipidic antibodies, lupus anticoagulant, anti-smooth muscle antibody, LKM antibody, anti-Ro/SSA and anti-La/SSB antibodies) were negative. This findings allowed us to diagnose an Hashimoto's encephalopathy. Therefore a therapy with high-dose of steroid and levothyroxine was started. The patient showed a progressive improvement and he has had no more seizures. At last visit he had normal thyroid function test and a decrease of autoimmunity but he presented an impairment of cognitive functions with involvement of short term memory and attention. Therefore he is actually supported both psychologically and neurologically. We underline that is necessary a high degree of suspicion for a prompt diagnosis of this rare disease in pediatric patients with neuropsycological symptoms not well defined by other disorders.

P 34

Severe Acne Conglobata after Treatment of Constitutionally Tall Stature

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Background: Sex steroids are used in the treatment of tall boys and girls with the aim to accelerate bone maturation leading to height reduction. The decision to initiate a treatment for tall stature is generally based on psychological reasons, but may also prevent orthopaedic complications related to this condition.
Methods: Illustrated case report and review of literature.
Findings: We present a 16-year-old male adolescent with a predicted height of 204.8 ± 5.4 centimetres according to Greulich and Pyle. He was started on a two weekly intramuscular therapy of 500 mg testosterone. After nine months on this regimen he developed on his face and thorax a severe acne conglobata grade 8–10 according to Leeds. Therefore the testosterone therapy was discontinued and the patient was put on antibiotics and isotretinoin. After 3 months skin lesions were partially healed with visible remaining skin defects and severe scars. Height reduction was successful with a final height of 191 cm.
Discussion: Height reduction therapy in boys using testosterone is associated with several side effects as weight gain, gynecomastia, muscle ache, edema, and hypertrichosis. Changes in psychological and sexual behavior rarely exceeded the normal range seen in adolescence. Although testicular volume is temporarily decreasing, sperm quality and paternity is not significantly altered. Acne is by far the most reported side effect. A causal relationship with androgen therapy is likely. Acne fulminans has been reported occasionally.
Conclusion: Height reduction therapy with sex steroids is an effective treatment of constitutionally tall stature but is associated with potentially severe side effects. The indication should be previously discussed with a pediatric endocrinologist and patients wishing hormonal height reduction should be fully informed about possible side effects. In the particular case of testosterone-induced acne conglobata, discontinuation of hormone therapy and dermatological counseling are mandatory.

P 35

Preschool obesity in Geneva: overweight surveillance in a pediatric emergency department

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Background: The prevalence of obesity remains insufficiently assessed in preschool children in Switzerland. Early prevention could reduce teenage obesity and its morbidity. Emergency departments could be an excellent entry-point for many children who do not attend regular checkups.
Methods: This is a prospective cohort study of children under 5 years attending the Geneva Children's Hospital Emergency Department, between September 2010 and March 2011, with any accident or acute disease. Data included sex, age, postal code, disease, and emergency degree. According to the new Swiss Pediatrics Society references, the World Health Organization (WHO) ANTHRO Software™ was used to calculate the Z-scores for Body-Mass-Index (BMI)-for-age (BAZ),

excluding implausible values. Multiple regressions analyzed disease predictors using STATA 11.0™.
Results: We included 2814 children aged 0-5 years (median 1.9). We found a total of 441 children (15.7%) at risk of overweight, 129 (4.58%) overweight and 54 (1.92%) suffering obesity. Obesity rates were lower under the age of one (1.06% vs. 2.24%, p = .044), stable in other age-categories. Multivariate analyses showed no area-code geographical pattern. Sex, types and severity of disease did not confound the levels of overweight.
Conclusions: Compared to the WHO recent growth standards for well-nourished children, the rates of overweight and obesity in preschool children in Geneva are high. Based on our data, no specific district can be targeted for health-promotion. The cause of consultation did not bias the level of overweight, suggesting that Pediatric Emergency Services could be excellent "sentinel sites" for obesity-malnutrition surveillance.

P 36

Acute changes in secretion of the hormone amylin following a meal challenge in lean and obese adolescents

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Background and Aims: Amylin is a pancreatic B-cell hormone, which is stimulated in response to nutrient intake and plays a critical role in the control of postprandial glucose regulation by lowering inappropriate post meal glucagon secretion and has inhibitory effects on gastric acid secretion, gastric emptying, and eating. The best-characterized function of amylin is its role as a satiation signal. Animal work suggests that amylin functions as an adiposity signal and that amylin secretion may be altered by increased adiposity. In adults, amylin concentrations correlate with the degree of overweight; furthermore fasting amylin levels are higher in obese than in lean persons. No data are available on amylin kinetics in overweight adolescents.
Objective: To characterize amylin, insulin, glucagon and glucose plasma kinetics in response to meal ingestion in lean and obese adolescents.
Setting: Observational case-control study.
Methods. Thirty healthy adolescents were recruited, 14 were lean (5 males, 9 females; mean age = 14 years, BMI range = 19.8–23.9 kg/m^2) and 16 were obese (8 males, 8 females; mean age = 13 years, BMI range = 31–41 kg/m^2). After an overnight fast, they consumed a mixed 500 kcal meal (bread, butter and chocolate milk) during which plasma samples were collected at multiple time points for measurement of several feeding-related hormones. Fasting glucose and insulin levels were used to calculate insulin sensitivity using the HOMA index.
Results: Obese adolescents had higher fasting and greater postprandial amylin concentrations (p <0.05, respectively) with associated increased postprandial glucose and insulin levels (both p <0.05). As a result of higher fasting insulin levels 31 ± 3 µU/ml vs 9 ± 1 µU/ml, p <0.01, the HOMA index was 4.0 ± 0.4 in obese and 1.2 ± 0.1 in lean subjects (p <0.01) documenting insulin resistance. Plasma concentrations of glucagon were not different between obese and control groups.
Conclusions: 1. Obesity in adolescents is associated with hyperamylinemia. 2. The increase in amylin in childhood obesity is associated with hypersecretion of insulin in obesity with consequences for metabolic control. 3. The high amylin levels in obese adolescents do not induce augmented inhibition of glucagon suggesting amylin resistance. Our studies support the idea that amylin acts as a regulator of glucose metabolism and satiation and warrant further investigation.

P 37

Quality of life of young adults treated with Recombinant Growth Hormone during childhood

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Introduction: Recombinant human Growth Hormone (rhGH) prescribed since 1985 in Switzerland is used with increasing frequency. Short term safety is good, but little is known on long term outcomes including quality of life (QoL). We aimed to assess QoL in young adults treated with GH during childhood.
Methods: A postal questionnaire was sent to patients registered in the Swiss Growth Registry (N = 700), born 1967–1993, who had been treated with rhGH. QoL was assessed with SF-36, containing 36 items that measure 8 dimensions of health status. Scores were normalized with the German normal population mean score (age and sex specific) and median was set at 50 with a standard deviation of 10.
Results: We received 375 / 700 questionnaires, corresponding to a response rate of 54%. Mean scores of all 8 dimensions were comparable with reference data from Germany (Swiss norm data unavailable) and were as follows: physical functioning (47.6), role physical (49.1), bodily pain (55.5), general health (51.0), vitality (53.9), social functioning (49.3), role emotional (48.0) and mental health (52.1).
Conclusion: There was a similar QoL in young adults who had been treated with rhGH during childhood and the general population. In a next step we will determine if there are differences between diagnostic groups, and if there is an association between QoL and final height.
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Poster SGP/SSP – Neuropaediatrics – Genetics

P 38

New Genetic Tests: What is the impact in patients with mental retardation with/without dysmorphic traits from the southern part of Switzerland

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Introduction: Children with mental retardation are commonly encountered in child clinics and establishing an etiological diagnosis is a challenge for pediatricians. The new ARRAY based Comparative Genomic Hybridization (array-CGH) is a revolutionary approach which allows us to characterize very small genetic abnormalities undetectable by standard approaches. The aim of this study was to describe the impact of new genetic tests on a population of children from the southern part of Switzerland, with mental retardation along with their features and therapy and follow-up.
Methods: All children born between 1.1.2000 and 31.12.2010 with mental retardation evaluated at the Paediatric Neurology Unit of the Ospedale San Giovanni in Bellinzona, with/without dimorphic traits, were enrolled in our data bank and their clinical characteristics and genetics results were studied.
Results: 118 patients with mental retardation (65 male and 53 female) were evaluated. 25 of these patients had not previously had genetic tests and hence, were excluded. In 27 patients with typically dimorphic traits it was possible to make clinical diagnosis. In some cases we have carried out tests to confirm the diagnosis. In 4 patients an MRI disclosed the diagnosis. In the 62 remaining patients (42 with unspecific dimorphic traits and 20 without) 19 had abnormal array-based comparative genomic hybridization results
Conclusion: Our results are interesting and show that the array-CGH allows us to find a definitive diagnosis in 19 patients where until now it wasn't possible to have safe aetiology to their mental retardation. The clinical implementation of array comparative genomic hybridization has revolutionized the diagnosis of patients with syndromic or nonsyndromic mental retardation. Array CGH may merit consideration as a first-tier test in the context of a child with unexplained mental retardation.

P 39

When 36 is bigger than 63: Numbers in the brain of children with developmental dyscalculia

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Introduction: In every classroom sits a child that struggles to decide whether 36 or 63 is larger. These children suffer from developmental dyscalculia (DD), a learning disability affecting specifically number processing and calculation. The present project represents the first

attempt to evaluate neuro-plastic effects on brain structure of a custom-designed training program for dyscalculic children.
Methods: We have developed a training program based on latest neuropsychological concepts of DD. Children with and without DD were examined before and after completion of the 5 weeks training by means of magnetic resonance imaging (MRI) and behavioural tests.
Results: Obtained results are promising and showed an improvement in numerical skills and a modulation of brain function. Children needed less neuronal effort to solve the numerical task after the training [1]. The investigation of training effects on brain structure is still under evaluation, but our recent data point to clear differences in fibre connections between dyscalculic children and controls [2]. Therefore, also structural changes in the brain are also expected due to our training.
Conclusion: Our results shed further light on the behavioural and neuronal characteristics of this still unexplored learning disability with respect to learning. Finally, this study provides important insight into the manner in which educational software games support learning efforts in affected children and further enhance the prospects of linking changes in brain structure to educational experimental manipulations.

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P 40

Unilateral parenchymal venous haemorrhagic infarction in preterm infants: A population based study on neurodevelopmental outcome

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Purpose: Unilateral parenchymal venous haemorrhagic infarction (PVHI) is an important problem in preterm infants and usually occurs after typical subependymal haemorrhage. Its prognostic significance is not well established. In this retrospective analysis we describe the neurodevelopmental outcome of preterm infants with this type of lesion.
Method: A population based retrospective analysis of all preterm infants with unilateral PVHI cared for at the Children's Hospital of Lucerne between January 1999 and January 2012. Diagnosis was either made by cerebral ultrasonography and/or by magnetic resonance imaging (MRI). Neurological outcome was based on most recent neurological examination and measured with the Gross Motor Function Classification Scale (GMFCS) for motor and Mental Developmental Index (MDI) for cognitive outcome.
Results: A total of 2731 preterm infants (gestational age <37 weeks) were admitted during the observation period. Among these, 15 had been diagnosed with unilateral PVHI (prevalence 0.5%). These 15 infants had a median gestational age of 27 3/7 weeks (range 23 6/7 – 32 3/7 weeks) with a median birth weight of 1063 g (range 560 g – 1950 g). Median age at the end of follow up was 5.6 years (range 12 months – 10.8 years). 2 children (13%) had died in the neonatal period. At follow-up, 8 children (72%) were at level I of the GMFCS, 2 (18%) at level II and 1 (9%) at level III. All children were ambulatory. Five children (45%) had an MDI >100, 1 (9%) had an MDI between 85–100, 3 (27%) an MDI between 70–85, and 2 (18%) an MDI between 50–70 (two patients were lost to follow-up). Thus, severe neurosensory impairment was observed only in a minority of patients following unilateral PVHI.
Discussion: Our experience in this small cohort suggests that neurodevelopmental outcome in premature infants with unilateral PVHI is not uniformly devastating. We consider these findings to be relevant for ethical decision-making in very low birth weight infants, particularly regarding redirection of care following unilateral PIVH.

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Myotonic dystrophies – analyzis of incidence, age of presentation and primary symptoms in the population of the central part of Switzerland from 1995–2010

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Introduction: Myotonic dystrophy type 1 (DM 1, M. Curschmann-Steinert) is a complex multisystem disorder caused by a dynamic mutation of the DMPK-gene on chromosome 19. In the pediatric population, it mainly manifests with neuromuscular, cognitive, gastrointestinal or unspecific symptoms of varying degree at different ages. In this report, we analyse the population of the central part of Switzerland for incidence, age of presentation and primary symptoms of DM 1.
Methods: Retrospective analysis of the clinical presentation and medical history of all children with confirmed DM1 – mutations (>60CTG-repeats) born between 1995–2010 in the Central Switzerland and comparison of the results with published data.
Results: Between 1995 and 2010, 12 Patients with DM 1 were registered at Childrens Hospital in Lucerne. In 4, the diagnosis was made in the neonatal period due to typical severe muscular hypotonia/ respiratory insufficiency and/or feeding difficulties. The remaining children were diagnosed beyond the neonatal period because of developmental delay with hypotonia (n = 4), bladder/bowel incontinence (n = 2), dysphagia with severe esophageal reflux disease (n = 1), orthopedic feet deformity (n = 1). The mean age for diagnosis after the neonatal period was 3.8 years (range 2–11.5), but retrospectively all of these patients had shown symptoms in their first year of life. The mean value of CTG-repeats was 1000 (range 700–1500). All children had inherited the disease by their mothers, who mostly did not show overt clinical symptoms of the disease. During follow-up, all patients diagnosed as neonates improved substantially; the disease course was non-progressive in most of the others. The incidence of DM 1 can be calculated as 1/10´000 live-births using epidemiological data from the federal office for health, comparable to the incidence reported worldwide (range 1/8000–1/20000).
Conclusion: In this population-based cohort, the majority of children with myotonic dystrophy presented in the post-neonatal period, often with unspecific symptoms. Considering the impact of diagnosis on patient management and family councelling, myotonic dystrophy should be considered in children with psychomotor retardation, "myopathic" facies, skeletal muscle weakness, incontinence, unexplained feet deformity or gastrointestinal symptoms.

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Isolated neonatal bilateral palsy of the n. radialis

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Aims: There are some rare case reports in the literature describing isolated paralysis of the n. radialis in newborns. We report the case of an unusual neonatal bilateral palsy of the n. radialis.
Methods: Case report and review of the literature
Results: We report the case of a fullterm girl with isolated n. radialis palsy of both hands diagnosed at the age of 4 weeks during an inpatient stay due to a respiratory infection. She was delivered normally after an uneventful pregnancy in the 38th gestational week. At four weeks of age she showed bilateral palsy of the n. radialis with drop hands, abduction of the thumbs and ulnar deviation. Other neurological findings were normal. After 8 weeks of ergo- and physiotherapy there was only marginal improvement of the palsy, but at the last follow up there was a significant recovery of function to almost normal. Approximately 60 cases of neonatal radialis palsy have been reported in the literature. The palsy was observed within a few hours and a few days after birth and was usually unilateral. The most common underlying cause according to the literature is subcutaneous fat necrosis or ecchymosis over the course of the radial nerve suggesting the possibility of a trauma to the nerve. Isolated radialis palsy can be clearly differentiated from plexus paresis and in nearly all presented cases full recovery between one week and five months has been reported.
Conclusion: There have been only four cases of bilateral radialis plasy reported in the literature. All of them have been seen in the context of subcutaneous fat necrosis of the upper arms. In our case there was no indication of fat necrosis or ecchymosis at the time of diagnosis or earlier. In spite of the delayed diagnosis there was an almost full recovery of function. This case shows that isolated palsy of the n. radialis is likely to have a favourable outcome.

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Do children and young adults with cerebral palsy profit from the supplementation of ω-3 and ω-6 fatty acids? – 5 years experience with Equazen Eye Q® as part of a multimodal management

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Introduction: Several studies showed that the polyunsaturated fatty acids are not only involved in the development and maturation of neuronal structures, but in particular play a central role in the functioning of the brain.
Objectives: What is the impact of Equazen Eye Q® on the motor impairments and the associated disabilities of children and young adults with cerebral palsy (CP)?
Methods: Since 2008 our open-label study followed 81 patients with CP aged 2–30 years who have been treated for at least 1 year with Equazen Eye Q®, based on the specific combination of the long-chain ω-3 fatty acids eicosapentaeonic (EPA) and docosahexanenoic acid (DHA) and ω-6 fatty acid (α-linolenic acid, GLA) with a ratio of 9:3:1. In the first 6 months all other therapy was kept unchanged. Symptoms, treatment results and adverse effects were recorded using standardised questionnaires and qualitative methods.

Results: Most patients with GMFCS level 1 and 2 improved in quality and velocity of the fine motor skills when supplemented with Equazen Eye Q®. These patients had a significant improvement in behaviour and cognitive impairments in general (attention, hyperactivity, anxiety, language processing, memory etc) compared to the patients with GMFCS level 3-5. These showed better vigilance, stabilized mood and health situation in general (e.g. less infections). The quality of life was improved in the study population.
Conclusion: These results show that Equazen Eye Q® can safely and effectively integrated in multimodal treatment concepts for children and young adults with CP, especially for the associated symptoms.

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Mutism in Adeno-/Rhinovirus Encephalopathy with a Reversible Splenial Lesion: A Case Report

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Introduction: Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a rare clinical-radiological syndrome almost exclusively found in South-East Asia. Common features include severe encephalopathy after 1 to 3 days of prodromal illness and an involvement of the splenium of the corpus callosum demonstrated on MRI. All patients with MERS reported previously recovered completely within a month from clinical and radiologic abnormalities.
Case Report: A 2 10/12-year-old Swiss girl was admitted to our hospital with apathy, somnolence (Glasgow Coma Scale 9), atactic truncal instability and mutism following a 3-day prodromal illness with fever, cough and vomiting. Laboratory investigations demonstrated elevated C-reactive protein (58 mg/l) and white blood cell count ($17.4x10^9$/l), and slight pleocytosis (5/mm^3) and increased protein (0.5 g/l) in the cerebrospinal fluid (CSF). EEG showed mild slowing of background activity, but no epileptic discharges. Brain MRI revealed high-intensity signal abnormality in the central splenium of the corpus callous in T2- and diffusion-weighted images. Other CNS structures including cerebellum showed normal signal intensities. Adenovirus and rhinovirus were identified by PCR from a nasopharyngeal swab. While her vigilance normalized over the first days, she recovered only slowly from atactic and mutistic abnormalities. Follow-up MRI-study on day 22 showed complete normalization. After 5 months of physio-, speech and occupational therapies, the girl showed only slight remnants of language and coordination problems.
Conclusion: Our case expands the spectrum of MERS showing that this entity can occur in very young Caucasian children in association with adenovirus infection and mutism. A longer time course of recovery is possible without changing its benign outcome.

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Malignant Neuroleptic Syndrome due to Tetrabenazine in a Boy with an Extrapyramidal Disorder

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A 7-year-old boy with a known extrapyramidal disorder was admitted with fever, sporadic vomiting, respiratory distress and worsening dystonia for one day. An intrathecal baclofen (ITB) pump had been placed 12 months before for severe dystonia insufficiently controlled by oral baclofen and tetrabenazine. Reduction of tetrabenazine had been unsuccessful after placement of the ITB pump because of rebound dystonia and irritability. On admission, the patient presented in a reduced general condition, dehydrated, febrile and with clinical signs of obstructive bronchitis. CSF and urine analysis were normal, radiological exam revealed a pulmonary infiltrate. Suspected pneumonia was treated with intravenous rehydration and antibiotics. Additional severe hypernatremia, mild metabolic acidosis and renal failure were ascribed to dehydration. Because of persisting somnolence, dystonia, hyperthermia, hypernatremia and metabolic acidosis despite adequate fluid replacement and antibiotic treatment, laboratory evaluation was extended. Severe rhabdomyolysis was noted. Oral baclofen was added until dysfunction and disconnection of the ITB pump was excluded and acute baclofen withdrawal was ruled out. Neuroleptic malignant syndrome (NMS) was diagnosed. Tetrabenazine was stopped, and replaced by diazepam. The patient recovered within 11 days under supportive therapy. NMS is a potentially life threatening disorder characterized by hyperthermia, autonomic instability, mental status change and rigidity as well as multiple additional findings such as elevated CK levels, electrolyte abnormalities and leukocytosis. Important differential diagnoses include acute systemic or central nervous infection, acute baclofen withdrawal, serotonin syndrome and malignant hyperthermia. Treatment of NMS consists in removing the causative agent and aggressive supportive care. Acute baclofen withdrawal has to be considered in patients with an ITB pump and NMS in patients on neuroleptic agents presenting with an unclear clinical picture, as prompt recognition has important therapeutic consequences.

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Mutations in the *ROGDI* gene cause epileptic encephalopathy and amelogenesis imperfecta (Kohlschütter-Tönz syndrome)

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Introduction: We report on a girl with left-sided hemiconvulsive seizures beginning at age 6 months, later she showed febrile and complex focal seizures. Imaging of the brain by MRI was normal. Her primary and secondary dentition showed the typical abnormality of the enamel, known as amelogenesis imperfecta. The motor and speech development was delayed. Kohlschütter-Tönz syndrome (KTS) is a rare autosomal recessive disorder characterized by the combination of epilepsy, psychomotor regression and enamel defects. The molecular basis has not yet been elucidated. Here we report that KTS is caused by mutations in the *ROGDI* gene.
Methods: Using a combination of autozygosity mapping in consanguineous families and exome sequencing we identified *ROGDI* gene mutations in several unrelated families.
Results: In our index case, we found compound heterozygosity for the splicing mutations c.531+5G>C and c.532-2A>T in the *ROGDI* gene, respectively. The latter mutation was also found heterozygous in the mother of the Swiss index patient with KTS reported in 1974. Beside the enamel defects, the dysmorphologic findings included a lateral flaring of the eyebrows, prominent nasal bridge, thin vermillion border of the upper lip, clinodactyly of fifth fingers and some café-au-lait spots.
Conclusion: We report for the first time that Kohlschütter-Tönz-Syndrome, an autosomal recessive disease characterized by the unusual combination of epilepsy, psychomotor regression and enamel defects, is caused by mutations in *ROGDI*. The protein coded by the *ROGDI* gene is predicted to contain a leucine zipper domain but its function has not been investigated in detail so far. Our finding indicates that this protein plays an important role in neuronal development as well as amelogenesis, opening interesting perspectives for research into the molecular causes of epilepsy.

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Severe recurrent headache in an adolescent boy with obesity: not always a migraine

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A 12-years old boy, known for overweight and recurrent headache, was admitted to our department with complaint of severe disabling headache with nausea and vomiting. In the past he was already investigated with different exams including CT and MRI, which were normal: the diagnosis of migraine was done at that time. On admission the physical and neurological examination revealed no pathological signs except a light neck stiffness. Later on, we observed a further worsening of headache and vomiting and the appearance of a paresis of the N. abducens with diplopia. A fundoscopic examination at this time showed a papilla with slightly blurred margins. An urgently performed MRI permitted to exclude an expansive process or other pathologies. The lumbar puncture revealed a normal CSF composition. Following the CSF drainage sudden improvement of headache and vomiting and disappearance of the VI nerve palsy. A few days later, reappearance of headache and vomiting, which again disappeared completely after a new lumbar puncture. The opening CSF pressure was clearly elevated (higher than 50 cm H_2O). We made the diagnosis of Idiopathic Intracranial Hypertension (IIH) and started a therapy with Acetazolamide, which was well tolerated and was successful in controlling the symptoms.
Conclusion: Idiopathic Intracranial Hypertension (pseudotumor cerebri) is a rare condition (1 : 2/100'000) of unknown pathogenesis, defined by clinical criteria, that include symptoms and signs related to the increased intracranial pressure (headache, papilledema, vision loss, VI nerve palsy), normal CFS composition and no cerebral abnormalities on the neuroimaging. Obesity is a known risk factor in adolescents and young adults (not in prepubertal children). IIH is not a life threatening condition, can however disrupt normal life and cause significant and also permanent visual loss. Early recognition is important as timely intervention may preserve vision and permit to start an appropriate treatment to control headaches.

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Familial macrocephaly – not always harmless

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Introduction: Infantile progressive macrocephaly is a frequent concern in paediatric praxis. If cranial ultrasound is considered normal and another first degree relative is affected as well, it is usually due to harmless familial variant. We report a case in which assumed familial megalencephaly was associated with autosomal dominant Gorlin syndrome (also known as nevoid basal cell carcinoma syndrome, OMIM 109400), characterized by a range of developmental anomalies and an increased risk of developing medulloblastoma.
Case report: A boy, born at term after an inconspicuous pregnancy, had a head circumference of 37 cm (P 75-90) at birth. Mothers family history was unremarkable. The father has a head circumference of 64 cm (+ 3.9 SD). His three brothers – all healthy up to now – also show macrocephaly suggestive for familial megalencephaly. The paternal grandfather was treated for a facial basal cell carcinoma and is macrocephalic. At the age of 6 months, the boy showed muscular hypotonia and impaired control of head- and body posture and physiotherapy was started. At that time, head circumference had increased above P 97. The patient was referred for further evaluation of progressive macrocephaly and developmental delay at the age of 8 months. He presented with muscular hypotonia, mild truncal ataxia and oculomotor apraxia but without signs of raised intracranial pressure. Cranial MRI revealed an enhancing tumour of the 4. ventricle with mild ventricular dilatation due to occlusive hydrocephalus. The boy underwent complete resection of the tumour that was classified histologically as a WHO IV° medulloblastoma of extensive nodularity. Chemotherapy according to HIT-SKK 2000 protocol was started. The paternal family history and the specific histology with extensive nodularity raised the suspicion of a Gorlin syndrome that was confirmed by the detection of a heterozygote mutation in the PTCH1-gene in the patient and his father.
Conclusion: Familial macrocephaly is not always benign. Gorlin Syndrome can be associated with macrocephaly and should be included in the differential diagnosis of this symptom. As about 5% of patients with this syndrome develop medulloblastoma, cranial MRI should be performed in infants at risk.

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Headache, unilateral facial nerve palsy and arterial hypertension: atypical presentation of an otherwise well known neurological disease

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Introduction: Headache and acute facial nerve palsy opens up a broad spectrum of differential diagnosis. Clinicians could primarily consider it neuroborreliosis, brain tumor or pseudotumor cerebri.
Case: We report on a 15 year old girl who initially presented as outpatient with severe headache, gait instability and high blood pressure. Two days later she was reevaluated because of persisting headache, a newly occured unilateral peripheral facial nerve palsy and double vision due to unilateral abducens nerve palsy. The patient showed normal strength and normal deep tendon reflexes. Further investigation revealed high protein level and normal cell count ("Dissociation albuminocytologique") in CSF. Cerebral imaging (IRM) was unremarkable. Neuroborreliosis was excluded by negative intrathecal serology. General condition deteriorated within three days accompanied by persistent severe headache, appearance of a bilateral peripheral facial nerve palsy, complete areflexia, extenuated strength of cough and inability to walk, primarily due to pronounced ataxia. The course of the symptoms in combination with the test results led to the diagnosis of Guillain Barré Syndrome / Miller Fisher Syndrome. The diagnosis was supported by slow nerve conduction velocity. An intravenous immunoglobulin therapy was given for 5 days and arterial hypertension was treated with a calcium antagonist. Breathing function remained stable. Recovery of all symptoms except a slight persistent one-sided peripheral facial nerve palsy and minimal ataxia was seen at a follow-up after 4 weeks.
Conclusion: Classic leading symptoms of Guillain Barré Syndrome / Miller Fischer Syndrome are ascending progressive motor weakness respectively cranial nerve palsy, areflexia and ataxia. Our patient presented initially with headache and arterial hypertension followed by acute unilateral facial nerve palsy. Patients with Guillain Barré Syndrome / Miller Fischer Syndrome can present initially and first line with pain and only progression of the disease gives hint for right diagnosis.

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Refractory epilepsy and ring chromosome 20 syndrome

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Background: The Ring chromosome 20 syndrome is characterized by intractable epilepsy, mental retardation and behavioral problems. No malformations or dysmorphology are associated. Although already described in 1976, the number of cases reported in the literature is low. Epilepsy is diagnosed mostly in childhood but may appear later. Seizures are typically of several types, including complex partial, tonic, tonic-clonic, as well as nocturnal frontal lobe seizures, and non-convulsive status epilepticus. In most cases, seizures are drug resistant. In order to avoid any diagnostic delay and to prevent costly unnecessary investigations, it's important to report the clinical features of this rare entity. We describe the case of a 5 year-old-child suffering from this syndrome and perform a literature review on this topic.
Clinical Case: The child was referred at the age of 5 to our Institution with daily intractable seizures. Epilepsy started when the child was 2 years-old and was rapidly characterized by frequent and variable seizures type uncontrolled by standard antiepileptic drugs. In addition the child had absent speech, and a global developmental delay. Brain MRI was normal and prior extensive genetic and metabolic was negative. Due to the development of recurrent episodes of prolonged absences and an increase of nocturnal seizures with predominantly bifrontal ictal abnormalities on EEG, ring chromosome 20 was suspected and confirmed by cytogenetic analysis.
Discussion: Ring chromosome 20 epilepsy syndrome is a rare and possibly underdiagnosed epilepsy syndrome, but whose clinical and electroencephalographic characteristics are well defined. Despite being an easy and readily accessible test, a karyotype is often omitted in the context of refractory epilepsy with developmental delay but should be included in the work-up before more complex and costly investigations. Currently, the best predictor of outcome remains the control of seizures, which is unfortunately often difficult.

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Acute encephalopathy with fever: look at the thalami!

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Introduction: Febrile encephalopathy in childhood is a diagnosis challenge, early recognition allows an appropriate management often leading to a better prognosis.
Case-Report: This 22-month-old boy presented with behavioral changes and irritability 24h after febrile streptococcal pharyngitis. At admission he was febrile (38.5 °C), drowsy with a right head and eyes deviation, brisk deep tendon reflexes and bilateral Babinski sign. Lumbar puncture was hemorrhagic, and blood sample showed: PCT 30.58 mcg/l, WBC 6.9G/l. Intravenous antibiotherapy and acyclovir were administered. A cerebral CT-scan revealed hypodensities in both thalami leading to the suspicion of ***Acute Necrotizing Encephalitis (ANE)*** which was confirmed by a brain MRI. The boy required intensive care unit with artificial ventilation for 5 days and received high dose methylprednisolone for three days. His consciousness improved rapidly. Brisk deep tendon reflexes, Babinski sign and extrapyramidal rigidity of upper limbs persisted for 2 weeks. One month after disease onset his clinical examination was nearly normal. A repeated brain MRI 3 months later, showed only small residual thalamic lesions.
Discussion: ANE is a potentially fatal acute encephalopathy characterized by rapid alteration of consciousness ± epileptic seizures after viral illnesses (Influenzae,...). Serum aminotransferase activity and cerebrospinal fluid protein are usually elevated. Diagnosis is made by characteristic findings on CT-scan and MRI showing symmetric lesions in the thalami with variable involvement of the white matter, basal ganglia, brainstem or cerebellum. ***Rapid recognition can allow a good outcome by early administration of high dose steroids.*** A predisposing RANBP2 gene mutation was found in some cases; a genetic counseling is recommended in patients with relapses or a family history of unexplained neurologic symptoms.

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A complicated rota-story

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Background: Rotavirus gastroenteritis is a common entity that usually carries an uncomplicated course leading to good outcome. At the age of 3 years, over 95% of children have been affected. Neurological

complications, due to both direct infection and immune-mediated neuronal dysfunction, are considered to be rare with seizures occurring in 4% and meningo-encephalitis in less than 2%. We report a case with an unusual course and distinct imaging findings most probably resulting from a rotavirus gastroenteritis.
Case report: A previously healthy 15-month-old boy presented with recurrent partial-complex seizures during an acute rotavirus gastroenteritis. With a 48h-course of phenobarbitone, the seizures stopped and the boy recovered fully. Two weeks later, the seizures recurred without any infectious trigger. A brain MRI showed an extensive signal alteration in the mesial temporal lobe, the corpus callosum and the septum pellucidum, evoking the differential diagnosis of an encephalitic or a neoplastic process. The seizures stopped with carbamazepine and the boy continued to develop normally.
On follow-up imaging, the signal alteration slowly decreased to a circumscript area in the mesial temporal lobe.
Conclusion: The causal effect of the rotavirus is very likely in the case presented even though we did not detect the virus itself in the CNS. Signal alterations on brain MRI are described in rotavirus encephalitis, but in our case, the extent and space-consuming character of the signal alteration are unheard of and initially lead to the differential diagnosis of a neoplastic process. Watchful waiting and observing of the benign clinical course held us from invasive investigations such as brain biopsy. Whether the remaining signal alteration fully disappears or may reveal an underlying epileptogenic malformation will be discovered on the follow-up imaging planned in the near future.

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Seizures, a clinical presentation of intraventricular hemorrhage in a full term newborn

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Introduction: Neonatal seizures are a frequent phenomenon resulting in most cases from neonatal asphyxia. It may be associated in preterm infants with intraventricular hemorrhage (IVH). Nevertheless, we report this association in a full term newborn.
Case Report: A 10 days old full term infant presented with tonico-clonic movements of limbs and loss of eye contact while breastfeeding. Physical exam reveals tachycardia, irritability, opisthotonos, hypertonia, sunset eyes, bulging anterior fontanel, positive Babinski bilaterally and osteotendinous hyperreflexia. Coagulation disorders were excluded. Cerebral ultrasound and MRI showed a tetraventricular hemorrhage with hydrocephalus and no evidence of vascular malformation. Serial lumbar punctures were ineffective, thus a ventriculo-peritoneal shunt was performed with a favourable postoperative course.
Discussion: Neonatal seizures reveal in 10% of cases an IVH which is frequent in preterm infants and mostly related to asphyxia or hypotension. IVH is infrequent in term infants and when it occurs, it is mostly due to vascular malformation, rupture or sinovenous thrombosis. Neonatal seizures are mostly related to metabolic disorders, infection, stroke, or neonatal epilepsy. However our case report shows that IVH in term infant can manifest by seizures. The diagnosis is made by cranial ultrasonography and confirmed by MRI to exclude other anomalies, mainly vascular ones.
Conclusion: Neonatal seizures revealing IVH are mainly frequent in premature infants. This association still rare in term infant and should be considered so that IVH could be diagnosed early to ensure adequate treatment and prevent complications.

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Möbius sequence following prenatal exposition to misoprostol (Cytotec)

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Introduction: Möbius syndrome is a rare disorder identified in 1888 by Paul Julius Möbius, which consists of congenital facial palsy, with or without limb defects. We report a new case that developed following administration of misoprostol, a prostaglandin E_1 analog, which has potent uterotonic properties and is used either as abortifacient or for upper gastrointestinal ulceration.
Case report: We recently made the diagnosis of Möbius syndrome in an African male newborn admitted because of clubfeet, poor feeding and expressionless face. The careful clinical examination disclosed a bilateral palsy of the nerves VI, VII, IX, and XII. In retrospect the mother reported the use of misoprostol during the first trimester of pregnancy in an unsuccessful attempt to terminate pregnancy. Magnetic resonance imaging failed to disclose significant brainstem abnormalities (the image quality was degraded by the appearance of some motion artifacts).
Conclusion: 1. The diagnosis of Möbius sequence is made on a clinical basis and requires a high index of suspicion by the clinician. 2. Many case reports associating Möbius sequence with the use of misoprostol during pregnancy have appeared in the scientific literature. 3. Exposure to cocaine or ergotamine during gestation has also been associated with Möbius sequence. It has been therefore assumed that these agents decrease blood flow and subsequently hemorrhage or cell death occur in the cranial nuclei.

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Acute psychotic disorder – what else matters?

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Background: Differential diagnosis of first-episode psychosis in children and adolescents is large. Psychotic symptoms may be caused by somatic disorders that require immediate therapy.
Method: We describe a patient that presented four times on our emergency department, until we finally diagnosed an anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis.
Case report: A 14 years old, previously healthy girl presented after a few short episodes of paraphrasia, which were accompanied by absence. She had complained about headaches afterwards, and one of the episodes had been followed by a generalized tonic-clonic seizure. Neurological examination, laboratory tests and cerebral magnetic resonance imaging were all normal. Seven days later, she showed up again. She was confused and agitated, didn't answer appropriately and was affected by visual and auditory hallucinations and paranoid perceptions. Phenomenologically we had to deal with an acute polymorphic psychotic disorder for which reason the patient was transferred to a psychiatric institution. Because of disturbances in level of consciousness and unstable blood pressure she was sent back to rule out an underlying somatic disorder. Upon return, she presented with aphasia, dysphagia, orofacial dyskinesia and autonomic instability. Lumbar puncture test results were unspecific initially, and anti-psychotic medication was continued. To rule out limbic encephalitis, anti-NMDA receptor-antibodies were searched and found in cerebrospinal fluid and serum. Intravenous high dose steroids and antiepileptic prophylaxis were initiated, intravenous immunoglobulins were added. Thereafter, disorientation, agitation and fluctuating consciousness all subsided slowly. After intensive neurorehabilitation the patient could be discharged two months later with only few persisting neuropsychological deficits.
Conclusion: In pediatric patients with new onset psychotic disorder encephalitis is an important differential diagnosis and mostly caused by viral infection. Rare autoimmune disorders such as anti-NMDAR encephalitis need to be considered. Immunotherapy has to be tailored to the individual treatment response. Timely diagnosed and adequately treated outcome can be expected to be good.

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Anti-NMDA receptor encephalitis presenting as an acute psychiatric syndrome, abnormal movements and sleep disturbances in a 7 year old child

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Introduction: Anti-NMDA receptor encephalitis is a newly recognized antibody-mediated inflammatory brain disease that causes severe psychiatric and neurologic deficits in previously healthy children and young adults, with or without tumor (ovarian teratoma) association.
Methods: We describe a 7 year old female child who presented to the emergency room with a history of behavioral changes (delirium, incoherent speech, auditory and visual hallucinations) since 10 days, sleep disturbances (insomnia), choreiform movements of the upper and lower limbs, orofacial dyskinesia, seizures and tachycardia.
Results: Cerebrospinal fluid analysis showed lymphocytic pleocytosis and oligoclonal bands, EEG showed right sided focal slowing and right frontotemporal seizures, and cerebral MRI showed diffuse cortical lesions in the right parietal region and the cerebellum. Anti N-methyl D-aspartate receptor antibodies were positive in both serum and CSF. Tumor screening was negative. She was treated with intravenous steroids followed by IV immunoglobulin with no initial response, and further with plasma exchange and rituximab. Clinical improvement was observed 3 days after starting the plasma exchange, with continued progress until she recovered completely, 8 weeks after the hospital admission. At follow up, her neurological examination is normal and she has resumed all her normal daily activities.
Conclusion: Anti-NMDAR encephalitis is a severe but treatable disorder and is likely under-recognized. The syndrome is highly predictable on clinical grounds and should be suspected in children with acute behavioral changes, seizures, abnormal movements and sleep disturbances. Auto antibodies against the NMDA-type glutamate receptors in the CSF and serum should be sought specifically since the clinical outcome is highly dependent on an early diagnosis and immunotherapy without delay.

P 57

A new NKX2-1/TTF1 mutation causing benign hereditary chorea and congenital hypothyroidism in familial brain-lung-thyroid syndrome

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Background: Brain-lung-thyroid syndrome is characterized by the combination of congenital hypothyroidism (CH), benign hereditary chorea and surfactant deficiency at birth. It is caused by mutations in the homeobox containing transcritpion factor NK homeobox 2 / thyroid transcription factor 1 (NKX2-1/TITF1). The clinical spectrum varies from the complete triad (50%), to brain and thyroid disease (30%), or isolated BHC (13%). The thyroid form presents at birth, in infancy or in early childhood with overt or, more commonly, subclinical hypothyroidism / hyperthyrotropinemia.
Methods: Case report and direct sequencing of the *NKX2-1* gene.
Results: A newborn presented with a slightly increased level of TSH of 17 mU/L at day 3 in the neonatal screening. The confirmatory test revealed subclinical CH (TSH 25 mU/L, fT4 normal). Levothyroxine (LT4) was started immediately. Neurologic development remained normal at 12 months of age. The father also suffered from CH due to athyreosis. LT4 was started at day 6 of life. Despite good compliance and normal TSH and T4 under LT4, he developed progressive hypotonia during the first year of life, evolving to severe choreoathetotic cerebral palsy by the age of 5 years. The neurologic symptoms were neither explained by CH nor by hypoxia during birth. The patient is non-ambulatory and wheel chair dependent. The combination of choreoathetosis and CH in the father suggested brain-lung-thyroid syndrome without pulmonary disease. Direct sequencing of *NKX2-1* revealed a new heterozygous missense mutation (c.515A>T, p.Q172L) in the father and his daughter. The mutation lies within the homeodomain of NKX2-1 in exon 3. Pathogenicity of the mutation is further supported by in silico analysis. The daughter is under close neurologic follow-up.
Conclusions: 1. The combination of subclinical CH and benign hereditary chorea is pathognomonic for the syndrome. 2. Haplo-insuffficiency of *NKX2-1* may result in autosomal dominantly inherited brain-lung-thyroid syndrome. 3. Unexplained unfavourable neurological outcome in patients with CH despite adequate substitutive therapy may be due to *NKX2.1* gene defects.

P 58

Gowers' sign in a 3-year-old boy

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Introduction: The British neurologist William Richard Gowers 1879 first described the clinical sign of patients "climbing" up their own body when standing up from the floor. Although it is commonly associated with muscular dystrophy, Gowers' sign actually is a nonspecific manifestation of proximal muscle weakness with a broad spectrum of differential diagnoses.
Methods: We present the case of a 3-year-old boy with Gowers' sign whose final diagnosis was juvenile dermatomyositis. The differential diagnoses of Gowers' sign and the characteristic features of juvenile dermatomyositis are revisited.
Case Presentation: A 3-year-old boy presents to his paediatrician with diffuse pain in his legs waking him up at night. He is reluctant to walk and wants to be carried more often. When asked to stand up from a supine position, he shows the Gowers' sign. A highly elevated creatine kinase supports the suspicion of Duchenne muscular dystrophy. The boy is referred to the children's hospital for further work-up. In the meantime, the proximal muscle weakness is further progressive; the boy is less active and has difficulties climbing stairs. Because of the nightly pain, the avoidance to walk and the rapid progression of weakness, a myositis is suspected. Magnetic resonance imaging shows signs of muscular inflammation consistent with a diagnosis of juvenile dermatomyositis. At the first visit he had a mild heliotrope rash which became gradually more prominent, and Gottron's papules developed on follow-up.
Conclusion. – Gowers' sign is an unspecific sign of proximal muscle weakness. – Most degenerative neuromuscular diseases are free of pain. Think of other causes in painful muscle weakness! – In patients with suspected juvenile dermatomyositis, look for the pathognomonic skin rashes.

Poster SGP/SSP – Gastroenterology

P 59

Fetal cholelithiasis – prenatal findings and postnatal outcome

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Fetal cholelithiasis is a rare finding on prenatal ultrasound and its incidence unknown and only a few cases have been described in the literature. The incidence of gallstones in children is about 1.5%. Causes include hemolytic disorders, cholestasis or intestinal malabsorption. We report three cases of hyperechogenic foci detected prenatally by ultrasound and their postnatal outcome.
Patients & findings: All three patients were term-born (two males). There were no prenatal or perinatal complications. In all patients, hyperechogenic foci were detected in the third trimester, at 33 and 38 weeks of gestation. In two patients they were described as calcifications in an enlarged gallbladder with an irregular wall. One patient presented with gallbladder sludge.
Laboratory investigations: there was no significant perturbation in serum aminotransferase levels or conjugated bilirubin levels. One patient showed a significant gGT elevation at birth. Neonatal assessment did not reveal any evidence of abnormal extrahepatic biliary tree, hypothyroidism, sepsis or hematological incompatibilities.
Management: Two patients were treated by ursodeoxycholic acid at first week following birth. On follow up US, hyperechogenic foci resolved after 1 week and 1 month. The third patient still presented micro-lithiasis on follow-up ultrasound at 1 month of life.
In conclusion, our findings suggest that fetal cholelithiasis is probably a self-limited, uncomplicated disease which usually does not require any form of therapy, confirming the findings of others [1–3]. Nonetheless the treatment of ursodeoxycholic acid may have a positive influence. However a close follow-up should is necessary until resolution is demonstrated by abdominal ultrasound. Non-resolution by 3 months of age should lead to work up for underlying conditions including hemolysis, intrahepatic familial cholestasis, cystic fibrosis, and choledocal cyst.

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P 60

Infliximab induced dermatologic complications in Adolescents with Crohn's Disease: A report of 3 cases

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Background: TNFα-inhibitors are increasingly used to treat inflammatory bowel disease, rheumatologic and inflammatory cutaneous diseases. So far only a few case reports and case series have been published describing cutaneous adverse reactions related to treatments with infliximab and adaluminab. We herewith contribute another three cases illustrating the broad clinical spectrum of cutaneous side-effects.
Case-Reports: We report the cases of 3 adolescents with Crohn's disease (CD) receiving infliximab therapy, who experienced severe dermatological complications. All patients showed rapid improvement of their dermatitis after discontinuation of infliximab. *Case 1:* A 16-y old female with refractory CD developed amicrobial pustulosis of the folds, a recently described entity, involving the scalp, face and cutaneous folds. First skin manifestations appeared after the second dose of infliximab, histology revealed a non-specific dermatitis and topical treatment with steroids and antibiotics was started. After initial improvement, the dermatitis progressed rapidly after dose 6 of infliximab, showing the typical clinical and histological features of this newly described entity. *Case 2:* A 17-y old male with CD who tolerated

infliximab for >3 years without any adverse events showed a new onset psoriasis with a rapid progression over the last 3 infusions of infliximab, involving his face, trunk, arms and legs. *Case 3:* A 17-y old male with severe CD tolerated infliximab well for >1 year prior to develop a worsening of a previously diagnosed seborrhoic dermatitis involving mainly the forehead and scalp. Despite intensive local therapy the dermatitis progressed.
Conclusion: From our experience and review of the literature, there is a spectrum of cutaneous adverse events related to infliximab that can occur at any time in the course of treatment. Early recognition and, thus, start of adequate treatment might alleviate the symptoms of cutaneous adverse events and also allow more time for difficult treatment decisions regarding the complex underlying inflammatory diseases.

P 61

An atypical form of Crohn's Disease

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Introduction: Crohn's disease (CD) is a main form of Inflammatory Bowel Disease(IBD). Classical symptoms include chronic abdominal pain, weight loss and diarrhea. We report a case with an atypical acute presentation.
Case report: A previously healthy 8 y.o. boy was admitted for dehydration due to profuse diarrhea and vomiting associated with abdominal pain and high fever (39 °C) since 3 days. Clinical picture and elevated CRP (156 mg/l) suggested an infectious enterocolitis. Ceftriaxone was given followed by metronidazole 3 days later because of poor initial response. Appendicitis was excluded by echography which showed thickening of the intestinal wall, multiple adenopathies and effusion in the Douglas, confirmed by CT. One week later, ESR was normal, there was no aphtous stomatitis or perianal disease. Stool cultures were negative. Fecal calprotectin was moderately elevated (87 mg/kg). GI loss up to 3.5 L/d led to hypoproteinemia, hypogammaglobulinemia and hyponatremia. Digestive panendoscopy showed congestive duodenitis, severe terminal ileitis and colitis. Histopathology confirmed the diagnosis of CD. Corticotherapy and azathioprine led to complete remission.
Discussion: CD presents with intestinal, extraintestinal and general symptoms. Typically symptoms are of gradual onset. At diagnosis, patients' age range between 10 and 20 y.o. Laboratory tests usually reveal anemia, thrombocytosis, elevated ESR and hypoalbuminemia. Fecal calprotectin is often elevated(>200 mg/kg). This case is atypical because of the young age of the patient, the hyperacute onset, with initial absence of typical symptoms, normal ESR and moderately elevated fecal calprotectin.
Conclusion: Acute symptoms with high fever and elevated CRP do not exclude CD, neither do so young age, absence of aphtous stomatitis or perianal disease, normal ESR or mildly elevated fecal calprotectin. Patients suspected for a CD should undergo digestive panendoscopy to confirm diagnosis.

P 62

Eosinophilic colitis as a risk factor for protein – losing enteropathy

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Background: A subset of patients with eosinophilic enteropathy develops hypoalbuminemia caused by protein-losing enteropathy (PLE). PLE is a rare complication of a variety of intestinal disorders, characterized by an excessive loss of protein into the gastrointestinal tract due to impaired integrity of the mucosa. Gastrointestinal symptoms are not necessarily present. The diagnosis is confirmed by the finding of increased faecal concentrations of alpha-1-antitrypsin (α-1-AT).
Case Presentation: A 18 month old girl presented with generalised oedema and a significant increase in weight. At physical examination praetibial oedema and abdominal distension were present. Laboratory results showed hypoalbuminaemia (17 g/l), elevated serum triglycerides (TG 5.58 mmol), and a severe anaemia (Hb 52 g/l) with iron deficiency (Ferritin 4 µg/l). No proteinuria or haematuria was found. Stool test was negative for bacterial or viral infections, but an elevated concentration of α-1-AT was found. Ascites was confirmed by abdominal ultrasound. Further work-up excluded liver dysfunction, celiac disease, intestinal lymphangiectasy or other systemic diseases. Macroscopic appearance at colonoscopy was normal, but biopsies showed an eosinophilic colitis. As the child was almost nourished on a exclusive cow's milk diet, a cow's milk protein allergy (CMP) associated eosinophilic colitis with a severe PLE was postulated. After introduction an amino acid based formula and iron supplementation, oedema resolved rapidly, serum albumin normalized and haemoglobin was found normal 2 month later.
Conclusion: PLE is rare disorder in children, the diagnosis should be considered in children with hypoproteinaemia in whom other causes, such as proteinuria or impaired protein synthesis due to liver disease have been excluded. The combination of eosinophilic colitis, CMP allergy, severe iron deficiency seems to be a risk factor for development of protein losing enteropathy. Children respond to an amino acid based formula and iron supplementation.

P 63

Giardiasis with protein losing enteropathy

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Introduction: Giardia lamblia, a flagellated protozoan, causes both epidemic and sporadic disease. Although infection is most commonly asymptomatic, it may occasionally manifest as invasive disease resulting in malabsorption, which can lead to hypoalbuminemia.
Case Report: A 2 y.o Eritrean girl who was born and always lived in Switzerland, presented with lower limbs edema, weight loss, fatigue and loss of appetite since 2 weeks. During this period she had episodes of watery diarrhea without blood or mucus, associated with vomiting. There was no history of fever or recent travel. Physical exam showed a pale, tired infant with muscle hypotrophy and lower limbs edema. Investigations revealed microcytic hypochromic anemia (Hb 98 g/l) with normal ESR, and hypoproteinemia (42.3 g/l). Hepatic, renal and cardiac causes of edema were excluded as well as celiac disease and cystic fibrosis. First stool examination was negative but later positive for Giardia cysts. The child was treated with metronidazole for 10 days and high protein diet, and showed complete improvement and cysts eradication.
Discussion: Although protein losing enteropathy is rarely reported in Giardia infection, its recognition is important after ruling out other causes of hypoproteinemia. It should always be kept in mind especially when it comes to healthy carriage (immigrant parents). Identification of cysts in stool specimens has higher sensitivity by examining more than 3 specimens collected every other day. When giardiasis is suspected clinically but no proof on stool examination, duodenal biopsy is to be considered. Therapy with metronidazole lasts 7–10 days and results in eradication of infection with rapid recovery.
Conclusion: Giardiasis is often asymptomatic but our case report shows that it must be included in the etiology of protein losing enteropathy.

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A duodenal phytobezoar as a rare cause of vomiting in a 19 month otherwise healthy child

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Introduction: In the pediatric emergency department vomiting is a common symptom, mainly related to acute gastroenteritis. However, if diarrhea and fever are missing, a variety of other entities need to be considered. Gastrointestinal (GI) obstruction due to a bezoar resulting from accumulating nonabsorbal foreign bodies is a rare but potentially life-threatening differential diagnosis.
Case: We discuss a case of a 19 month old toddler who was presented to the pediatric emergency department with recurrent nonbilious and nonbloody vomiting for 48 hours. There was no history of abdominal pain, fever, diarrhea, abdominal trauma. Physical examination revealed a slightly reduced general condition, with signs of moderate dehydration, and normal abdominal examination. Laboratory evaluation including a complete blood count, serum electrolytes, blood gas analyses, and a liver panel were performed and did not provide an explanation for the vomiting. An abdominal radiograph was normal. The abdominal ultrasound showed a marked gastric distention with presence of a round structure that obstructed the duodenum, as well as a thickened wall of the antrum and duodenum. The child was transferred to a tertiary care centre. Upper gastrointestinal endoscopy was performed and a 25 mm large phytobezoar trapped in the duodenum was removed. Histological analysis confirmed a phytobezoar consisting of apple or pear fibers. Two days after the endoscopy the child did well and could be discharged in a good condition.
Discussion: GI phytobezoars result from poorly digested and accumulated fruit and vegetable fibers. Predisposing factors in children include inadequate chewing or previous GI surgery. If untreated, potential serious complications include intestinal bleeding or perforation. Appropriate imaging as well as a high index of suspicion plays an important role. Therapy for bezoars should be tailored to the composition of the concretion and the underlying pathophysiologic process. Available treatment methods include chemical dissolution, endoscopy or surgery.

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Intussusception following appendectomy: a case report

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Introduction: Intussusception is a common pediatric surgical emergency, rarely seen postoperatively as a cause of obstruction. Its incidence is reported to be 1.5–6% as a postoperative complication. Due to this low incidence, the possibility of postoperative intussusception (POI) in the pediatric patient is often either forgotten or overlooked. We here present such a case.
Case report: Five days post appendectomy by Mc Burney with otherwise unenventful recovery, a 7-year-old boy presented with acute abdominal cramps in left iliac fossa with nausea and absence of stool for 2 days. An enema relieved the pain for a while but he came back with lethargy and exacerbation of the abdominal pain in right iliac fossa this time. The abdomen was mildly distended, tender and guarded in the right hemiabdomen. The blood count showed leukocytosis 17.2 G/l, CRP 34 mg/l and 137.9 mg/l the next day. A plain x-ray abdomen was normal and ultrasound showed no collection nor mass, but small quantity of liquid in the Pouch of Douglas, air in the colon and a left pyelocalicial dilation suggesting a left nephrolithiasis. As the pain worsened, a CT was performed and showed a 6 cm diameter ileo-caeco-colic intussusception but no nephrolithiasis. The patient underwent surgery. There was no intestinal necrosis and he fully recovered.
Discussion: Postoperative obstructions are most commonly due to intestinal adhesions (78%), while intestinal intussusception may be responsible for as many as 5–10% of postoperative obstructions in the pediatric age group.The clinic usually occurs after a symptom-free postoperative interval of less than a week and the classical triad (abdominal pain, palpable mass and strawberry stools) of intussusception is absent in most cases. Therefore high degree of suspicion is needed for diagnosis. The etiology of POI remains unclear but there is evidence that the operative procedure leads to an edematous reaction with subsequent perfusion deficits and motility disturbances of the intestine.
Conclusion: As an early diagnosis and treatment is necessary to avoid intestinal necrosis and mortality, POI must be suspected in every child with intestinal obstruction following abdominal surgery.

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Multiple Magnet Ingestion in Children

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Objective: To raise awareness of the dangers associated with magnet ingestion in children.
Design: A case report and review of the literature.
Patient: A one-year-old girl with minimal initial physical findings but with history of magnet ingestion (3 pin wall magnet). Imaging suggests that the magnets stick close together and thus there is no intestinal wall between them. It was initially assumed that the magnets would pass in his stool. However, after 16 hours, the child began to develop acute abdominal pain which prompted to laparotomy.
Intervention: Surgical removal of magnets which caused intestinal obstruction of two jejunal sling, greater omentum and colon transversum. Repair of magnet induced enterotomies were performed.
Result: Full recovery after surgical intervention.
Conclusion: Ingestion of multiple magnets can result in significant complications, including bowel perforation, volvulus, ischemia, and death. Imaging is not reliable and clinical vigilance should be exercised in these cases. Early surgical consultation and intervention can prevent significant morbidity and mortality and thus is an aggressive surgical approach is recommended.

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Magnet Ingestion: A Dangerous Attraction

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Introduction: Magnet ingestion is common in young children, because of the increasing availability of powerful small magnets in toys and other products. One single magnet is usually small enough to easily pass through the digestive tract. However, ingestion of multiple magnets can lead to serious gastrointestinal complications due to the attraction of the objects across intestinal walls. The need of prompt removal of multiple ingested magnets is now well recognized. The case of magnet ingestion we present illustrates how indistinct history and clinical presentation can lead to delayed diagnosis and serious complications.
Case: A 15 months old girl presented with repeated non-bilious vomiting without fever or diarrhea. After four days of intravenous rehydration, she developed abdominal distension and bilious vomiting. A plain abdominal X-ray revealed signs of intestinal occlusion as well as the presence of multiple small radio-opaque foreign bodies stuck together in two adjacent rows projecting over the small bowel. The mother recognized the objects as magnets having been stuck to the fridge at home. The clinical picture now prompted for immediate laparotomy. Seventeen small magnets, magnetically attracted across the jejunum and the caecum, causing necrosis of the intestinal walls and a subsequent fistula, were removed. Another intestinal loop was squeezed between magnets, showing lesions. Furthermore, necrosis of the mesentery had caused an internal hernia with half of the small intestine herniated trough, with impaired vascularization. The patient required resection and primary anastomoses of two portions of the jejunum and direct repair of the bowel wall at 3 locations.
Discussion: A great proportion of ingested foreign bodies are not witnessed. When magnetic and multiple, serious complications can occur such as intestinal obstruction, bowel perforation, fistulae and volvulus. Moreover, initial signs and symptoms are often mild and nonspecific leading to delayed diagnosis.
Conclusion: Our aim is to remind health-care providers to have a high degree of suspicion for potential foreign body ingestion in any child with persistent unspecific abdominal symptoms, such as isolated vomiting or unspecific abdominal pain. Abdominal X-ray should then be considered. Furthermore, prevention should focus on teaching caregivers to keep products with magnets out of reach of young children.

Poster SGP/SSP – Cardiology

P 68

Chest pain in children and adolescents: a frequent complaint

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Introduction: Chest pain is a frequent presenting complaint in children and adolescents. It is frequently perceived by both children and parents as heart related, therefore causing a lot of worry and emotional upset. It frequently leads to referral to a pediatric cardiology outpatient clinic for more specific evaluation. In the pediatric population, chest pain is very rarely due to a heart problem. Noncardiac chest pain is by far the most common cause of chest pain in the pediatric population.
Methods: Retrospective review of all cases of chest pain referred to our pediatric cardiology outpatient clinic over a one year period (2011). Charts, ECG, Holter, echocardiography studies and exercise test results were reviewed.
Results: From January1st to December 31th 2011, 82 patients presented with chest pain. The mean age at presentation was 11 years old (range 4–17). There were 36 boys and 46 girls. In 36 cases chest pain was the only complaint. In 60% of cases symptoms occurred with exercise. Patients were evaluated with ECG (n = 82), Holter (n = 16), R-test (n = 6), echocardiography (n = 81) and exercise stress test (n = 35). In 17 patients chest pain was triggered and patients could be examined while being symptomatic. In 90% (74 patients) of patients chest pain was due to a noncardiac cause, of which 86% (64 patients) presented with musculo-skeletal or chest wall pain. Other noncardiac causes included hyperventilation and vasovagal malaise. In only 10% (8 patients) chest pain was due to a cardiac cause, of which 7 presented with an arrhythmia and 1 patient with signs of myocardial ischemia in the context of a severe aortic stenosis.
Conclusion: All patients presenting with chest pain warrant a thorough evaluation. In the vast majority of cases chest pain has a musculoskeletal origin. Reassuring both parents and patients about

the benign nature of chest wall pain is of great importance. Although rare, a cardiac cause for chest pain should be sought for. It is most likely to be associated with abnormal cardiac findings and to occur upon exertion.

P 69

Arterial switch: medium-term outcome of neoaortic root and peripheral pulmonary arteries

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Introduction: Arterial switch is the standard operation for correction of transposition of the great vessels. Several long term complications have been described such as neoaortic root dilatation and peripheral pulmonary stenosis (PPS). We reviewed all our patients with arterial switch operation as to these problems and their correlation.
Method: Retrospective review of all patients after arterial switches at our Institution since 1993 and followed at least one year. Measured variables were diameters of aortic annulus, aortic root, pulmonary valve, pulmonary trunk and peripheral pulmonary arteries, normalized for surface area, aortic and pulmonary pressure gradients and peripheral pulmonary gradients. These measurements were taken prior to arterial switch, 10 days, 3 months, 6 months, 1 year, 3 years and 5 years after arterial switch.
Results 29 pts were included in the study.
Neoaortic root: There was a progressive decrease in normalized neoaortic valve diameter starting 6 months after switch ($p < 0.0001$). Normalized ascending aorta diameter increased at 10 days ($p = 0.0007$) but progressively decreased after 1 year ($p = 0.0007$). Compared to standard norms, neoaortic valve and ascending aorta diameters were larger after switch than in the normal population with Z-scores > 6 five years postop. *PPS:* there was a significant increase in peripheral pulmonary gradient in the first year postop ($p = 0.01$), however it was not significant thereafter. The normalized diameter of the peripheral pulmonary arteries decreased significantly after 3 months post switch ($p = 0.004$) until the end of study. Compared to normal peripheral pulmonary arteries tended to be slightly less large with Z-score <0 at 5 years. No correlation was found between neoaortic root dilatation and PPS.
Discussion: our study shows significant, rapidly occurring aortic root dilatation after switch operation probably due to rapid growth in the first few months of life with stabilization thereafter as is shown in decrease in normalized values over time. However it never completely normalizes. PPS is common with decreased growth of the pulmonary arteries compared to normal with likelihood of the necessity for angioplasties or stent placement. Contrary to hypothesis in the literature no correlation could be found in our study between aortic root dilatation compressing the peripheral pulmonary arteries causing stenosis.
Conclusion: Neoaortic root dilatation and PPS are common problems after arterial switch operation and need close follow-up in these patients.

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Cardiogene: an innovative multidisciplinary consultation for genetic arrhythmias

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Introduction: Over the past decade clinically relevant progress has been made regarding the genetic origin of sudden cardiac death due to arrhythmic syndromes such as congenital long QT syndrome (LQTS), Brugada syndrome (BrS), catecholinergic polymorphic ventricular tachycardia (CPVT) and short QT (SQTS). An increased number of patients are diagnosed and their offspring sent for screening. In order to optimize care of these families we have set up a multidisciplinary consultation, "Cardiogene", consisting of a pediatric and an adult cardiologist and a clinical geneticist. All families are seen at a common consult in order to take the family history, genetic background and to explain the disease to patients and their families. Appropriate cardiac investigations and genetic testing are then performed and the families seen again in a multidisciplinary fashion for the results. We have reviewed all our cases over the past 5 years.
Methods: retrospective review of all cases seen at Cardiogene Clinic for suspicion of arrhythmic syndromes since 2007.
Results: 23 families were seen at the Cardiogene Clinic with a total of 41 children. The suspected arrhythmic syndrome was LQTS in 14 families (26 children), BrS in 7 families (14 children), SQTS in1 family (2 children) and CPVT in 1 family (3 children). Of the 41 children 17 were genetically positive for an arrhythmic syndrome: 14 were for LQTS, 3 for BrS. 24 children were genetically negative however 4 of those were phenotypically positive: 2 LQTS, 1 BrS and 1 CPVT. In 3 families the diagnosis was initially made in a child and then found in the parent. In 2 families the diagnosis was made after a sudden death of one of their children, 1 LQTS (3 week old child), 1 BrS (20 year old).
Discussion: Genetic testing is an essential part of diagnosis and permits an improved targeting of patients needing follow-up and treatment. In our series, a mutation has been found in most families with LQTS. In all other genetic arrhythmias, the yield of genetic testing is less but nevertheless helpful for medical care of these pts.
Conclusion: A multidisciplinary approach to genetic arrhythmias permits a better and more efficient screening and therapy in affected families. It helps families to better understand their disease and improves follow-up in the affected individuals.

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Scimitar Syndrome – clinical presentation, management and outcome

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Introduction: Scimitar syndrome (SS) is defined by a partial or complete anomalous pulmonary venous drainage of the right lung to the inferior vena cava with various additional cardiopulmonal anomalies. Depending on the time of clinical presentation, an infantile form is distinguished from an adult form. Data on clinical presentation, cardiac comorbidities and outcome after surgical repair is sparse.
Methodes: Retrospective review of all patients (pts) diagnosed with SS between 1979 and 2010 in our institution. Our specific aim was to evaluate clinical presentation, therapeutic interventions and long-term outcome after surgery.
Results: A total of 14 pts (42% males) were identified. Median age at diagnosis was 3 years (range 0–37). 6 pts (42%) were diagnosed within (infantile form) and 8 pts (58%) after the first year of life (adult form). While the infantile form usually presented with respiratory distress, the adult form was mainly suspected casually on the chest x-ray. Most associated cardiac and non-cardiac abnormalities were dextroposition of the heart 13 (93%), right lung hypoplasia 13 (93%) and hypoplasia of the right pulmonary artery 13 (93%). Pulmonary hypertension was present in half of all cases at time of diagnosis. In all pts diagnosis was established by transthoracic echocardiography. Additional examinations were required before surgery and consisted of cardiac catheterization in 8, computed tomography in 7 and cardiac magnetic resonance imaging in 6 pts. Surgical repair was performed in 10 patients and 1 is currently on the waiting list. Median age at operation was 3 yrs (5 m–30 yrs). During a median follow-up time of 8.5 yrs (range 4–30 yrs) mortality was 7%, with one patient dying after surgical repair. In 5 of 10 repaired pts (50%) significant obstruction/ occlusion of pulmonary veins occurred requiring redo-surgery in 4. Pulmonary hypertension persisted in 3 pts (14%). At last follow up 10 patients (71%) were in NYHA class I, 2 (14%) in NYHA class II and 2 (14%) in NYHA class III.
Conclusion: SS is a complex malformation of the heart and the lung that can be surgically repaired with good results. While overall functional outcome after surgery is satisfactory, residual pulmonary vein stenosis and persistence of pulmonary hypertension represent the most common residual findings, determining need of reintervention and long-term morbidity.

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The Swinging Heart

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Introduction: Large and significant pericardial effusions (PE) up to an acute tamponade are infrequent in children. Clinical presentation may be nonspecific and there is a wide spectrum of underlying causes. We present 3 children with pericardial tamponade of different etiologies necessitating acute intervention.

Results:

Age (years)	4.5	5.5	14
Underlying disease	Mycoplasma pneumonia with encephalitis	Hematopoietic stem cell transplantation for IL10R-deficiency, HHV6 reactivation	Ross-Operation for valvular aortic stenosis six weeks ago
History	Fatigue, fever	Discomfort, restless, tachypnea	Chest pain, fever
General condition	Good	Reduced	Reduced
Heart rate/ Blood pressure	↑ ↓	↑ ↓	↑ Normal
Heart sounds	Muffled	Quiet	Normal
ECG	Normal	Normal	Discrete ST-elevations
Echocardiography	3–4 cm circular, septated PE with compression of the right atrium (RA) and right ventricle (RV)	2–3 cm circular PE with compression of the RA and RV; congestion of the vena cava inferior (VCI)	1.3–2.2 cm circular PE with compression of the RA and RV; congestion of the VCI
Emergency procedure	Surgical drainage	Pericardiocentesis and drainage	Pericardiocentesis and drainage
Pericardial fluid	600 ml hemorrhagic-serous, sterile	700 ml hemorrhagic-serous, growth of HHV6	500 ml hemorrhagic-serous, sterile
Therapy	Diuretics, NSAR, steroids	Diuretics, Cymevene	Diuretics, NSAR
Interpretation	Pneumonia with concomitant PE	Infective PE	Post pericardiotomy syndrome

Conclusions: Our patients illustrate that even with discrete and unspecific clinical findings (fever, tachycardia, hypotension) a PE with an acute tamponade can be the underlying cause. In doubt an echocardiography is indicated to exclude or confirm the diagnosis and assess the hemodynamic impact. A conservative approach with diuretics and anti-inflammatory agents can be discussed initially but if there is evidence of hemodynamic compromise (with the heart "swinging" in the fluid) an immediate release of the fluid (open surgical drainage or pericardiocentesis) is necessary. Infection (often viral), previous cardiac surgery or trauma, autoimmune, metabolic or neoplastic disorders are among the major causes for PE.

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An exceptional cause of sudden death in infants: histiocytoïd cardiomyopathy

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Introduction: Most sudden deaths infants don't have an identifiable cause although some are thought to be related to channelopathies. We report here an exceptional cause of sudden death.
Case report: A 5 months old infant, known for mild hypotonia and developmental delay of unknown origin, became suddenly limp and pale and developed respiratory arrest while sitting in an infant seat and playing with her mother. The mother started mouth – to mouth resuscitation. The emergency physician found the child 3 minutes later in ventricular fibrillation (VF). After 2 defibrillations and 2 doses of adrenalin she regained sinus rhythm. Upon arrival at the hospital lactate was 14. She recovered rapidly without neurological sequellae. ECG showed Wolff-Parkinson-White (WPW) syndrome, echocardiogram was normal. Intravenous amiodarone was introduced for suspected antidromic tachycardia and subsequent VF secondary to her WPW. However she continued to have multiple runs of ventricular tachycardia with hemodynamic compromise necessitating defibrillation, cardiac massage and adrenaline. ECG's immediately prior to those episodes were variable, some showed a long-short-long coupling making a channelopathy more likely, and some resembled a His's-Purkinje tachycardia. Intravenous betabloquers were introduced without recurrences of arrhythmias. However 48h later she presented extensive ischemic bowel disorder, sepsis and died. Autopsy revealed histiocytoïd cardiomyopathy (HICMP).
Discussion: HICMP is a rare cause of sudden death affecting predominantly girls under 2 years of age consisting of subendocardial or epicardial nodules formed of histiocytoïd cells in both ventricles, particularly in the His-Purkinje system causing incessant severe arrhythmias. Extracardiac manifestations include abnormalities of the central nervous system, hypotonia, Peter's anomaly, congenital glaucoma. Antiarrhythmic drugs are usually inefficient. Treatment may include resection or thermoablation of the nodules as well as heart transplant. Without these the outcome is usually fatal.
Conclusion: This diagnosis should be considered in all infants with severe uncontrollable arrhythmias and in aborted sudden death in order to insure appropriate treatment rapidly.

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When atrium goes crazy; two cases with atrial flutter and concomitant atrial ectopic tachycardia

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Introduction: Atrial flutter (AFL) and atrial ectopic tachycardia (AET) are uncommon arrhythmias in infants and toddlers. They can occur isolated or in combination and can lead to tachycardia induced cardiomyopathy. We present two cases with refractory AFL and additional AET.
Case I: After uncomplicated pregnancy, delivery was induced at term due to tachycardia with a heart rate of 200 bpm. Postnatal ECG showed AFL with a maximum heart rate of 220 bpm and 2:1 to 3:1 atrioventricular-conduction. Echocardiography revealed moderately reduced left ventricular systolic function (LV-EF 40%) without any clinical evidence of congestive heart failure. Because repeated cardioversion up to 10 Joule and i.v. amiodarone bolus were unsuccessful, amiodarone drip was started, which led to conversion into sinus rhythm for a short time until intermittent AET occurred. By increasing the dose of amiodarone, rate control of AET could be achieved and subsequently amiodarone was switched to oral medication on day 12. The last follow-up at 4 month of age showed no more arrhythmias by 24h-ECG.
Case II: A two year old boy with acute bronchitis presented with tachycardia. Initial ECG showed multifocal atrial tachycardia with a heart rate of 240 bpm. Laboratory tests, echocardiography (LV-EF 17%) and clinical signs were consistent with tachycardia induced cardiomyopathy. Amiodarone at increasing dose was unsuccessful and heart rate control was only achieved after adding i.v. esmolol, which was later switched to oral propranolol. Heart failure was treated with diuretics. After rate control was achieved, systolic function recovered completely. Before discharge 24h-ECG revealed surprisingly episodes of AFL. As these episodes were non-sustained, medication with amiodarone and propranolol remained unchanged and further 24h-ECG showed no recurrence of AFL or AET.
Conclusion: AFL and AET are uncommon arrhythmias in childhood, but can lead to tachycardia induced cardiomyopathy if not treated timely. Heart rate above 200 bpm should lead to immediate further investigation by 12 lead ECG and cardiac evaluation. Even though therapy can be challenging, especially in those with combined arrhythmias, prognosis is generally good.

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Cardiogenic shock due to myopericarditis as a presentation of H1N1 influenza A virus infection

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Introduction: Myopericarditis is a rare pediatric emergency, mostly associated with viral infections. Among the viruses, influenza is a recognised cause of myopericarditis. We report the case of a previously healthy 13-year-old boy presenting with cardiogenic shock associated with a H1N1 2009 influenza virus infection
Case report: 5 days before his admission , the patient developed tiredness with coughing and sneezing without fever. The tiredness worsened, with a stage III NYHA dyspnea. The boy experienced intermittent epigastric pain on exertion and bilateral upper palpebral swelling with ocular pain and diplopia. At arrival his temperature was 35.9 °C, BP 120/93, HR 106/min, RR 18/min. He was asthenic, pale,

with cold, mottled extremities and delayed capillary refill (7 sec). There was no signs of right or left congestive heart failure. BP quickly decreased to 76/54 after 15 minutes. He received 3 bolus of NaCl 0.9% and an infusion of dobutamine. The blood tests showed normal WBC, CRP <5, lactate 8 mmol/l, pH 7.37, CK 5551 U/l (<190), CK-MB 35.6 µg/l (<4.87), troponine 0.19 µg/l (<0.15), and proBNP 1937ng/l (<450). The chest x-ray was normal and the ECG showed a right bundle block. An echocardiogram was performed and showed a pericardial effusion with a diastolic dysfonction and a left ventricular hypertrophy. Nasopharyngeal swab tested positive for influenza A subtype 2009 H1N1. He was transfered to the ICU and received inotropic support, Prednisone and Tamiflu with good clinical and radiologic evolution. He was discharged after 8 days.

Discussion and conclusion: The frequency of myocardial involvement in influenza infection is variable with rates of up to 10%, with lower incidence in pediatric patients. It occurs 4–9 days after the onset of the symptoms with worsening dyspnea, ECG abnormalities, elevation of cardiac enzymes, and impaired left ventricular fonction which may lead to cardiogenic shock requiring inotropic support. In our case the presentation was atypical with early symptoms of cardiac involvement (3ed day), absence of fever and no significant ECG abnormalities. This case reminds that severe cardiac events related to influenza virus may occur in young patients without known predisposing factors and strongly highlights the importance of early diagnosis and treatment.

Poster SGP/SSP – Pulmonology

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Comparison of different brushing techniques to obtain nasal epithelial cells from human subjects

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Introduction: Nasal epithelial cells are used in the clinical setting for diagnosis of primary ciliary dyskinesia and have been shown to be good surrogate markers for bronchial epithelial cells in inflammation studies. We aimed at comparing different available brushing techniques allowing collection of nasal epithelial cells with regards to efficiency in establishing cell cultures and acceptability to subjects.
Methods: Nasal epithelial cells were obtained by brushing the inferior surface of the middle turbinate of both nostrils (each nostril was brushed twice) using three different instruments: a 3-mm cytology brush, a neonatal flocked nasal swab and a nasal mucosal curette. Primary cell cultures were established by seeding freshly brushed nasal cells into growth medium. Cell count, cell viability (assessed by trypan blue staining), and success rate in establishing cell cultures (assessed by time to confluency) were compared between groups. A standard numeric pain intensity scale was used to assess the acceptability of each method to subjects.
Results: 60 human subjects were brushed. Higher number of cells were obtained using brushes (9.8 [7.0-28.5] x 10^5 cells/mL) compared to swabs (2.4 [1.5–3.4] x 10^5 cells/mL, p <0.0001) and curettes (1.3 [1.1–1.9] x 10^5 cells/mL, p <0.0001). Viability was higher for cells obtained using curettes (54 [29–68]%) and swabs (54 [16–69]%) compared to brushes (42 [15–70]%). Cells obtained by brushes grew fastest (6 [6–9]d), followed by cells obtained by curettes (11 [10–13]d) and swabs (19 [13–21]d). Success rate in establishing primary cell cultures (100% confluent cell layers within 21 days in a 12.5 cm^2 cell culture flask) was 95% with brushes, 65% with swabs and 85% with curettes. Pain intensity was highest with the brushes (5 [3–7] out of 10 on the pain scale) compared to the other two instruments (3 [1–4] out of 10 for swabs and 3 [2–5] out of 10 for curettes).
Conclusion: All three types of instruments allow collection and growth of human nasal epithelial cells. The most efficient but also most painful type is the nasal brush.

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Arterial stiffness in asthmatic children

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Background: Increased arterial stiffness is an independent risk factor for cardiovascular disease. It occurs in inflammatory diseases indicating an aging of the vasculature. In the present study we aimed to assess arterial stiffness in children with asthma, a chronic disease characterized by airway but also systemic inflammation.
Methods: Pulse wave velocity between carotid and femoral artery (PWV) was determined in 36 asthmatic children (10 female, median age 11, range 6–15 years, mean FEV_1 86.4% predicted = –0.61 SDS). Standard deviation scores (SDS) for PWV were computed with reference data from the general population (Ref: Reusz GS et al. Hypertension 2010;56: 217-24) and related to lung function parameters (FEV_1; MMEF 25–75; FVC) and the exhaled fraction of nitric oxide (FeNO).
Results: PWV (SDS corrected for height) was higher in male compared to female children (0.16 vs. –0.39; p = 0.01), but similar in asthmatic children compared to an age-matched control population (0.006 vs. 0; p = n.s.). PWV was inversely related to FEV_1 (R^2 = 0.23, p = 0.003) and to MMEF 25–75 (R^2 = 0.17, p = 0.01), but was not related to FeNO. Age, gender and FEV_1 remained significantly associated with PWV in multivariable regression analysis adjusting for possible confounders including body mass index, blood pressure and steroid use.
Conclusion: Arterial stiffness in our population of children with mild to moderate asthma is not increased when compared to the general population. However, arterial stiffness in asthmatic children was directly associated with impaired lung function, suggesting systemic effects of the disease on the cardiovascular system. These findings have important implications for the management of cardiovascular functions in patients with asthma and require further exploration so that cardiovascular health can be maintained.

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Can nitrogen multiple breath-washout measurements be shortened for clinical routine?

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Background: Multiple-breath inert gas washout (MBW) tests are increasingly used to assess small airway function in Cystic Fibrosis patients. Nevertheless, MBW is still not established in clinical paediatric routine. The main reason is the time consuming protocol requiring triplicate MBW measurements.
Aims: We examined whether lung clearance index (LCI) from the first valid MBW test provides reliable results, compared to the pooled information obtained from three tests.
Methods: We retrospectively analyzed data of 31 school-aged children with CF who performed triplicate MBW during their outpatient visits from January 2011 to January 2012. Nitrogen MBW was performed using a commercially available set-up (Eco Medics AG, Duernten, Switzerland).
Results: Children with CF were aged 11.9 (range 4.8 to 16.9) years. Mean LCI of the first measurement was 9.49 (95% CI 8.60–10.38), compared to a mean of 9.43 (95% CI 8.55–10.31) of all three measurements without significant difference (p = 0.37). R^2 from linear regression model showed a predictive value of 0.98 of first LCI for mean LCI of three. Bland-Altman plot did not show systematic differences, limits of agreements where within physiological variability (10%).
Conclusion: The first LCI reliably predicts the mean LCI of three MBW measurements, differences were within natural variability. Thus, using one measurement instead of three could be a promising way to shorten MBW protocols for clinical routine.

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Diagnostic value of nasal NO measurement using the NIOX MINO device

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Background: Screening for primary ciliary dyskinesia might become more widespread with the release of the new NIOX MINO hand held NO analyzer which includes an adapter for nasal nitrite oxide (nNO). However, no data on accuracy and quality of the measurements are

available. This study aimed to compare nNO measurement with the NIOX MINO to the NIOX FLEX gold standard device.
Methods: Nasal NO was assessed in healthy children and adults by NIOX FLEX, followed by NIOX MINO (flow rate 5 ml/s). For each device, measurements consisted of a tests with subjects holding their breath (BH), followed by a tests with tidal breathing (TB) through a medium-sized straw (Jung et al., 2012). A NIOX FLEX test was considered valid when nNO concentration reached a stable plateau.
Results: 48 subjects (median age 34.4 yrs, range 3.6–68.3) were included. 42 of them had both a valid BH and TB NIOX FLEX test. No optical quality control (nNO, CO_2 or air flow curve) was available for the NIOX MINO. A BH test with the NIOX MINO requires a breath hold of 45s, which only 12 subjects were able to perform (29%; median breath hold time 25s). In general, NIOX MINO nNO levels were significantly lower than for NIOX FLEX (all $p < 0.001$). For the conventional BH technique, median (quartiles) nNO levels were 861 (670, 1147) ppb for NIOX FLEX vs. 657 (445, 786) ppb for NIOX Mino, whereas median nNO values for the TB technique were 867 (692, 1187) ppb vs. 687 (537, 865) ppb.
Conclusion: Nasal NO values in healthy subjects are generally lower when the NIOX MINO is used, compared to the gold standard method. This might lead to interpretation problems when the technique is applied in patients with chronic rhinosinusitis or younger children with lower expected nNO levels (ongoing studies). No quality control is available for the device, making the correct interpretation of low values even more difficult.

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Case report: Rehabilitation after severe acute respiratory distress syndrome in a previously healthy adolescent girl

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Background: For patients suffering from severe pulmonary illness the requirement for medical care does not end with discharge from the acute or intensive care wards. Continuous in-patient specialist treatment for a long time period is required to help the patient with transition from hospital to ambulatory care. In view of the introduction of the DRG system more cost-effective solutions are required than can be offered by acute-care hospitals with their inevitable high costs.
Case: A 16-year-old previously healthy girl developed pneumonia and was hospitalized at the Children's Hospital St. Gallen. She developed ARDS, mechanical ventilation and Novalung showed unsatisfactory response. Extracorporeal membrane oxygenation (ECMO) was necessary in Zurich. After 20 days of ECMO and >6 weeks intensive care treatment she was transferred to the Children's Allergy and Asthma Hospital at the Hochgebirgsklinik Davos for rehabilitation. Upon admission in Davos she received nutrition via nasogastric tube, needed 2L oxygen via a tracheal cannula and her vital capacity (VC) reached 1L (23% of pred.). A multidisciplinary treatment approach was started. After a transfer to the ward for adolescents she increasingly could participate in the daily activities of her peer patients. 44 days later she was discharged to home, needed oxygen only during sports and could independently carry out activities of everyday life. 4 months after discharge her VC was 3L (78% pred.). She went back to her normal everyday life (no more oxygen needed).
Conclusion: The girl with a life-threatening course of pneumonia benefited from a multidisciplinary rehabilitation program following up a >9 weeks intensive care treatment. From a health economic point of view, the rehabilitation program allowed a medically optimal outcome to relevantly lower costs compared to a prolonged stay in an acute medical ward.

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Subglottic Hemangioma – Case Report of propanolol as a first line treatment

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Introduction: Infantile hemangiomas (IH) are the most common tumours of infancy. IH are proliferative vascular tumours that can occur in the paediatric airway, potentially causing airway narrowing and respiratory distress. Untreated, these lesions carry a mortality of nearly 50%, especially when they involve the narrowest portion of the paediatric airway, the subglottis.
Case report: A 3-month old, otherwise healthy, female infant presented on our emergency departement with recurrent episodes of inspiratory stridor during infections of the upper airways. There were no feeding difficulties and no apneic or cyanotic episodes in between. Because of the severity of the episodes and the skin examination, which did reveal multiple hemangiomas, the girl underwent a sonographic evaluation of the neck, which showed tracheal and subglottic masses. These masses could be confirmed as hemangiomas in CT scan and laryngobronchoscopic findings with a tracheal obstruction of >50%. The girl was started on treatment with propranol, gradually increasing over 24 h to a dose of 2 mg/kg/day divided to three doses. Eight month follow up revealed the patient to be asymptomatic and repeated laryngoscopy and MRI demonstrated an impressive involution of all lesions. Because of the persisting subglottic rest of IH, we decided to treat the child for totally 12 month. Regarding side effects of propranolol: Parents only reported fatigue during the first week of treatment.
Discussion: It is important to arrange further investigations in a child presenting with stridor and hemangiomas in the emergency room. The administration of propanolol in our patient with obstructing haemangioma in the airways avoided not only invasive surgical procedures, but also long-term treatment with oral corticosteroids. The effect of propranolol on cutaneous haemangiomas of infancy was described for the first time in 2008. Our case report is an addition to the few published case series, summarized in a meta-analysis in 2011, also demonstrating a favourable effect of propanolol alone. Further studies are needed to determine long-term effect, dosing strategy, treatment duration, and side effect profile of propranolol treatment for hemangiomas.

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Exercise induced dyspnea – not always asthma

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Introduction: Exercise induced breathlessness (EIB) is a common symptom of childhood asthma, most often combined with cough and wheezing. However, isolated EIB can also be the only leading symptom of asthma, but there are many other reasons for EIB. We report a child with a very uncommon cause of EIB.
Case presentation: An 11 year old boy was referred to our outpatient clinic with a two years history of recurrent EIB with chest tightness, especially while hiking with his family. The general practitioner (GP) assumed that the child has asthma and prescribed inhaled short-acting β2-agonist and corticosteroids, which was partly helpful. The child had no major limitations in sport activities and was regularly playing unihockey. The personal history is unremarkable with no severe diseases or admissions to a hospital. In August 2011, the GP performed lung function testing and was not sure about the assessment of the flow-volume curve. Finally, he referred the child for further evaluation with the suspicion of asthma. On auscultation, there was a hypoventilation of the whole left lung and lung function was reduced (FVC 67%, FEV_1 64%). Chest X-ray revealed impressive bulleous structures and a seropneumothorax on the left side. CT scan showed multiple bullae (max. 12 cm in diameter) derived from the left lower lobe. An earlier chest X-ray at the age of 14 months (due to an acute cough) showed normal pulmonary structure. A resection of all bullae could be performed by open lung surgery without any complications. Final histology described the lesions as idiopathic bullae. Four weeks later, a control chest X-ray was normal and lung function improved (FVC 78%, FEV_1 87%).
Conclusion: The origin of these multiple bullae remains unclear. There were no signs of a congenital pulmonary airway malformation (CPAM, former term: CCAM), neither on the chest X-ray nor in the histology. Most likely, all bullae were acquired, may be based on small congenital lesions. However, there was no history of foreign body aspiration, severe bronchiolitis or another lung infection. In children with EIB, a proper auscultation and – in case of partial hypoventilation – a chest X-ray should always be performed.

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Significant oxygen desaturation in persistent periodic breathing in term babies

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We report two cases of desaturations and apnea associated with persistent periodic breathing during the second month of life in 2 term newborn babies. Both infants without antenatal complications or significant past medical history were admitted to the emergency room for apparent life threatening event (ALTE) between 6 and 7 weeks of age. Clinical examination and laboratory investigations did not reveal any infectious disease and blood gases were normal. Monitoring revealed repeated desaturations associated with bradycardia. Non

acid gastro-oesophagal reflux disease was found in one case and successfully treated with metoclopramide. Neonatal MRI was performed to exclude brain malformation and was normal. Polysomnography (PSG) confirmed significant desaturations (more than 4%) due to central apnea, some of them followed by bradycardia, occurring mostly during periodic breathing. Caffeine citrate was introduced with a loading dose of 10 mg/kg/day followed by a maintenance dose of 5 mg/kg/day for 4 to 6 month with disappearance of apnea and bradycardia. Nocturnal oxymetry was performed before discontinuing the medication. Since this exam was normal, 3 days after stopping the caffeine, a second PSG was performed to verify the number of apnea and the periodic breathing.
Discussion: The literature describes the efficacy of caffeine treatment for periodic breathing in preterm newborns. At 30 weeks of gestational age, periodic breathing is frequent and account for 25% of the respiration time due to brain immaturity. In full-term newborn, periodic breathing is seen mostly during REM sleep until 5 weeks of age, and decreases with less than 1% of total sleep time at 6 months. Prolonged duration of periodic breathing in term babies is poorly studied and no clear guidelines for treatment introduction and duration are reported. A normal oxymetry under caffeine allows discontinuation of treatment. A second PSG is indicated to confirm the maturity of the respiratory control. We describe two cases presenting polysomnographic findings compatible with persistent periodic breathing successfully treated with caffeine.

Poster SGP/SSP – Oncology – Haematology

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Educational problems in school-aged childhood cancer survivors and siblings

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Objectives: Diagnosis and treatment of childhood cancer often occurs during school years and the patients may encounter educational problems. So far, few data are available on school problems in paediatric and adolescent cancer patients. We aimed to 1) describe how many childhood cancer survivors ever repeated a year in school compared to siblings; and 2) find risk factors associated with repeating a year in school in survivors.
Methods: As part of the Swiss Childhood Cancer Survivor Study we sent a detailed questionnaire to all survivors aged 8–21 years, ≥5 years after diagnosis and registered in the Swiss Childhood Cancer Registry. The same questionnaire was sent to siblings. We used multivariable logistic regression to determine clinical and socio-demographic characteristics associated with repeating a year in school.
Results: The sample included 812 survivors and 181 siblings, with a mean age of 15 years (range 8–21). Of these, 167 survivors (23%; varying by diagnosis (leukaemia 25%, lymphoma 20%, CNS 31%, other tumours 17%)) and 25 siblings (14%) had repeated a class ($p = 0.012$). Compared to siblings, survivors of leukaemia (OR = 2.3, CI = 1.4–4.0, $p = 0.002$) and CNS tumours (OR = 2.7, CI = 1.5–4.9, $p = 0.001$) had an increased risk of repeating a year. Within survivors, migration background (OR = 3.6, CI = 1.2–10.7, $p = 0.020$), radiotherapy (OR = 8.9, CI = 2.7–29.5, $p < 0.001$) and relapse (OR = 3.7, CI = 1.4-9.7, $p = 0.009$) were risk factors for repeating a class. Survivors of renal tumours had a lower risk (OR = 0.2, CI = 0.1–0.9, $p = 0.041$) compared to leukaemia survivors.
Conclusion: We found that a considerable proportion of survivors had had to repeat a year in school, particularly those with a prolonged (leukaemia) or intensified (radiotherapy) treatment and those who had suffered a relapse. This knowledge might help to further improve educational support for paediatric cancer patients during and after treatment.

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Recombinant human erythropoietin in surgical correction of pediatric spinal deformities: a two years experience

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Background: One of the major causes of morbidity in pediatric spinal deformity (SD) surgery is blood loss. Patients require up to 8 units of red blood transfusions. Recombinant human erythropoietin (r-EPO) is efficacious in reducing transfusion rate (TR) in surgical correction of SD.
Methods: We evaluated the TR and safety of blood conservation by administration of r-EPO in 39 pediatric patients undergoing surgical correction of SD from October 2009 until January 2012. Mean age was 14.2 years (2.7–18.3); mean body weight was 48.41 Kg (9.2–75). We recruited patients for blood conservation techniques 4-6 weeks before surgery. Patients were divided into 3 major groups: idiopathic scoliosis (IS) (n = 25), neuromuscular scoliosis (NMS) (n = 6) and Others (spondylolysthésis, etc..) (n = 8). Each group was further subdivided into r-EPO and control groups. We followed patients with weekly blood counts. In each category patients were in the control group if they had the followings: Hb at baseline >150 g/L, uncontrolled hypertension or epilepsy, oral contraception, smoking, personal and family history of venous thromboembolism and biological evidence of thrombophilia. The mean r-EPO dose was 518 U/kg /week (144–800). The r-EPO dose was adapted weekly according to Hb levels and reticulocyte counts for a target Hb of 150 g/L.
Results: In the IS r-EPO group (n = 16), the TR was 0%. In the IS control group (n = 9) the TR was 44.4%. In the NMS group (NMS r-EPO; n = 3) (NMS control; n = 3), all patients (100%) needed transfusion. In the group Others (Others r-EPO; n = 4), (Others control n = 4) TR was 0% in both groups. One patient with heterozygous factor V Leiden, which was diagnosed after introduction of r-EPO, had deep venous thrombosis. There were no other side effects.
Conclusion: These results are consistent with the current literature that shows the lack of efficacy of r-EPO in NMS pediatric patients. Therefore we recommend the administration of r-EPO in order to diminish the peri-surgical TR and morbidity related in the pediatric IS.

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Bleeding Disorders in Noonan Syndrome

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Purpose: Noonan Syndrome (NS) is a common genetic disorder with heterogeneous clinical manifestations such as distinctive facial features, short stature, chest deformity, congenital heart disease, cryptorchism, lymphatic vessel anomalies and other comorbities. In 20–89% of the patients, laboratory abnormalities of primary or secondary haemostasis are found. As a large number of patients will require surgery, detecting and characterising haemostatic disorders in patients with NS is important.
Patients and Methods: Clinical features, bleeding history, blood smear and laboratory results for platelet function and coagulation parameters were reviewed in patients with NS followed at our institution.
Results: Sixteen patients (5 female, 9 male) with a median age of 10.4 years (0.7–25.5 years) were included. In seven patients (43%) either a positive history for bleeding (increased bruising or bleeding) and/or abnormal laboratory results (factor deficiency, abnormal platelet function) were found.
Conclusion: The existence of various bleeding types within one syndrome is unusual but might be explained by several mutations on several genes. As bleeding disorders can lead to serious complications, coagulation screening tests in every patient with NS is highly recommended for an optimal clinical management. Laboratory results and bleeding history may not correlate and require repeated testing and close follow up.

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Follow-up for paediatric survivors of childhood cancer– a survey of paediatric oncology / haematology institutions across Europe

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Introduction: Treatment for childhood cancer has improved, but due to cancer- and treatment-induced late effects regular follow-up is necessary for most survivors. Our aims were to: 1) assess the availability of specialised follow-up programmes for paediatric survivors across Europe, 2) describe activities performed during

follow-up and 3) document the perceived advantages and disadvantages of these programmes.
Methods: We contacted 179 institutions from 21 European countries and asked them to complete an online survey. The questionnaire included questions on respondents, their institution, available follow-up programmes, follow-up for paediatric survivors (<20 years of age), and guidelines used for follow-up. We used descriptive statistics.
Results: We received 110 (62%) responses and 61/93 (66%) reported to have a formal follow-up programme for their paediatric survivors. Most programmes were headed by a paediatric oncologist (73%) and situated in the paediatric oncology ward (98%) with close access to other specialities. Most respondents reported to use guidelines (89%) Activities were according to guidelines, but checks for problems (cancer recurrence 90%, late effects 97%, second malignancies 95%, and psychosocial problems 91%) were performed more frequently than education of survivors (about former disease 77%, treatments 75%, potential future health problems 86%, health behaviours 77%). Major barriers concerned institution-related problems (lack of: personnel 68%, dedicated time 58%, funding 53%,), but also survivor-related problems (patients lack of knowledge about need for follow-up 42%, distance to clinic 39%).
Conclusion: Our study showed that in many European countries, including Switzerland, there is still a lack of follow-up programmes for young survivors of childhood cancer. Close international collaboration will help to build programmes according to needs of countries, institutions and survivors. Funded by SNF-Ambizione-grant PZ00P3_121682/1.

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Challenge of misleading diagnostic results – when renal tumor mimics renal abscess – a case report

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Introduction: Ewing's sarcoma (ES) is a rare however wellknown tumor of childhood and represents the second most frequent primary malignant tumor of the bone following osteosarcoma. The majority of patients are in their second decade of life. Besides the bones, ES may also arise in soft tissue such as chest wall. However, there are only a few case reports on renal ES.
Case description: We report a case of primary renal ES in a 12-year-old boy. He presented with fever and flank pain in otherwise good condition. Elevated C-reactive protein (180 mg/l) and micro-hematuria were suggestive of urinary tract infection but urine culture was sterile. Ultrasound showed two lesions of the right kidney (largest diameter 4 and 2.6 cm), both with small fluid filled cysts and faint vascularisation. Further diagnostic including computed tomography of the abdomen revealed discrete contrast enhancement of one of these intra-renal lesions. First differential diagnosis was renal abscess or hemorrhagic cysts; however, a malignant tumor could not be excluded. Therefore, a true needle cut biopsy was performed. Unfortunately, the results of the biopsy were inconclusive, showing only normal renal tissue. In retrospect it is clear why; the tumor consisted of almost liquid material, so the only part that made it to the pathologist was the normal renal tissue. Antibiotic treatment was started, followed by a close monitoring with ultrasound. Since the lesions remained unchanged and the performed MRI investigation could not define the entity of the lesion, an open biopsy with resection of the tumor was undertaken. Unexpectedly, we received the diagnosis of extrascelettal ES. Adjuvant chemotherapy was started 10 days later. The patient is currently under ongoing treatment, nephrectomy is planned with further chemotherapy and probably also radiotherapy.
Conclusion: This case presents a rare type of tumor manifestation and shows the difficulties of making the diagnosis, when radiologic features are inconclusive, and the sample of the needle biopsy is not representative in a mainly cystic lesion.

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(N)ICE – or HDC: innovative approaches to treat pediatric relapsed sarcomas

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Introduction: Soft tissue sarcomas are rare and heterogeneous tumors of mesenchymal origin. The incidence in children less than 16 years of age is 8 per 1 Mio. The prognosis of undifferentiated sarcomas is poor and is similar to alveolar rhabdomyosarcomas. We present a boy with an intraabdominal undifferentiated sarcoma. Treatment included surgery, chemotherapy and irradiation according to the German CWS protocol. Relapse within the muscles of his forearm was treated with ICE chemotherapy resulting in substantial shrinkage of the tumor. Arm-saving surgery and irradiation, as well as consolidation with high-dose chemotherapy were performed.
Case report: A 14-year old boy presented with acute appendicitis. Complete blood count was normal and inflammation markers were not elevated. Sonographically the appendix was enlarged. However a ruptured tumor in the right abdomen was seen by laparoscopy, instead of the expected appendicitis. After R1 resection the patient was referred to our oncology department for further investigations. Staging excluded distant metastases. According to CWS 2002 , high risk group, the patient was treated with chemotherapy (ifosfamid, adramycin and vincristin) and an adjuvant radiotherapy with 24 Gy of the abdomen including a boost on the mesenteric area of a cumulative dose of 40,2 Gy. Complete remission was maintained during 3 years. 44 months after diagnosis an tumor was found by sonography in the proximal part of his right forearm which was not associated with bone. MRI revealed a 2.8 x 2.7 x 3.5 cm measuring tumor in the region of brachialis and flector digitorum superficialis muscles with involvement of the median nerve. An individual treatment was started consisting of 4 ICE cycles followed by local hyperfractionated neoadjuvant radiotherapy. A marked reduction of tumor volume was achieved. Complete surgical removal avoiding injury to the median nerve was undertaken. Surgery was followed by 2 HDC cycles with autologous stem-cell transplantation.
Conclusion: Relapsed undifferentiated sarcomas have a very poor prognosis. No significant progress has been made despite efforts in the treatment of metastatic sarcomas. High dose chemotherapy potentially may be of benefit for patients, however timing and composition of therapy remain unclear. Innovative prospective trials are warranted to demonstrate progress in this field of medicine and to confirm results which have been achieved in our patient.

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Transient acute myeloid leukemia in a newborn without Down Syndrome or a GATA-1 mutation: a new entity?

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Introduction: Transient myeloproliferative disorder (TMD), restricted to newborns with Down Syndrome (DS), is a megakaryocytic leukemia (FAB M7) that is characterized by spontaneous resolution. It is estimated that TMD occurs in 4–10% of patients with DS. Recent discoveries showed that somatic mutations in GATA1, a gene that encodes an essential hematopoietic transcription factor, occurred in clonal cells originating from nearly all patients with these malignancies. Rare patients with TMD but without DS have already been reported in the literature: however all the patients showed a blast-population with numeral or structural chromosome 21 abnormalities (+21, i(21q) or t(21)) or GATA1 mutation. We present a newborn with M7- leukaemia without molecular or cytogenetic abnormalities. No treatment was given and the leukemia resolved without complications 5 months later.
Case report: A 5 hour-old newborn was referred to the division of neonatalogy because of hypoglycaemia and acute respiratory distress. The blood count showed a severe thrombocytopenia, a moderate anemia and a leukocytosis of 45 x 10e9/l with 52% atypical cells. Further haematological investigations including bone marrow cytology revealed a M7 leukaemia without any genetic abnormalities. Neither clinical examination, nor fibroblast investigations provided evidence for a mosaic form of trisomy 21, or a partial or a translocation trisomy. Also no GATA1 mutation was found. Marrow and fibroblast cells were also investigated in Toronto for GATA1 mutations, as classical cases of TMD have been observed with absence of mutation in the investigated exons. The reason in these cases, are large deletions encompassing the primer sites typically used to detect exon 2 mutations. However, no such mutations were found. Clinically the patient appeared to be healthy and the leukemia disappeared spontaneously within 5 months. The patient is now 2 years old and in complete remission.
Conclusion: Neonates with DS have a unique predilection to develop TMD. A similar picture was seen in a small cohort of patients without DS, but in these cases the leukaemic clone showed abnormalities of chromosome 21, including the GATA1 gene.
To our knowledge this is the first patient with TMD in the absence of the known genetic abnormalities.

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Falling and leg weakness in a child with a history of cerebro-spinal anaplastic ependymoma: Relapse or complication of the therapy?

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A nine-year old boy, K., present with progressive leg weakness and frequent falls. He had a cerebro-spinal anaplastic ependymoma at the age of 2 and 8 months, treated with a two step-surgery followed by severe complications (cerebrospinal fluid leak, meningits, sepsis, right

cerebellar infarction). Unresectable residual tumor remained close to the basilar artery. Subsequent treatment consisted of chemotherapy and proton-beam radiotherapy (54 CGE on tumor region plus 6 CGE boost on residual disease). The residual tumor have appeared to remain dormant after six years of follow-up. Consequences of the tumor and the therapy have been a right hemisyndrom, deafness of the right ear and growth-hormone deficiency needing substitution. Follow up spinal MR imaging had shown a secondary Chiari Malformation due to significant scar tissue formation at the craniocervical junction and a syringomyelia down to Th 8, however stable over the following years, without correlated clinical signs. Five years have gone by and these conditions have not stopped K. from living a normal life, with sport activities, playing with his friends and going to normal school. Suddenly, at the age of 9, about 6 years after the diagnosis, K. beginns to fall more times a day. In few weeks he's able to walk just a few steps. A MRI reveals a progression of the syrinx throughout almost the entire spinal cord, without suspicion of tumor relapse. In order to prevent further progression of lower extremity weakness and anticipate upper extremity dysfunction a posterior craniovertebral decompression combined with lower thoracic laminotomy and placement of a syringosubarachnoid shunt was performed on a semi-urgent basis without perioperative morbidity. On short term follow-up a significant improvement of walking and leg strength was observed as well as a significant reduction in syrinx volume.
Conclusions: Follow up by children with a history of tumor is extremely important, and it is necessary to be aware of the possible late effects in order to detect them, which can develop quickly and be the cause of permanent damages if not handled on time. Pediatric neurosurgical intervention may be needed in children even after many years of follow-up after complicated brain tumor treatment.

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Severe anaemia due to chronic bleeding in a 5 year old boy with delayed diagnosis of a rare subtype of von Willebrand syndrome (vWS 2A IIE)

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Introduction: vWS 2A IIE is a rare form of vWS that first was described in 1986. It is defined by a lack of large and medium sized vWF-oligomeres in the plasma (defining "2A") and a specifically aberrant pattern of the multimer triplets (defining "IIE"). The subtype IIE displays autosomal dominant inheritance.
Case report: A 5 year old patient with an incidentally detected, severe anaemia (Hb 56 g/l) and a history of recurrent epistaxis was referred for further diagnostics. He had been tired during the last five month and suffered from epistaxis 3–5x a week since the age of 15 month. There was no other history or signs of bleeding. A blood test in Canada at the age of two seemed to show a vWS, but the tests were never completed, and no therapy was initiated. The family history showed recurrent epistaxis in the father during childhood. Clinically we found a pale 5 year old boy in a good general condition with a low systolic murmur as sole abnormality. Laboratory results showed severe iron deficiency anaemia, a decreased vWillebrand-Ristocetin-Co-Factor and vWF-Ag, a normal vWF-Ratio and Factor VIII and a prolongation of the closure-time in the platelet function analyzer (PFA-100) with epinephrine and ADP. The desmopressin-test revealed a short-lived normalization oft the PFA-100 and vWF values with return to pathological values at 2 hours. Multimer-analysis revealed a pattern compatible with vWS 2A IIE with a relative decrease of the large and middle vWF-multimer and a pathological triplet pattern. The father and the 3 year old sister (asymptomatic) showed the same laboratory findings. On therapy with oral tranexamic acid and iron substitution the epistaxis ceased and hemoglobin normalized. However, some month later epistaxis recurred despite tranexamic acid, and a prophylactic substitution regime with plasmatic von Willebrand factor (Hämate P) was started. The epistaxis has now decreased to an acceptable frequency without any signs of anemia or iron deficiency.
Conclusion: Any child with anemia and a bleeding history should have a thorough clotting analysis. The differential diagnosis of vWS requires multimer analysis and desmopressin testing up to hour 4 to indentify rare subtype as 2A IIE, as a misinterpretation as vWS type 1 is possible. The short duration of desmopressin effects in vWS 2A IIE has therapeutic implications.

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Basal ganglia germinoma in a 6-year-old boy – a diagnostic challenge

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Background: Basal ganglia germinoma are very rare malignant CNS tumours almost exclusively observed in South East Asia. Due to the lack of diagnostic neuroradiological features, diagnosis may be difficult. We present the diagnostic features of a 6-year-old Swiss boy with a supranuclear hemiparesis due to a basal ganglia germinoma.
Case Report: A previously healthy boy presented with slowly progressive right sided supranuclear hemiparesis beginning with clumsiness of the right hand, newly established left-handiness and problems to walk as well as mild facial palsy. Magnetic resonance imaging (MRI) of the CNS showed a slight atrophy oft the left hemisphere and a small left striatal non-expansive lesion with cystic parts that was hypointense on T_1- and hyperintense on T_2-images and showed discrete gadolinium enhancement. Differential diagnosis included an inflammatory process or a basal ganglia germinoma. A cranial CT scan revealed calcification of the lesion. Cerebrospinal fluid analysis showed no abnormal cells and elevated β-HCG (0.8 IU/L) with normal serum beta-HCG. The boy underwent stereotactic biopsy and the diagnosis of a pure germinoma was confirmed neuropathologically. Dedicated chemotherapy, followed by fractionated precision conformal proton radiation therapy (whole ventricular irradiation to 24 Gy (RB) and tumour boost to total dose of 40 Gy (RBE), SIOP CNS GCT 96 protocol) was performed with good response. Two years after initial diagnosis, the boy shows minor cognitive impairment and a right sided spastic hemiparesis without evidence of tumour recurrence.
Discussion: Basal ganglia germinoma are very rare in non-Asian patients; less than 10 cases have been reported in the western world. They usually occur unilaterally in male children and young adults, bilateral presentations are possible. They are highly sensitive to radio- and/or chemotherapy and prognosis with early adequate therapy is good. Due to close proximity to the internal capsule, acquired progressive supranuclear hemiparesis is a typical clinical presentation. We suggest that basal ganglia germinoma should be considered in patients with typical symptoms and non-specific lesion on initial MRI. Asymmetric isolateral brain atrophy, calcifications on CT and an intrathecal β-HCG-secretion are hallmarks of the tumour and should prompt confirmation by stereotactic biopsy.

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Pneumatosis intestinalis in a 3-year-old with acute lymphoblastic leukaemia

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Purpose: To describe symptoms, diagnostic features, treatment and outcome of pneumatosis intestinalis (PI) in a child being treated for acute lymphoblastic leucemia.
Case Report: After being diagnosed with acute lymphoblastic leukemia (ALL), a 3-year old boy was treated with prednisolon according to BFM-ALL 2009. During a mild episode of rotavirus gastroenteritis, abdominal sonography revealed intrahepatic portal venous gas but no free intraperitoneal air confirmed by an abdominal radiograph. At that time, clinical examination revealed good peristaltic movement and no abdominal guarding. One week later, the child's condition deteriorated with severe abdominal pain and signs of peritonitis. Abdominal CT suggested free intraperitoneal air indicating intestinal perforation and therefore a laparotomy was performed. Intraoperatively, no perforation was seen but massive air-filled cystic lesions along the whole mesocolon. Antibiotic treatment was carried out for ten days and enteral nutrition could be started one week after surgery. Treatment for ALL could be continued 2 weeks later.
Discussion: Well known as sign of necrotizing enterocolitis in premature newborn infants, PI is rare in older children. Pathogenesis remains unclear, mechanical and infectious causes are discussed as possible reason. In addition, PI following chemotherapy or long-term steroid treatment has been described. In our patient, a combination of rotavirus infection, steroid treatment and leukemia may have been involved. CT scan has proven very helpful in detection of PI to distinguish intramural from free intraperitoneal air, however, sometimes, massive intramural cystic lesions may mimic free intraperitoneal air. In most cases, conservative treatment might be sufficient, as outcome usually is excellent. Surgical intervention may be indicated in cases of fulminant forms with peritoneal signs and progressive deterioration. Although a rare condition, awareness of PI and its imaging appearances during immunosuppressive treatment is important to establish a safe management, reserving surgical approach for fulminant courses.

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Fatal hyperammonemia following autologous hematopoietic stem cell transplantation

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We present a 2-year-old male patient with a neuroblastoma stage IV, who developed severe hyperammonemia (33–475 umol/l) after receiving high-dose chemotherapy and autologous hematopoietic stem cell transplantation. Despite nitrogen scavenging therapy and hemodialysis, ammonium levels remained elevated and two weeks after the onset of hyperammonemia he died due to cerebral edema. So far only few fatal cases of hyperammonemia following autologous or allogeneic bone marrow transplantation have been described. In these cases the pathogenesis of hyperammonemia remains to be elucidated and has been suggested to be multifactorial due to a combination of infections, mucositis, gastrointestinal bleeding, protein catabolism and parenteral nutrition. We hypothesize that in our patient the acute onset of hyperammonemia may be due to a secondary (e.g., drug-induced) mitochondrial dysfunction with consecutive deficiency of the oxidative phosphorylation and urea-cycle. Investigations of these mitochondrial functions are currently examined and will be presented.

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Hyperleukocytosis and its role in the Pediatric Emergency Department

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Introduction: Leukocytosis (total WBC count >11'000/µL) is frequently seen in the pediatric emergency department due to various etiologies. It is most often caused by diverse infections and commonly due to an increase in the absolute number of mature neutrophils. Hyperleukocytosis (HL) refers to a total WBC >50'000/µL. It may result in leukostasis which is a clinicopathological syndrome caused by the sludging of circulating leukemic blasts in tissue microvasculature provoking neurological, pulmonary and metabolic signs and symptoms. Younger patients are particularly at risk. HL represents a medical emergency due to the increased risk of mortality (20%).
Case Report: We report 2 pediatric cases of leukemia: Patient I a 15 year old boy diagnosed with T-LLA and Patient II a 2 & ½ year old girl diagnosed with preB-LLA. At initial diagnosis HL was identified in both patients (total WBC count of 256'000/µL and 875'000/µL respectively). Patient I had partial (40 ml/kg) exchange transfusion (ET) with induction chemotherapy, hyperhydration, forced diuresis, treatment of hyperuricemia, blood transfusions and correction of coagulopathy with fresh frozen plasma. Patient II had double-volume ET (160 ml/kg) and was intubated because of the pulmonary leukostasis symptoms. She also received additional therapy as with Patient I. Both patients survived the initial stages of treatment and are currently continuing on their leukemia therapy.
Discussion: It is critical to anticipate the risks and severe complications of leukostasis. The decision and choice of exchange transfusion versus leukapheresis depends on patient age/size, central venous line access and availability of local facilities and expertise.
Conclusion: Hyperleukocytosis, although rare, requires immediate recognition and appropriate emergency treatment. These 2 case reports illustrate the importance of leucocytoreduction in the emergency setting.

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Methemoglobinemia in a 10-month old girl: another swimming pool danger

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Introduction: Acquired methemoglobinemia is a rare but potentially fatal condition. Children are at higher risk of poor outcome due to the impairment in oxygen delivery to the tissues and the slow compensatory response. Immediate recognition of this pathology in cyanotic children is important.
Case Report: We report the case of a 10-month old girl who presented with vomiting, pallor, cyanosis and asthenia. She showed no fever but tachycardia (190/min) and her blood O_2 saturation was 89%. She did not show any signs of respiratory distress and the pulmonary auscultation was normal. An infectious process with septic choc was suspected on admission. Chest x-ray, abdominal and cerebral echography, ECG, and liver function tests were normal. Leukocytosis was present but CRP was low (<10 mg/l). A urinary tract infection was suspected due to a pathological urinary dipstick (presence of nitrite and leucocytes) and intravenous ceftriaxone was initiated prior to her transfer. Upon arrival at our hospital, the child remained cyanotic despite oxygen therapy. The differential diagnosis was therefore enlarged to include an eventual cardiac abnormality, a neurological process or possible intoxication. Complete venous blood gases were obtained, showing a pathological methemoglobinemia of 11.6%. The child's swimming pool water was incriminated as the water had not been changed for several months although formal proof was not obtained. Stagnant water is known to contain nitrates that are converted to nitrites by intestinal bacteria, which subsequently oxidize hemoglobin to methemoglobin. Under intensive oxygen therapy (up to 8L), her methemoglobinemia reduced to 2% in 12 hours, permitting discharge from hospital.
Conclusion: It is important to recognize acute cyanosis in the emergency setting and to conduct appropriate investigations following a systematic algorithm differentiating between central and peripheral origins. Acquired methemoglobinemia is due to a multitude of ingested therapeutic agents and toxins, but also to environmental conditions such as exposition to stagnant water.

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Consumptive hypothyroidism due to infantile hemangioendothelioma

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Introduction: Infantile hepatic hemangioendotheliomas are the most common benign hepatic tumor of infancy. About half of cases occur as solitary masses and half are multifocal. Although it is a benign tumor, serious clinical complications can occur. We present an infant who presented with a giant panhepatic multifocal infantile hemangio-endothelioma and clinical consumptive hypothyroidism due to excessive inactivation of thyroid hormones suggesting type 3 idothyronine (D3) hyperactivity. After giving beta-blocker there was a considerable decrease in size of the liver tumor.
Case report: A four-month old girl was referred to our hospital for further investigation after detecting hepatomegaly by routine check-up (U4). The mother reported that the infant showed increasing signs of prostration while breastfeeding and paleness within the last few weeks. Initial complete blood count showed hemoglobin of 79 g/l, platelets of 312 x10^9/l and leukocytes of 7.27. PTT was 28 sec and PT 77%. Further radiologic investigations including sonography of the abdomen following MRI revealed a giant panhepatic multifocal tumor with largely replacement of the liver. Further blood investigations showed a manifest hypothyroidism with a highly elevated TSH and low fT3. A high thyreoglobuline concentration suggests improved synthetic capacity of the thyroid. No signs for abdominal compression syndromes including abdominal caval occlusion, disseminated intravascular coagulation (Kassabach-Merritt syndrome) and congestive heart failure was seen. The child was treated with propranolol and subsequently showed a significant decrease in tumor size. In parallel TSH decreased under thyroid hormone substitution from initially 198 mIU/l to 92 mIU/l within six days. The child was discharged two weeks after admission.
Conclusion: Giant diffuse hemangioendotheliomas may cause hypothyroidism, congestive heart failure and Kassabach-Merritt syndrome. Consumptive hypothyroidism is mostly seen in the diffuse variant and less often in multifocal variant of liver hemangioendothelioma.

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External Validation of The Lab-Score to Detect Serious Bacterial Infections in Children with Fever without Source

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Introduction: Serious bacterial infections (SBI) are often difficult to detect in children with fever without source. The Lab-score, combining procalcitonin (PCT), C-reactive protein (CRP) and a urine dipstick, has been developed to overcome the weaknesses of the markers taken individually. Our objectives were to evaluate the diagnostic properties of the Lab-score in a North-American population.
Methods: A prospective cohort study was conducted on a convenience sample that took place in a tertiary pediatric hospital emergency department. We included every child between the ages of 1 and 36 months with history of a rectal temperature over 38 °C with no identified source of infection. A blood test for complete blood count, PCT, CRP, blood culture, and a bladder catheterization or suprapubic aspiration for urine analysis and culture were performed. The primary outcome was the diagnostic properties of the newly described Lab-score to detect a SBI.
Results: A total of 341 children were included. 55 children (16%) were diagnosed with a SBI. The area under the ROC curve (AUC) for Lab-score was 0.92 (95% CI 0.88, 0.94). It was 0.88 for CRP (95% CI 0.84, 0.91), 0.82 for PCT (95% CI 0.78, 0.86) and 0.80 for WBC (95% CI 0.75, 0.84). The lab-Score AUC was statistically superior to the AUC of CRP, PCT and WBC. The Lab.score had a sensitivity of 84% (95% CI 74, 91) and a specificity of 89% (95% CI 87, 91) to detect a SBI. Positive and negative predictive value were 60% (95% CI 53, 65) and 97% (95% CI 95, 98) respectively.
Conclusion: The Lab-score combining PCT, CRP and a urine dipstick is a valuable tool to detect a serious bacterial infection in children between 1 and 36 months with fever without source. It is superior to the other markers taken individually.

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Antimicrobial resistance of *E. coli* febrile UTI in children less than 1 year including clinical data of young infants

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Introduction: Urinary tract infections are common, usually well treatable bacterial infections in children. They are a top differential particularly when evaluating young infants presenting with fever of unknown origin in the emergency department. Accurate diagnosis, i.e., processing urine obtained via clean catch (MSU) or catheterisation only, is pertinent. The most common pathogen involved in children without an underlying urological pathology, is *Escherichia coli*. Frequent re-evaluations of local epidemiological resistance data are necessary to review the current antibiotic agents used for initial treatment.
Aim: Review of our local resistance data for *E. coli* to revise our empirical antibiotic treatment regime and presentation of clinical findings in young infants, 3 to 6 months.
Methods: Retrospective review of urine cultures growing *E. coli,* supplied by the microbiology lab, and their antimicrobial resistance patterns in children less than 1 year diagnosed at the University Childrens' Hospital Bern during 2011. Exclusion criteria: children with known underlying uropathies and urine bag samples. Review of clinical data (type of urine specimen, dip/microscopy, CRP, blood culture) in children 3–6 months presenting with UTI.
Results: Ninety-five specimens were obtained from 78 children (54% female). Fifty-nine (62%) specimens grew *E. coli* with 47(80%) Amox/Clav and 42(71%) Cotrimoxazole sensitivity, respectively. Ceftriaxone sensitivity was detected in 57(97%) of *E. coli* isolates. ESBL was not a problem in this cohort. Twenty-one(27%) children were 3 to 6 months. In 27 specimens 17(63%) *E. coli* were detected: 16(94%) and 12(71%) were sensitive to Amox/Clav and Cotrimoxazole, respectively, and all were sensitive to Ceftriaxone.
Conculsion: Starting with a third generation cephalosporin empirically is the safest option to avoid treatment failure. Particularly Cotrimoxazol and possibly also Amox/Clav are not sufficient as first choice to cover for an *E. coli* febrile urinary tract infection at our centre.

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Performance of Rapid Antigen Diagnostic Test for Group A β-Haemolytic Streptococcal Pharyngitis in a tertiary paediatric emergency department

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Objectives: The main objective of this study is to determine the performance of rapid antigen diagnostic test (RADT) for group A β-haemolytic streptococcal (GABHS) pharyngitis on children who presented a sore throat in a paediatric emergency department. The secondary objective is to evaluate the performance of RADT by physicians.
Methods: We conducted a prospective study between January 2010 and July 2011. We included all children aged 3-18 years who presented a sore throat and did not received any antibiotic during the previous seven days. For all children, two pharyngeal swabs were taken for rapid antigen detection test (RADT) and throat culture. We evaluated RADT performance to compare with culture (Gold standard) by calculating sensitivity (Se), specificity (Sp), positive likelihood ratio (LR+), negative likelihood ratio (LR-) with 95% confidence interval (95%CI) and pre and post- test probability.
Results: We included 2089 patients. Prevalence or pre-test probability of GABHS is 36–95%CI (34–38) with throat culture. Sensibility of RADT is 81–95%CI (78–84), Specificity is 87–95%CI (85–89), LR+ is 6.4–95%CI (5–8.2), LR- is 0.2–95%CI (0.2–0.3). Positive probability post-test is 78%. Negative probability post-test is 11%. RADT performance varied by physicians with variations in sensitivity from 60 to 100% and specificity from 50 to 100%.
Conclusion: RADT performance among children who presented sore throat in paediatric emergency department is overall insufficient to diagnose the GABHS pharyngitis. RADT performance varied significantly depending on the physicians. The establishment of RADT in paediatric emergency department needs instructions, individual evaluation and training for the physicians.

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Deep suppurative neck infections in children

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Introduction: Deep suppurative neck infections generally occur in children between two and four years. That can be explained by the fact that the deep neck spaces, as the retropharyngeal and the latero-pharyngeal spaces, contain chains of lymph nodes that are prominent in the young child, but atrophy before puberty. Infection of the areas drained by these lymph chains may lead to suppurative adenitis.
Methods: We present 4 children hospitalized with deep neck infection. The ages of these children (1, 5, 9 and 12 years) differ from the typical age described in the literature. All the patients presented similarities in their clinical pictures.
Results: Three retropharyngeal abscess were diagnosed, one with a mediastinum infiltration. The fourth patient presented with a latero-pharyngeal abscess. All of them presented with torticollis, lateral or posterior cervical adenitis and fever. Dysphagia was present only in 2 out of 4. Trismus was present in only one patient. All of them were positive for Streptococcus A. CT or RMN were done in all. 3 / 4 were treated with surgical drainage and amygdalectomia. I.v. antibiotherapy was given to all patients.
Conclusion: Independently of the age of the patient, some clinical signs and symptoms should evocate a deep neck infection. Torticollis, cervical adenitis, and fever seem to be signs that should alert a clinician because this entity remains potentially fatal.

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Idiopathic facial aseptic granuloma: high frequency of ocular involvement

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Introduction: Idipoathic facial aseptic granuloma (IFAG) is a newly recognized pediatric entity characterized by abscess-like painless red to violaceous nodules located on the cheeks of toddlers/preschool-aged children with slow spontaneous healing. The occurrence of chalazions has been reported in a few patients. We aimed to assess the frequency of ocular lesions in children with IFAG.
Methods: We prospectively collected demographic and clinical data of all patients presenting with IFAG at our Department of Pediatric Dermatology during 2 years. Values are presented as median (range).
Results: We identified 9 children (5 female, 4 male) with IFAG who presented at the age of 2.7 (1.8–8.3) years after a disease duration of 2.9 (1–36.5) months. Six patients had a solitary facial lesion at the time of presentation and three had 2 or 3 lesions. Six of the 9 children had a history of documented chalazions, with usually recurrent course, and three had mild keratitis. In 5 of these 6 patients the ocular lesions antedated the occurence of facial nodules. They were treated with ocular antibiotics and steroids. Four patients with rather new and fluctuating facial nodules were treated with systemic antibiotics (azithromycin, metronidazol) for 4 weeks resulting in gradual improvement. For all facial nodules zink containing creams were applied until full recovery.

Conclusions: This case series reports a high frequency of ocular lesions, in particular chalazions, in IFAG. This suggests that IFAG belongs to the spectrum of childhood rosacea; thus the use of metronidazole may represent a beneficial treatment option. Children with IFAG should routinely be investigated for ocular involvement.

P 105

Atypical skin complications of *Mycoplasma Pneumoniae*

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Introduction: *Mycoplasma pneumoniae* (MP) is a well-known cause of childhood pneumonia. Dermatologic manifestations such as exanthematous skin eruptions, erythema nodosum, urticarial, and Stevens-Johnson syndrome (SJS) may occur in 25–33% of patients. Rarely, dermatologic complications such as bullous erythema multiforme or *MP*-associated mucositis (Fuchs syndrome) may occur.

Clinical cases: We present four cases of dermatologic complications linked to MP.
Discussion: There are 34 cases of bullous erythema multiforme caused by MP in the literature. This entity is considered to be in the spectrum of disease that includes SJS, but unlike SJS there is little morbidity and no mortality reported. There are ten cases of MP-associated mucositis described in the literature. Differentiation from SJS is made by the absence of skin lesions. Treatment includes antibiotics, corticosteroids, and rarely immunoglobulins. Hypotheses exist that immune complex-mediated vascular injury, cell-mediated immune response/cytotoxic injury to epithelial cells, and autoimmune mechanisms may be responsible.
Conclusion: Dermatologic manifestations of M. pneumoniae may be similar to Stevens-Johnson syndrome and needs to be considered in the differential diagnosis of mucocutaneous lesions.

Description	Diagnosis	Skin Lesions	Treatment and Outcome
12-yr-old boy with fever, cough, rales, skin lesions, conjunctivitis, mucositis	Positive Mycoplasma PCR Chest x-ray confirmed pneumonia	Bullous Erythema Multiforme	Macrolide Corticosteroids Immunoglobulins Complete resolution after two weeks
11-yr-old boy with fever, cough, rales, skin lesions, conjunctivitis, and mucositis	Positive Mycoplasma PCR Chest x-ray confirmed pneumonia	Bullous Erythema Multiforme	Macrolide Corticosteroids Complete resolution after 3 weeks.
15-yr-old girl with fever, cough, rales, skin lesions, conjunctivitis, and mucositis	Positive Mycoplasma PCR Chest x-ray confirmed pneumonia	Bullous Erythema Multiforme	Macrolide Corticosteroids Complete resolution after 2 1/2 weeks
15-yr-old boy with fever, cough, mucositis and conjunctivitis	Positive Mycoplasma PCR	MP-associated mucositis	Corticosteroids Complete resolution after 2 weeks

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Epidemic Invasive Pneumococcal Disease in Child Day-Care Center: Diagnostic Problems, Prevention and Implications

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Introduction: The overall number of invasive pneumococcal disease (IPD) is reduced since introduction of the 7-valent pneumococcal vaccine (PCV-7), but a shift in the isolated subtypes in IPD to non-covered strains occurred in Switzerland as well as in other countries with pneumococci type 3 now presenting the most common causative strain of IPD in 2-4 year olds. Epidemic outbreaks of pneumococcal infections are rare. Diagnosis of IPD is difficult in the outpatient setting. We report on 5 children with suspected IPD observed within one week in one child day-care facility.
Discussion: We present an epidemic of invasive pneumococcal disease (IPD), a rare but still existing condition in PCV-7 vaccinated children. In children presenting with IPD who are not critical ill and cared for as outpatients, eliciting the genesis of disease remains difficult. In IPD, blood cultures are positive in only a minority of cases (patient 1), pneumococcal antigen excreted in the urine is not a clear indicator for IPD. Detection of pneumococci either by culture, PCR or pneumococci antigen in the pleural effusion is regarded superior (1). However good clinical condition of children in an outpatient setting hinder a more invasive diagnostic approach. In the presented case series the suspicion of pneumococci type 3 as the causative agent of infection is high, but could not be proven beyond doubt. It is well established that pneumococcus type 3 is one of the major causes of IPD and the most common detected strain in affected children with pleural effusions. The existence of more aggressive subtypes of type 3 strains is described (2). Nevertheless an underlying viral infection although not provable must be equally considered and is a discussed causative link. As clinical symptoms of all five reported children were equivalent no efforts diagnosing a paving viral infections were made, but should be considered in similar cases. All but one patient was vaccinated with PCV-7 comprising the subgroups of pneumococci accounting for 70% of all IPD. A shift in the detected types of pneumococci in IPD in children was shown since introduction of PCV-7. Type 3 pneumococci are now responsible for the majority of these infections in the 2-4 year olds in Switzerland (3). As type 3 is included in the new 13 valent PCV-13 the diseases described above may be preventable by vaccination. We conclude that epidemics of IPD are rare but still occur despite vaccination (PCV-7). In day-care facilities attendees should be vaccinated against penumococci with PCV-13. In suspected epidemic outbreaks of IPD detection of pneumococci and underlying viral infection should be urged for. It remains to be seen whether the effect of PCV-13 will reduce epidemics of IPD.
Literature: 1 Werno et Murdoch, Clin Infect Dis. 2008;46(6):926–32.
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P 107

Cluster of severe group A beta-haemolytic streptococcal infections

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Background: The spectrum of diseases caused by group A beta-haemolytic streptococcus (GABHS) includes superficial, invasive, toxin-mediated and post-infectious diseases. Various surface structures of GABHS influence its virulence by mediating adherence, colonization, and invasion of human skin and mucosa. Among these, the M protein, which is encoded by the *emm* gene, plays a pivotal role. Especially *emm1* and *emm3* encode for M-protein subtypes associated with invasive GABHS infections. In addition, various cellular toxins and enzymes are produced, and super-antigens mediate the streptococcal toxic shock syndrome (TSS). On the other side, disease severity is dependent of the host's immunological profile that determines susceptibility for severe invasive infections.
Case Series: We present a series of 4 previously healthy children with invasive GABHS infections admitted to our ICU within 2 weeks in January 2012. Case 1: an 11 year-old girl of Sri-Lankan descent was admitted with TSS after a 2-day history of vomiting, diarrhea and leg pain. Blood cultures were positive for GABHS. Despite antibiotic treatment with ceftriaxon and clindamycin, she developed GAS positive septic arthritis of the left ankle on day 7 after admission; Case 2: a 2 year-old Caucasian girl with a 4-day history of an upper airway infection was admitted in septic shock with a scarlet rash and a lobar pneumonia with pleural empyema. GABHS was cultured from the pleural fluid and from a pharyngeal swab; Case 3: a 2 year-old Sri-Lankan boy was admitted in septic shock with bronchopneumonia. He has had signs of a mild upper airway infection for 3 days before and GABHS was isolated from tracheal secretions; Case 4: a 2 year-old Caucasian boy with a 4-day history of croup was admitted in septic shock, with a scarlet rash, and lobar pneumonia with pleural empyema. Both a pharyngeal swab and the pleural fluid grew GABHS, the nasopharyngeal aspirate was positive for human metapneumovirus. All 4 patients survived.
Comments: Local epidemics of severe GABHS infections have been reported world-wide for many years, presumably due to the emergence of particularly virulent strains. Genotyping and other microbiological tests are under way to characterize our isolates in terms of their genetic relationship and the production of various virulence factors. The cluster of severe GABHS infections was reported to the local public health authorities.

P 108

Meropenem-associated agranulocytosis in an infant with brain abscess

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Introduction: Meropenem is a broad-spectrum antibiotic which is commonly used for the treatment of severe life threatening infections. It is generally safe and well tolerated. The most common clinical adverse events include diarrhoea, rash, nausea, vomiting and reaction at the injection site. Haematological adverse events have rarely been reported in children. In children under the age of three months meropenem is not licensed as a result of limited data on safety and pharmacokinetics. Nevertheless there is considerable off-label use in particular for severe sepsis, intra-abdominal and cerebral infections.
Case Report: We report the case of a preterm infant who, at the postnatal age of nine weeks, developed agranulocytosis after 19 days of treatment with meropenem for intracerebral abscess caused by *Enterobacter cloacae*. As meropenem was suspected to be the most likely cause of his agranulocytosis antibiotic treatment was switched to ciprofloxacin. After discontinuation of meropenem the neutrophil blood count normalised within 10 days.
Discussion and Conclusion: A literature search revealed only one other case report of meropenem-associated bone marrow aplasia in a 3-year old child. An additional search using the World Health Organization Global Individual Case Safety Report database from the Collaborating Centre for International Drug Monitoring showed eight reports of haematological adverse events in children between 2 and 9 years of age. Agranulocytosis is a rare but serious and potentially life-threatening adverse event of meropenem and should be considered in children at any age who present with leucopoenia or agranulocytosis.

P 109

Taking headache and vomiting in a young child serious: a case of pneumococcal brain abscess

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Introduction: Vomiting without diarrhoea and/or headache presenting in a pre-schooler are serious symptoms. A low threshold for early imaging should be part of the work up. Brain abscess is a well known but rare entity in children. Otic infection and cyanotic heart disease are leading predisposing conditions. *Streptococcus pneumoniae* as a causative microbe is rare. Little is found in the literature on epidemiology and management particularly in children. Our 5 year old girl, with above presenting signs, was found to have a pneumococcal brain abscess.
Case: A 5 year old immunocompetent girl was referred to our emergency department with intermittent headache since 1 week. Just prior admission mild pyrexia, nausea, vomiting, photophobia, nocturnal headache and loss of appetite was reported. Besides a symptomatically treated otitis media on the right 3 weeks prior, the past medical history had been uneventful. Migraine runs in the family. On examination she was afebrile, had stable vitals and a GCS of 15. Except mild photo-phobia the general and extended neurological exam was unremarkable. No inflammatory markers. MRI Brain showed a left temporal brain abscess (2.5 x 2.6 cm) thought to be originating from the left mastoid. Stereotactic aspiration was performed by the neuro-surgical team and paracentesis by the ENT team. She was started on Meropenem 40 mg/kg/dose tds. Twenty four hours later gram positive cocci were found in the aspirate, which were identified as *Streptococcus pneumonia* serotype 3, the antibacterial treatment was reduced to Amoxicillin thereafter. She made a rapid and full recovery. Eight weeks of parenteral antibiotics were given. A follow up MRI week 12 post admission showed a normalised left temporal lobe.
Conculsion: Brain abscesses without known predisposing risk factors are often diagnosed late. If treated in a multidisciplinary approach (medical, neurosurgical) outcome is favourable. This child was diagnosed early, taking her presenting symptoms serious and appropriate investigations were initiated. She made full recovery without sequelae to date.

P 110

Does tick-borne encephalitis cross the borders?

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Introduction: Tick-borne encephalitis is a well known cause of encephalitis in Switzerland in endemic areas. Long-term consequences are numerous and can be severe. Vaccination is recommended for people >6 years who live or travel in endemic aeras. We report here the case of a meningo-encephalitis in a six years old girl with confusion and behavioural disorder, without any evidence of travel to an endemic area.
Case description: This 6 years old girl presented severe headaches and vomiting, which became more acute over a 6 days period. Unusual behaviour prompted hospitalisation for further investigations, despite no febrile episode was present. At admission, aggressiveness, temporary contact loss, mood swings and sudden crying prevented a thorough physical examination. Blood test demonstrated light inflammation (CRP 33 mg/l, L 12.9 G/l, N 9.5 G/l). CT-scan and lumbar puncture were performed under general anaesthesia because of aggressiveness. Inflammation compatible with viral meningitis was found in cerebrospinal fluid, without evidence of bacterial infection (leucocytes: 105/µl, 12% neutrophiles, 87% monocytes; proteins: 458 mg/L, glucose: 2.7 mmol/L, lactate: 1.3 mmol/l, negative culture). *Borrelia burdorferi,* Herpes and Enterovirus infections were excluded. Flavivirus serology (IgM and IgG) suggested a tick-borne encephalitis. The recent history revealed flu-like symptoms after a tick bite three weeks earlier in the forest close to her home (Apples/VD). The girl received supportive treatment and rehydratation during the following days. Six weeks later she still had light headaches, gait disturbance and possibly absence epilepsy.
Conclusion: Tick-borne encephalitis is rarely firstly thought of when facing a child with signs of encephalitis, in particular outside endemic areas. Behavioural disturbance and atypical neurological symptoms must therefore suggest such a diagnosis.
This case reveals a flavivirus infection outside the endemic area. Should we then vaccinate adults and children even outside the endemic region? And should we vaccinate children earlier than 6 years old?

P 111

Cytomegalovirus associated polyradiculitis mimics meningeosis in a boy with medulloblastoma

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Background: Cytomegalovirus (CMV) infections of the central nervous system (CNS) are rare in both immunocompetent and immunocompromised patients. PTCH1 mutations causing Gorlin syndrome have recently been shown to compromise immune privilegy of the CNS.
Case report: A 20-months-old boy with Gorlin syndrome (PTCH1 mutation) under chemotherapy for medulloblastoma presented with acute onset of irritability and lower extremities weakness. The clinical examination showed meningeal irritation with symmetric flaccid paralysis of lower extremities, absent deep tendon reflexes, ataxia and ophtalmoplegia. Bladder and bowel control were not affected. Cerebrospinal fluid (CSF) examination showed cytoalbuminary dissociation. Spinal MRI revealed thickening and contrast enhancement of the distal nerve roots and cauda equina interpreted as tumor seeding. CMV DNA could be detected in the CSF and a ten-fold increase of CMV IgG antibody in serum was observed.
A 5 days treatment with intravenous prednisone (5 mg kg^{-1} per day) followed by an antiviral therapy with intravenous ganciclovir (10 mg kg^{-1} per day) led to a slow recovery with consistent clinical improvements. The clinical course is compatible with an inflammatory caudal polyradiculitis triggered by CMV-infection.
Conclusion: CMV infection as a potentially treatable cause of polyradiculitis in the CNS needs to be ruled out when meningeosis in patients with malignant brain tumors is suspected. A predisposition to the triggering of an autoimmune aggravation of CMV disease of the CNS in Gorlin syndrome is possible.

P 112

Osteoarticular tuberculosis of the wrist – a case report

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Background: The incidence of tuberculosis is generally rising due to rising cases of HIV- patients and the emergence of multidrug-resistant mycobacteria. Musculoscelettal manifestations of tuberculosis (TB) is rare (2–3%) and its occurence mainly consists of TB located in the spine (tuberculous spondylitis). Extraspinal musculoscelettal involvement is among the least common manifestations of TB. We present our experience of a patient with a tuberculosis of the wrist.
Case report: The patient, a 5-year-old otherwise healthy girl, displayed a progressive painful swelling and loss of motion in the right wrist over a period of 4 months. A rheumatologic disease was suspected and an anti-inflammatory treatment with Ibuprofen was initiated with no success. Rheumatologic markers were negative and the leucocyte count and c-reactive protein were within normal ranges. Diagnosis of TB was made by a positive quantiFERON test. The affection of the wrist was confirmed in the biopsy specimen, which

revealed a granulomatous epithelio-gigantocellulary inflammation with acid-fast rods. The MRI of the wrist showed severe inflammatory changes of the carpal and partially of the metacarpal bones. A CT scan of the thorax showed enlarged lymph nodes in the mediastinum and both hili, another enlarged lymph node could be detected in the right axilla. A multidrug anti-tuberculosis therapy and splinting was initiated and is still going on.
Conclusion: Diagnosis of TB in a joint is difficult due to its non-specific clinical presentation and imaging features. Because early diagnosis and treatment ist vital in order to prevent irreversible osteoarticular destruction and function, differential diagnosis of a painful swallen joint should include TB, especially if the patient doesn't respond to a anti-inflammatory therapy.

P 113

Parinaud oculoglandular syndrome – an atypical presentation of Bartonella henselae infection

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Background: Parinaud oculoglandular syndrome was first described in 1889 and is the most common ocular presentation of Bartonella henselae infection, affecting about 5% of patients with cat scratch disease. Typical eye symptoms include foreign body sensation, unilateral redness, increased tear production, conjunctivitis and regional swelling of the preauricular, submandibular, or cervical lymph nodes.
Method: Case report
Results: A 10-year old girl presented in the emergency room with preauricular lymphadenitis on the left and an ipsilateral red eye with increased tear production starting 3 weeks ago. She did not remember being scratched by her two cats and had no fever. Her pediatrician prescribed fusidic acid gel without any effect. Her left eye was mildly injected with moderate subtarsal papillae and she had marked, painful left preauricular lymphadenitis. CRP (35.7 mg/l) and erythrocyte sedimentation rate (24 mm/h) were elevated. Indirect fluorescence assay (IFA) demonstrated IgG antibodies to Bartonella henselae at a titer of 1:254 which is diagnostic for cat-scratch disease. After starting antibiotic therapy with oral clarithromycin for 10 days, all the clinical symptoms resolved over the next 2 weeks.
Conclusion: Knowing Parinaud ocularglandular syndrome as an atypical presentation of Bartonella henselae infection, the diagnosis can be done straight forward with the help of IFA. Although cat-scratch disease is a self limited illness that resolves within 2 to 6 months, treatment with macrolides can shorten the duration of the illness.

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Primary presentation of an IL-7 receptor deficient SCID in a 4-months old girl

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Introduction: Infants with persistent infections and failure to thrive should be identified as early as possible by pediatricians to exclude primary immunodeficiency (PID). We review the clinical and laboratory features that identified a patient with severe combined immunodeficiency (SCID) caused by an Interleukin-7 receptor defect (IL-7R SCID).
Case report: The 4-months old daughter of consanguineous parents presented with failure to thrive (FTT), fever, cough and rhinitis for weeks and a history of one episode of acute otitis media. A partial respiratory insufficiency, fever, and an oral thrush were present. A chest x-ray showed peribronchial thickening. Laboratory parameters revealed a persisting lymphocytopenia, negative blood cultures and no viral agents in the nasopharyngeal secretions at that time. Serum immunoglobulines were low. Antibiotic therapy with amoxicillin/clavulan acid and clarythromycin did not influence the clinical course. A bronchoalveolar lavage (BAL) grew E. coli and candida albicans in culture. HIV testing was negative. The patient got subsequently stabilized on a therapy with meropenem, amphotericin B, Trimethoprim-Sulfamethoxazol**.** Lymphocyte subtyping identified a SCID with missing T-cells, but existing B and NK cells (T-B+NK+). IL-7R deficiency was proven molecular genetically (OMIM #608971). The child was referred to the University Hospital Zürich for allogeneic hematopoietic stem cell transplantation (HSCT), and is currently doing well 90 days after stem cell transplantation. The viral cultures/PCR before HSCT showed a chronic H1N1 virus infection which was not detectable in conventional culture media.
Conclusion and summary: Early lymphocyte subtyping in lymphocytopenia and suspected ID is essential. Consanguinity augments the risk of an autosomal recessive (AR) defect. Patients with the AR IL-7R SCID display a T-B+NK+SCID with low immunoglobulines and present in early infancy with FTT, candidiasis, chronic diarrhea, Pneumocystis jiroveci pneumonia (PJP) and severe viral infections, and sometimes with an Omenn-syndrome phenotype. The condition affects 1–10% of the 1/50000–1/100000 newborns with SCID. Life vaccines should be avoided, blood products have to be irradiated and intravenous immunoglobulin/PJP prophylaxis should be started. Allogeneic HSCT is the only available cure of the otherwise fatal condition.

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Regeneration of a functional thymus from adult murine thymic epithelial cells

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Introduction: The thymus serves as the primary lymphoid organ for the physiological development of T cells and hence is critical for the successful establishment and maintenance of the adaptive immune system. Thymic epithelial cells (TEC) exert a critical role in selecting an individual's specific repertoire of T cell antigen receptors and thus establish the capacity to distinguish between vital "Self" and injurious "Non-Self". Thymus function may be congenitally absent, defective or prematurely compromised as a consequence of a number of infectious and malignant diseases and as a result of different treatments. Hence, possibilities to gain thymus function using regenerative medical techniques would be highly desirable. TEC isolated from adult mice, however, have failed so far to regenerate a functional thymic structure either *in vitro* or when transplanted *in vivo*.
Methods: Enriched TEC isolated from adult mice were propagated and manipulated in different 2D and 3D culture systems and their functional capacity was tested *in vitro* and *in vivo*.
Results: Seeded on a supportive scaffold substrate and grafted directly *in vivo*, freshly isolated TEC retain the potential to rebuild a functional thymic microenvironment able to attract blood-borne hematopoietic precursors and to support their survival, expansion, maturation and eventual selection to mature T cells. Upon prolonged *in vitro* culture, however, this capacity, together with TEC identity as defined by expression of TEC associated genes, is lost. Therefore, cultures were modified that now allow for retention of specific TEC gene products and endow these cells with the ability to self-reaggregate into thymic organoid-like structures, that mediate some aspects of T cell selection *in vitro*. Furthermore, these culture conditions are permissive for gene replacement therapies.
Conclusion: Isolated adult TEC retain their potential to re-organize a functional thymic micro-environment, but displaying this capacity after prolonged culture times critically depends on specific culture conditions. The ability to grow, expand and manipulate TEC *ex vivo* provides an essential condition for thymus regenerative medical efforts.

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

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Introduction: The thymus is the primary lymphoid organ responsible for the formation and maturation of functional T cells. These essential processes are effected by a stromal micro-environment that is mainly composed of cortical (cTEC) and medullary thymic epithelial cells (mTEC). Together, these cells excert distinct functions relevant for T cell development. This includes the attraction of T cell precursors, and the subsequent maturation, selection and export of functional T cells, that are tolerant to self-peptides but reactive to foreign antigens. The evolutionary conserved protein mammalian target of rapamycin (mTOR) is a central controller of cellular proliferation and growth. Its activity is inhibited by Rapamycin, an immunosuppressant drug broadly used in clinical transplantation to inhibit T cell activation.
Methods: We investigated the function of mTOR in TEC. For this purpose, we generated mice that specifically lack mTOR activity secondary to the TEC targeted absence of the mTOR specific regulator Raptor, which is essential for mTOR1's catalytic activity.
Results: The targeted loss of Raptor expression in TECs results in a significant reduction of thymic cellularity and an increased fibrotic remodeling of the organ.These effects are concurrent with substantial alterations in the epithelial composition of the thymus. The qualitative TEC changes are characterised by the expression of distinct surface markers, a reduced cell size and an increased degree of autophagic activity. Inhibition of the mTOR pathway further impairs TEC cell cycle activity causing a reduced TEC cellularity in postnatal but not fetal thymic epithelia. These quantitative changes affect mainly the mTEC compartment. Together, these changes correlate with a low T cell output that results in a substantial peripheral lymphopenia.
Conclusion: The targeted loss of mTOR activity in TEC not only disturbes TEC cell size, differentiation potential and cell proliferation but also negatively impacts on the generation and export of T cells. We have thus uncovered a new immunological effect of Rapamycin which is independent of its direct immunosuppressive role on T cells but has significant clinical implications.

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DEEP look into Thymic Epithelial Cell Transcriptome

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Introduction: Cortical thymic epithelial cells (cTEC) dictate positive thymus selection and hence the generation of a self-MHC restricted T cell antigen receptor (TCR) repertoire whereas the corresponding epithelia in the medulla (mTEC) enforce negative thymus selection and thus secure immunological tolerance to self-antigens. This unique mTEC function is dependent on the ability to express ectopically antigens which are typically only detected in specific tissues. The transcription of some of these tissue specific antigens (TSA) is dependent on the presence of a nuclear factor known as autoimmune regulator, Aire. Mutations of Aire are the molecular cause for Autoimmune Polyendocrinopathy Candidiasis Ectodermal Dystrophy (APCAED) syndrome. To gain further insight into TEC physiology, we analyzed the transcriptome of wild type and Aire-deficient TEC subpopulations.
Methods: Ultra high-throughput sequencing was used for the first time to quantify the gene expression profile of separate TEC subpopulations isolated from either wildtype or Aire deficient mice. Genome-scale data is analysed and compared using advanced bioinformatics.
Results and Conclusion: The comparative transcriptome analysis revealed significant differences in the gene expression pattern of TSA, cytokines, transcription factors, peptidase, and signaling molecules for each TEC subpopulation. This distinction correlates with spatially distinct functional properties and allows the definition of developmental hierarchies. Moreover, this approach has allowed the genome-scale enumeration of genes whose expression is Aire-dependent. The information gained is invaluable in deciphering the mechanism by which the thymus induces and maintains central immunological tolerance.

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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 including the ability of these cells to attract lymphoid precursors. The loss of Foxn1 expression constitutes the molecular cause of a congenital disorder observed in humans and mice that is characterised by athymia and alopecia. The aim of this study is to define the temporal and quantitative requirements of the transcription factor Foxn1 for development and maintenance of a normal thymus.
Methods: Two different gene targeting approaches were chosen to create (a) mice in which the Foxn1 DNA binding domain is deleted once the thymus anlage has normally formed; and (b) mice expressing a hypomorphic Foxn1 allele resulting in a reduction of Foxn1 expression. The former model will investigate the consequences of a loss of Foxn1 expression after thymus organogenesis has been initiated (embryonic day 12) but not yet completed whereas the latter tests a gene dosage effect.
Results: The thymus was significantly reduced in size, the regular microarchitecture was lost and cysts had formed in both experimental models in comparison to wild type mice. With time, adipose tissue prematurely disrupted the lymphoid organ. In parallel to these significant microenvironmental changes, fewer T cell precursors homed to the thymus and their further differentiation was altered with an increase in immature $CD4^{-}CD8^{-}$ and a decrease in the $CD4^{+}CD8^{+}$ thymocytes. As a consequence, T cells are scarce in the periphery, albeit partially functional.
Conclusion: TEC differentiation and maintenance depend on continuous and adequate Foxn1 expression. Transient expression or low level expression of this unique transcription factor do not suffice to sustain regular thymus development and normal function. Once a thymus anlage has formed, both homing of T cells precursors and their maturation to T cells occur inefficiently in the absence of physiological Foxn1 concentrations.

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The role of Dicer-dependent miRNA in thymus development and function

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Introduction: Thymic T cell development requires a specialized microenvironment that is largely composed of cortical and medullary thymic epithelial cells (TECs). The molecular programs that control TEC differentiation and function remain, however, for the most part elusive. Because micro RNAs (miRNAs) have been implicated to play a role in the processes of cellular self-renewal and differentiation, we investigated their importance for TEC development and function.
Methods: We generated mice that are deficient in expressing in TEC the enzyme Dicer which processes the mature form of miRNA. As a consequence, these mice lack miRNA only in TEC.
Results: Severe morphological changes of the thymic microenvironment became apparent as early as 10 days of age, and resulted in a gradual decrease in the absolute number of both thymic T lymphoid and stromal cells. The alterations of the epithelial compartment first involved the thymic medulla but later also affected the cortex. Early functional consequences of a miRNA-deficiency in TECs related to altered intrathymic T cell differentiation including a reduction in positive thymocyte selection. With progressive age of these mutant mice, all stages of T cell maturation were affected and the microenvironment eventually ceased to support its thymopoietic activity in lieu of in-situ B cell maturation. Moreover, medullary epithelia were compromised in their capacity to express peripheral tissue antigens (PTA). As a consequence of an altered central tolerance induction, organ specific autoimmunity ensued revealing a pattern of tissue infiltrations linking specific defects in PTA expression to defined tissue pathologies.
Conclusion: Dicer-deficiency in TEC causes severe changes in the thymic microenvironment underscoring the importance of miRNA in TEC maintenance and function.

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The consequences of *in vivo* ablation of Aire-expressing medullary thymic epithelial cells

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Mature medullary thymic epithelial cells have been implicated in central immunological tolerance as they express a large number of tissue-specific antigens (TSA). Though typically produced by mature (i.e. MHC class II^{high}) medullary thymic epithelial cells (mTEC), some but not all TSA require the expression of the autoimmune regulator (Aire) for their transcription. To investigate the role of $Aire^{+}$ mTEC in expression of Aire-independent TSA, we specifically ablated these cells in mice by cell-targeted expression of diphteria toxin A (DTA) and compared these animals to mice deficient only in Aire expression. The constitutive absence of $Aire^{+}$ mTEC caused not only a smaller thymus medullary compartment that was focally replaced by fibroblasts but also concurrently resulted in a decrease in mTEC with an immature (i.e. MHC class II^{low}) phenotype. The ablation of Aire-expressing mTEC provoked defects in thymocyte maturation and in the expansion of regulatory T cells with specific TCR. These changes in the cellular composition and function of the medullary compartment correlated with serum autoantibodies and mononuclear infiltrations in different organs including thyroid, parathyroid, and the liver. A third of mutant mice became spontaneously sick as early as 6 weeks of age whereas none of the mice deficient in Aire-expression showed any signs of autoimmunity at this stage of life. Taken together, mature mTEC play an essential role in shaping the overall cellular composition of thymus medulla and exert a dominant effect on central tolerance induction that extends beyond the effect of promiscuous gene expression controlled by Aire.

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Collaboration between the "Centre Médico-Chirurgical Pédiatrique PERSIS" (CMCPP), Ouahigouya, Burkina Faso and the Departments of Pediatrics of the CHCVs and CHC, Switzerland

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Introduction: The "Centre Médico-Chirurgical Pédiatrique Persis" (CMCPP) in Ouahigouya/Burkina Faso is a private medical center for social purposes. Created in 2004 by a local pediatrician, Dr Zala, in collaboration with several european partners, its aim is to provide a high quality modern medicine as well as to prevent infant malnutrition by instructing mothers on feeding and hygiene, and thus to reduce general infant and child mortality.
Presentation: The collaboration between Dr Zala at the CMCPP and the "Centre Hospitalier du Centre du Valais" (CHCVs) and the "Centre Hospitalier du Chablais" (CHC) as well as other european partners has permitted to build a high quality hospital, composed of the following sectors: Ambulatory consultation, Emergency room and nursing ward, Hospitalisation rooms (13) with 2200 patients hospitalised annually, Nutrition and education center, Surgical ward with 250 operations annually, Radiology (ultrasonic and x-ray devices), Laboratory, and Pharmacy. Furthermore an exchange program permits interns of the Departments of Pediatrics of HV as well as medical students of the universities of Geneva and Lausanne and nurse students to get initiated in medical practice in an african country. In addition to their medical activities, they conduct a clinical study during their stay. Moreover training is offered to the local staff to improve their medical skills.
Discussion: The collaboration between CMCPP and CHCVs+CHC enables a high quality and modern medicine in Ouahigouya, Burkina Faso. In addition to financing medical structures and devices, it permits a productive cooperation between the burkinabé staff and swiss physicians and students. Actual projects include the setting up of a dentistry and the search for more surgical teams interested in missions at the CMCPP. Further goals should be to develop the exchange program between swiss and burkinabé physicians, to promote mutual teaching of physicians, students and nurses, to conduct small clinical studies aiming at the improvement of diagnosis and treatments at the CMCPP, as well as to develop further diagnostic possibilities (such as biopsies, blood cultures) to optimize treatment.
Conclusion: The collaboration between the CMCPP and CHCVs+CHC has already achieved many goals, and should be further developed.

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Paediatric Partnership Program Zurich – Yerevan (Armenia)

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Introduction: An acute relief operation (haemodialysis for the crush syndrome) after the earthquake in Armenia in Dec. 1988 initiated a long-term training and support program with the "Arabkir" paediatric hospital in Yerevan. – Armenia is a small country in transition and independent since 1991. As all post-Soviet countries it had an excess of hospitals and of physicians who are poorly trained. Hence, education has top priority. In 2007 it has become an official partnership program of the Kinderspital Zurich.
Methods: Education is done by training courses and bed side teaching in Yerevan and by special training of selected Armenian medical residents in Zurich. Up-to-date diagnostic methods are introduced and support for basic medical equipment is given. Funding is by charities (notably by Verein Armenienhilfe Direkt (VAD) until 2008) and by the Canton of Zurich (Lotteriefonds). Costs for the last 4 years were CHF 480'000: One third was spent for education, 2/3 for material/equipment and <3% for administration. Donations in kind amounted to CHF 280'000. No salaries are paid by the program.
Results: The program started with building up nephrology and related fields (radiology, infectious diseases, psycho-social and educational care) and shipping of material (mainly before 1995). Since 2004 the program has been strongly enlarged to include most paediatric disciplines. Professional skills have much improved as well as the ability to work in a team to allow comprehensive paediatric care. Motivation is stimulated by active participation at studies and publications (so far 25). Neonatal screening for congenital hypothyroidism was introduced in 2005 (so far 45 patients diagnosed) and for PKU in 2008. During 2008–2011 we had 68 teaching visits (average 10 days) in Yerevan, and 22 mostly young paediatricians came for further training to Zurich (average 1 month). Our partner hospital has meanwhile become the reference centre for paediatrics in Armenia and is at the same time a leading hospital for paediatric and adult nephrology in the Southern Caucasus.
Conclusions: Building up paediatrics in a post-Soviet country in transition and with limited resources is a particular challenge, but professionally, culturally and personally rewarding. Long-term commitment and stable partners are essential.
SGP Luzern, 31.5.-1.6.2012

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Copying medical letters to the patient and their families: a prospective satisfaction study

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Background: Trusted information exchange between the patient and his physician is important, and might increase patient's understanding of his disease and compliance. In a prospective study, we analyzed the reception and perceived usefulness of patients and their families visiting a pediatric renal outpatient clinic towards receiving copies of the medical letters addressed to their primary care doctors.
Methods: Prospective non randomized written questionnaire, regarding the transmission of the letter addressed to their primary care doctor. Anonymized questionnaires were sent to parents after consultation in pediatric nephrology clinic. Patients were aged 0 to 18 years, and classified according to the severity of their renal disease, and the presence or not of a renal genetic disorder.
Results: There were 86 and 64 valid questionnaires returned from patients and physicians, respectively. All families were completely or very satisfied with the procedure, and all thought this was a good idea, regardless of the severity of the disease of their child or the presence or not of a genetic renal disease. Receiving a copy of the letter did not induce anxiety, but improved in 50% of the cases the understanding of the disease, its treatment and/or prognosis. Only 25% wished to receive a better "adapted" letter. Regarding access to the internet after receiving the letter, only 30% of families did so, searching mainly diagnosis, treatment and/or alternative treatment information. Most of the families wished to receive a copy of the letter after the initial visit and then only when major changes occurred. Concerning the physicians' responses, 20% and 45% thought copying a letter would not increase patient's satisfaction or compliance, respectively. Thirteen percent of physicians did not agree at all with sending a copy of the letter, and only 65% were completely or very satisfied with the procedure.
Discussion: Copying the medical letter to the patient or their family was felt to increase disease comprehension and patient's global satisfaction by all families. On the other hand, physicians were more sceptical with the procedure. We propose that every new patient/family seeing a specialist should be asked about his/her preferences regarding the provision of such information, and how often they want it to be delivered. The strong discrepancies between the families' and physicians' evaluation regarding this procedure need to be explored.
NB: this work has been previously partly presented at the ESPACOMP meeting in Utrecht in November 2011

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Symptomatic management of fever by Swiss pediatricians: Results from a cross-sectional survey

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Introduction: Symptomatic management is often all that is recommended in children with fever. The aim of this study was to describe the management of children with fever by Swiss pediatricians.
Methods: A close-ended questionnaire was pilot-tested and subsequently corrected. The questionnaire was sent to the exactly 900 members (72% of the Swiss board-certified Pediatricians) of the regional societies of Pediatrics from 13 Swiss cantons (82% of the Swiss population). The survey was not commercially sponsored.
Results: 322 Pediatricians (36%) answered the questionnaire. Ninety-six percent of respondents identified ≥38.5 °C as the rectal temperature threshold for fever treatment, 64% indicated that they prescribe antipyretics for the treatment of general discomfort. A total of 95% of respondents prescribe paracetamol as the first choice antipyretic, and 91% often prescribe ibuprofen as well. An alternating regimen of 2 drugs and physical antipyresis were indicated as common practice by 77% and 65% of pediatricians, respectively. The most commonly prescribed routes of administration in children aged 18 months, 5 years, and 10 years were rectal (78%), oral (87%), and oral (99%), respectively. Ninety-two percent of respondents believe that fever phobia is common among parents, but 81% are not usual to lower the temperature threshold for initiating symptomatic treatment exclusively to calm parents. Most respondents (95%) believe that it is possible to educate families about the fear of fever.

Conclusions: The findings of the present survey indicate that, following the current guidelines, antipyretics are often prescribed to treat the general discomfort that accompanies fever. Nevertheless, a gap still exists between available evidence and clinical practice. Guidelines should take this fact into account.

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Pediatric dosage booklet: from a crude text file to a sophisticated smartphone application

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Introduction: Drug doses for children seem to challenge pediatricians daily. In many cases no regulatory approved dosage is available since drugs are prescribed in an "off-label" or "unlicensed" status. Therefore, professionals rely on dosages summarized by specialists. In 2009 the University Children's Hospital Zurich published a booklet containing regulatory approved as well as not approved but evidence or at least eminence based pediatric dosages in a highly structured version.
Methods: In spring 2011 we conducted a survey on our booklet. The electronic questionnaire was sent to 660 users and included questions about quality (layout, completeness of the drug list, possible errors and usefulness of the remarks). Further, the users were asked if they would appreciate our dosage booklet to be available in an electronic form over the internet and/or as a mobile application (for smartphones or tablet computers). In addition, the survey included some questions about a possible harmonisation of paediatric dosages through Switzerland.
Results: The answers of 165 participants (turnout: 25%) showed that the quality is very satisfying and that the users would appreciate our dosage booklet to be available in an electronic form over the internet and as application for mobile devices. In addition to that, the survey showed that the harmonization of pediatric dosages among Swiss children's hospitals seems to be of concern.
Conclusion: To meet the requirements of our users, we are working on the availability of our dosage booklet over the internet and for use with mobile devices. It is our goal to provide a tool that can be used in sophisticated applications such as the automatic dose calculation. And at the same time it seems very important to us that efforts are made towards a national harmonization of pediatric dosages.

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Unlicensed and off-label drug prescription at discharge from a Swiss children's hospital

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Introduction: For children, many drugs are used without marketing authorization ("unlicensed", e.g. imported drugs, drugs prepared by a pharmacy) or outside the terms of marketing authorization ("off-label")[1]. The aim of this study was to determine the proportion of unlicensed and off-label prescriptions, which has not been investigated previously, at discharge and the proportion of parents informed about such a prescription.
Methods: Prospective study including all discharge prescriptions of inpatients over a two-month period at the Children's Hospital of Aarau. Exclusion criteria: hospitalization for chemotherapy only, age over 18, re-entry during study period, no informed consent of parents. At discharge parents were asked using a questionary about the information they got on discharge medication as well as about their satisfaction with this information.
Results: During the study period 503 children where discharged, 231 children could be included. For 140 children (61%) discharge prescriptions were written. A total of 227 drugs were prescribed, especially antiphlogistic, antiasthmatic and antiinfective drugs. 38.5% of all prescriptions were off-label: 51% of these were off-label because of dosage, 40% because of age, 9% because of indication. Only 0.5% of drugs were unlicensed. Discharge questionaries were returned by 103 of 140 children. Most parents (>80%) were informed about purpose, dosage and use of the drugs for their child, and satisfied with obtained information, but only 9% of parents getting an off-label / unlicensed prescription for their child were informed about the off-label / unlicensed use.
Conclusion: There is a high percentage of drugs prescribed off-label at hospital discharge. Most drugs are well known substances and regularly prescribed for children. This emphasizes the need for an update of marketing information of older substances, or the need of a national database for drug use and dosage in children.
1) Paolo, E et al, 2006. Swiss. Med. WKLY. 136, 218–22.

P 127

Pediatric pre-hospital care in an urban setting: a 4 year review

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Introduction: In Switzerland, pediatric prehospital care is mostly assumed by paramedics only. In Geneva, a trained medical pediatric team is available for these transports, either for children less than 5 years old or when the Emergency Medical Dispatcher (144) identifies any criteria of vital threat in any patient less than 16 years old. These cases benefit from rapid on-site medical evaluation, and initiation of the appropriate treatment. Few data concerning pediatric advanced life support (PALS) transports exists in Switzerland. Our goal was to describe the pediatric population using Emergency Medical Dispatch Center in our single urban setting, in order to better define dispatch criteria.
Method: Descriptive retrospective study. Data provided by the Emergency Dispatch Center 144 concerning age, daytime, major medical diagnosis and procedures, NACA scores, and 48 hours follow-up were reviewed and analyzed from 01.01.2008 to 31.12.2011.
Results: In Geneva, 1794 pediatric patients received ALS transport over 4 years. From these, 39.6% were less than 2 and 65.7% less than 5 years old. NACA scores showed a majority of non severe cases (NACA2: 28.6%, NACA3: 42%, NACA4: 13.9%, NACA5 and 6: 3.9%). The majority of transports were performed at daytime. 33.3% were related to medical complaints, 66.0% to injuries, burns or intoxications, and 0.67% to home births. Main medical diagnostic categories were convulsions (21.7%), respiratory troubles (19.1%), traumatic injuries except head trauma (11.8%) and head trauma (11.4%). Only 0.8% involved cardiac arrests (including SIDS). Among procedures, bag-mask ventilation alone was performed in 1.0%, intubation in 1.9%, IV cannulation in 17.7%, and intraosseous access in 0.5% of patients. Medications were required in 24% of transported patients and involved mostly: paracetamol (28%), bronchodilators (18%), fentanyl (17%), benzodiazepines (15%) and nebulized epinephrine (5%) administration.
Conclusion: Emergency Medical Dispatch for pediatric prehospital transport data show a majority of non severe cases requiring few life-savings procedures. The dispatch protocol should be revised in order to better define the indications to have the pediatrician on-site for non severe cases.

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Inter-hospital transportation of life threatening paediatric emergencies: a six year review in Lausanne

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Objective: Assess inter-hospital transportation of paediatric life threatening emergencies in Lausanne compared to places using specialized dedicated teams.
Methods: Retrospective analysis of data collected by the pre-hospital transportation and paediatric resuscitation quality control teams between May 2005 and June 2011 regarding each patient transferred to the resuscitation room of the University Hospital of Lausanne (CHUV) from another institution.
Results: 302 patients up to 16 years of age (median age: 3.6 [1.2; 9.0] years) were identified, including 172 boys (57%). Helicopter was used in 165 patients, ambulance with medical supervision in 120 and ambulance without medical supervision in 14. The median transportation time was 11 [7; 15] minutes. The activation of the resuscitation team was justified in 239 situations (79.1%). Adverse events were recorded in 61 cases (20.2%), and were mostly respiratory issues (50.8%). These critical incidents were noted in significantly younger patients, who had a higher NACA score. They also had a higher length of stay in the resuscitation room, in the Intensive Care Unit and in hospital.
Conclusions: The incidence of adverse events was lower compared to the literature (56.9 to 61% for non-specialised paediatric transport team and 4 to 41.1% for specialised teams). In our setting, a specialised paediatric transport team is not required, especially with regards to our relatively short transportation time.

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Measures to increase the security of medical care for pediatric patients in the county of Vaud

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Introduction: Around 80'000 pediatric patients are seen every year in the 7 pediatric emergency departments (PED) of the canton of Vaud. Due to historical reasons each centre is structured and organised

differently, resulting in different standard of care. This prompted the public health department to assess the necessity of unifying processes by implementing measures to increase the security of pediatric emergency care.
Methods: In 2010 all 7 PED were evaluated. Focus was laid on the security of structural and organisational processes.
Results: Six measures were identified and are being implemented: – In 2011 a triage course was given to all nurses caring for pediatric patients in emergency departments. The Australia triage system is being implemented in all hospitals. – A course on pediatric emergency care is being defined and should be given in 2012 to all nurses caring for pediatric patients in emergency departments. – Some hospitals received funds to increase their nursing staff, resulting in a higher quality and security of care around the clock. – All parental telephone calls are diverted to a centralized telephone counselling organization (CTMG), thus relieving nurses and doctors in hospitals of telephone counselling while attending emergency patients. – A common pedagogic concept is being implemented in all hospitals to ensure a structured education for all pediatric residents. – All transfers of pediatric patients in need of critical care from peripheral hospitals to the university hospital are accepted and dealt with rapidly, thanks to an increase in physician and nursing staff as well as organisational changes in the university hospital.
Conclusion: During the last year the canton of Vaud has implemented six measures aiming to increase the security of medical care given to all pediatric patients.

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Patient flow in two paediatric emergency units in the French speaking part of Switzerland: an observational study

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Introduction: Most paediatric emergency units experience a constant workload increase. Consequently, patients waiting time and risks of inappropriate triage as well as parental dissatisfaction may rise. Review of the literature reveals various studies, mainly North American, on very specific paediatric emergencies topics. To our knowledge, organisational aspects have not been reported however. To improve, and then share, our knowledge of patients flow, organisational and financial aspects of Swiss paediatric emergency units, we embarked in a prospective study to accurately describe our units.
Methods: In two paediatric emergency units, Hôpital Neuchâtelois Pourtalès (HNE, patients age 0–16 years) and Hôpital de l'Enfance (HEL, patients age 0–18 years), Lausanne, Switzerland, from April 1, 2011 to February 29, 2012, various indicators of patient flow and severity score (Australasian triage scale, ATS) as well as cost accounting have been prospectively recorded, statistically described and compared. Preliminary (April 1 to November 30, 2011) results are shown below.
Results: (HNE/*HEL* respectively): There were 5161/*20274* recorded visits. Severity scores were: ATS 1 12/*22* (0.2/*0.1%* of total), ATS 2 176/*537* (3.4/*2.6%*), ATS 3 767/*2387* (14.9/*11.8%*), ATS 4 1593/*2943* (30.9/*14.5%*), ATS 5 2613/*14385* (50.6/*71%*). Age distribution: <1 y 15/*12%*, <6 y 60/*55%*, <12 y 86/83%. Mean waiting time between admission and medical evaluation were 4/*5* min for ATS 1, 14/*14* min for ATS 2, 33/*27* min for ATS 3, 47/*55* min for ATS 4, 48/*68* min for ATS 5. Mean time spent in the units ranged between 1h29 and 2h29.
Conclusions: The majority of patients were young children. Mean waiting times were within ATS guidelines, patients safety being thus guaranteed. Further data (including cost analysis) will be shown.

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The new Interdisciplinary Emergency Department – one year's experience in the University Children's Hospital Basel

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The University Children's Hospital Basel (UKBB) is in a unique position in comparison with other Paediatric hospitals within Switzerland, having moved from 2 locations to one highly modern site at the end of January 2011. It is now one year since the move and merge of these two locations. The relocation has led to various changes, not least within our Emergency Department which is now, according to patient numbers, one of the leading Swiss paediatric emergency departments with a large increase over the last years (29'370 patients in 2011, a 19% increase since 2010 (24'555) or a 48% increase since 2004 (19'782)). Out of these, 12% of patients required hospitalisation. Next to looking at the range of patient presentations (16'409 paediatric (60%) and 10'957 surgical (40%) since the relocation, 121 patients in the resuscitation area in 1 year, 12% hospitalisations), we provide an overview and reasoning for the developments and changes which include the introduction of an interdisciplinary team and highly qualified "fast track" medicine (separate treatment of patients with acute but non-life-threatening conditions) with practice-paediatricians (5339 patients in 2011) as well as an observation ward within our emergency department.
Conclusion: the UKBB has seen a huge increase in emergency patients in the last years. Possible explanations for this rise in numbers are increasing demands for high quality care at inopportune times, the new central location, and not least the impact of our practice-paediatricians working within the Emergency Department at peak times.

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The potential impact of an additional ambulatory care centre at a Swiss University Children's Hospital

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Introduction: Many paediatric emergency departments (PEDs) are registering increasing numbers of patients. In 2010 30,807 children and adolescents were seen at the PED of the University Children's Hospital, Zurich, representing an increase in patient volume of 34% over 5 years. To improve the infrastructure of care provision at weekends and on holidays, care provision at an additional ambulatory care centre (ACC) located on the premises was piloted from Jan 9th, 2010. The aim of this study was to evaluate whether the ACC succeeded in reducing waiting times and patient throughput at the PED during the pilot phase. In addition sociodemographic factors, timing of and reason for consultation as well as triage category were evaluated.
Methods: Retrospective analysis of all patients attending the ACC in 2010 and comparison of the characteristics of this group with those of patients attending the PED in 2009.
Results: In 2010 30,807 children attended the PED. 39.7% of these visited the department on weekends and holidays. 2954 patients were given an appointment at the ACC. On weekends the ACC processed approximately a quarter of the total patient throughput. 26% of these patients were referred by the local on-call phone hotline. 97% and 50% of patients were from canton Zurich and the city of Zurich, respectively. The most common reason for attendance were symptoms typically seen in an office paediatrics setting such as respiratory tract infections, acute otitis and gastrointestinal symptoms. 73.4% of ACC patients were triaged as category 4 (non-urgent, to be seen within 60 minutes, Australasian Triage Score). Patients with triage category 3 to 5 on average waited 44 minutes in 2010. In 2009 the average waiting time was 49 minutes. For patients seen in the ACC the average waiting time was only 33 minutes, more than 56% of patients were seen by a physician within 30 minutes.
Conclusion: In 2010 2684 additional patients visited the PED compared with 2009. The ACC saw 2954 patients in total. The waiting times for patients with triage categories 3 to 5 were lower in 2010 compared to 2009 and patients seen in the ACC waited for even shorter periods. All in all, resources were more efficiently allocated according to clinical urgency and need. However, due to the continuing increases in patient volume additional strategies may be necessary to further optimise care provision in the PED.

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Preparedness and anxiety regarding critical clinical events among staff members of a Swiss Children's Hospital

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Children's Hospital Lucerne

Objectives: Optimal management of critical clinical events requires knowledge, technical skills and multidisciplinary collaboration and teamwork. Our objective was to determine self-evaluated preparedness, comfort and anxiety regarding performance in a possible future critical event among staff members at the Children's Hospital Lucerne.
Methods: Multidisciplinary, cross-sectional survey of staff members at the Children's Hospital Lucerne. Classification of answers regarding preparedness (P), knowledge (K) and anxiety (A) with a 5-point Likert scale: 1 = very low P/K and very high A, 2 = low P/K and high A, 3 = satisfying P/K and moderate A, 4 = good P/K and low A, 5 = very good A/P and no A.
Results: 121 staff members participated in the survey. 39/121 (32%) were physicians (paediatricians including subspecialists and paediatric surgeons of all level of expertise), 82/121 (68%) nurses (all level of expertise). 98% (118/121) of all participants felt adequately trained (score ≥3) to recognize early a critical deterioration of a child, 79% (95/121) responded to have a good or very good competence in this

area (score ≥4). 69% (84/121) reported to be satisfying prepared to participate in the management of a critical clinical event (score ≥3), whereas 19% (23/121) of all respondents and only 10% of physicians (4/39) considered their preparedness as good (score ≥4). Looking at the competence of their current team to manage a critical event assessments of satisfying (score ≥3 in 78%; 69/110) and good preparedness (score ≥4 in 34%; 41/110) were slightly higher. A substantial number of respondents (24%; 27/119) didn't know what their role would be in such an event (score <3). 29% (35/119) of all participants have a good knowledge of their expected role (score ≥4). Nurses evaluated their competence in all categories higher than physicians. 36% (43/121) reported to have a high or very high level of anxiety (score <3). Only 14% (17/121) of all respondents and 10% of physicians (4/39) felt a low level of anxiety regarding attendance in a future critical event (score ≥4).
Conclusions: A substantial number of staff members at the Children's Hospital Lucerne felt inadequately trained regarding management of possible critical clinical events. This raises sufficient concern to launch a new multidisciplinary training programme (iSTaRT: interdisciplinary Simulated Team and Resuscitation Training).

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Needs assessment of training regarding management of critical clinical events among staff members of a Swiss Children's Hospital

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Objectives: A substantial number of staff members at the Children's Hospital Lucerne felt inadequately trained regarding management of possible critical clinical events. Our objective was to evaluate the perceived needs of training to improve performance and to diminish the level of anxiety for such an event.
Methods: Multidisciplinary**,** cross-sectional survey of staff members at the Children's Hospital Lucerne. Topics reported by more than 50% of participants were assessed as important, if chosen by more than 66% as urgent.
Results: 124 staff members participated in the survey. 32/124 (26%) were physicians (paediatricians including subspecialists and paediatric surgeons of all level of expertise), 92/124 (74%) nurses (all level of expertise). In the area of knowledge and technical skills more than 50% of the respondents reported educational needs in the following topics: Airway management (65%; 81/124), bag and mask ventilation (56%; 69/124), cardiac massage (54%; 67/124) and defibrillation (56%; 70/124). 81% (101/124) requested teaching regarding emergency medication. Regarding specific clinical situations there were respiratory problems (58%; 72/124), respiratory collapse (65%; 81/124), cardiac arrest (61%; 76/124), shock (62%; 77/124) and multiple trauma (53%; 66/124) reported to be important teaching topics. Assessed as urgent training requirement regarding management of critical clinical events was the topic team organisation in the emergency situation (68%; 84/124). Other training aspects considered as important regarding management of critical events were emergency algorithms (62%; 77/124), crisis resource management (CRM) principles (59%; 73/124) and equipment in the emergency department (56%; 69/124). Communication (66%; 82/124), role allocation / resource management (71%; 88/124) and error prevention (67%; 83/124) were reported as urgent training topics in crisis resource management.
Conclusions: Emergency medication, team organisation in the emergency situation and the CRM principles communication, role allocation / resource management and error prevention were perceived as urgent training requirements. This needs assessment helps to determine goals of our new multidisciplinary training programme iSTaRT (interdisciplinary Simulated Team and Resuscitation Training).

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Alcohol intoxication among adolescents: A five year experience of a postexposional brief intervention model

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Aims: Evaluation of a postexposional short intervention model for adolescents admitted for an acute alcohol intoxication at the paediatric emergency unit.
Methods: From january 2007 to december 2011 all patients seen for an alcohol intoxication at the emergency unit were followed by a control consultation within 10 days of their admission. The aim of a brief intervention was to give them information, to evaluate their risk behaviour and resources, thereby providing secondary prevention.
Results: Out of the 430 patients seen at the emergency unit, 356 (83%) were addressed for a follow up consultation. Among the other 74 patients almost 2/3 were admitted to the psychiatric department from the outset, and 1/3 lived outside of the canton of Geneva. Out of those convoked to the adolescent health clinic, 88% showed up for evaluation (12% refused), 2/3 were accompanied by one parent. The alcohol intoxication, mostly done with a mixture of vodka and Redbull, was judged to be accidental in more than ¾ of our population, and we didn't find any other major risk behaviour in this group. Nevertheless 20% of our group needed further treatment, the principal reasons being an alcohol problem in the family or a very complex family situation, school problems or questions concerning sexuality. Rehospitalisation was rare among this population and concerned less than 5%. During our interventions we observed that there is a lack of information especially concerning the somatic and psychosocial risk taken by the youngster, when consuming alcohol.
Conclusions: The high rate of participation to our programme is very encouraging and could be interpreted as a sign that adolescents and their family need a follow up consultation for discussion. It's also an opportunity for the adolescent to take up contact with a specialist early on. For the emergency unit this setting was evaluated as very useful, as it permits a more appropriate evaluation, outside of the emergency setting.

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Review of acute anogenital trauma in girls and boys (2005–2010)

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Background: Since 2005 the Childrens Hospital of Zuerich has an interdisciplinary emergency department (ED) and electronic chart documentation. The aim of this study was to define the injury patterns of acute anogenital trauma (AGT) in female and male patients.
Methods: 6 year chart review (2005–2010) of patients younger than 17 yrs with AGT (laceratios, abrasion, bruising) including sexual abuse (SA).
Results: 254 patients met the criteria of AGT. 159 (63%) were female, 95 (37%) were male. In **128** (80%) **girls** accidental straddle injury (soft tissues of the vulva are compressed against a hard surface) was the most frequent cause oft AGT: 63 (49%) through falls and climbing, 28 (22%) slipped out in bathroom or swimming pool. 26 (20%) fell down with the scooter or to a bicycle frame. Injuries to the labia were seen in 73 girls (46%), to the perineum in 17 (11%). 33 (25%) had hematoma, 34 (26%) abrasions, 84 (66%) lacerations. Only in 2 girls the hymen showed abrasions, detected by the gynaecologist. In 36(28%) girls the laceration needed surgical repair under anaesthesia. Acute anogenital injury due to SA was documented in 19 (12%) girls. In 12 (8%) girls the aetiology of AGT was unexplained. **80** (84%) **boys** had an accidental straddle injury: 25% (20) due to falls and climbing, 25 (31%) due to foot kicks. 12 (13%) fell down to a bicycle frame, 14 boys (18%) jammed the penis in a toilet-seat, 5 (6%) in a zip. AGT due to SA was documented in 4 (5%) boys. In 11 (11%) cases the aetiology was unexplained. 37% of all the patients presented to the ED within 12 hrs; 67% within 24 hrs. 80% were walk-in patients. The gynaecological service was consulted in 38% of straddle injury, in 58% oft unexplained AGT and in all cases of SA in girls. Description of genital anatomy and injuries by residents was often poor and lacking details.
Conclusion: Our data of AGT are consistent with the prospective study (n = 56) of Bond et al in Pediatrics 1995 and the retrospective study (n = 105) of Spitzer et al in Ped. Emerg. Care 2008: Accidental straddle injuries in girls involve primarily the labia and the perineum, rarely the hymen. The knowledge in female genital anatomy and examination technique (labial traction) should be improved, therefore we start a prospective study including teaching residents at the ED.

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Four days fever and diarrhoea in an adolescent: Kawasaki disease?

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Introduction: Kawasaki disease (KD) was diagnosed in an adolescent with febrile diarrhoea.
Case report: A 13-year-old boy, returning from a stay in South Italy, was hospitalised following a 4-days febrile watery diarrhoea, with abdominal pain, vomiting, fatigue, dehydration and rash. A high inflammatory reaction (CRP 254 mg/l) and platelets count (475G/l) were found. Six days later, despite antibiotics, intense fatigue and high fever persisted, with headache. Conjunctive and lips injection appeared, with "raspberry" tongue, suggesting a KD. Microbiology was negative, as were abdominal ultrasound, rheumatoid factor, antinuclear antibodies and ANCA. Treatment with intravenous polyvalent immunoglobulin and aspirin was followed by dramatic improvement and apyrexia within 24 hours. Fingers desquamation was then observed. Cardiac ultrasound showed tritruncular giant aneurysms (9mm), confirmed by a computerised tomography. No other vascular complication was found (cerebral and abdominal MRI). Treatment with

vitamin K antagonist was initiated and aspirin pursued at anti-thrombotic dose. Five months later, partial remodelling of the right coronary artery was observed.
Discussion: Atypical presentations of KD are often found in patients aged <6 months or >5 years (5–10% of all cases). Lacking specific criteria, the diagnostic delay often exceeds 7 days, which is the optimal limit for treatment. Differential diagnosis includes infectious or inflammatory states (Still disease, vasculitis,...). Corticotherapy may be discussed. Cardiac involvement, including giant aneurysms (>8 mm) is more frequent and severe. They could improve, with arterial remodelling. Other medium-size vessels must be controlled. Long-term use of anti-coagulant agents is warranted. Enteritis, and precocious giant tritruncular coronary aneurysms, as in our case report, were rarely described.
Conclusion: KD may be clinically atypical and incomplete. A therapeutic test should be considered as soon as possible (<7th day) to prevent coronary damage. Giant coronary aneurysms are a rare serious complication with uncertain evolution. Other arteries must be checked.

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Kawaski disease in adolescents

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Introduction: Kawasaki disease (KD) is a systemic vasculitis affecting predominantly young children, younger than 8 years. It can be responsible for coronary artery abnormalities such as dilatation and/or aneurysms. It is thus the leading cause of acquired heart disease in childhood. Older children and adolescents have a higher risk of developing coronary artery abnormalities. Diagnosis in older children or adolescents can be difficult because clinical presentation may be incomplete or atypical leading to delay in diagnosis and treatment.
Methods: Retrospective review of all cases of Kawasaki disease referred to our pediatric cardiology outpatient clinic over a one-year period. Patients over 8 years old were identified. Patient charts, ECG and echocardiography studies were reviewed.
Results: From January 1st to December 31st 2011, 16 patients presented with Kawasaki disease. Medianage at presentation was 2 years old (range 0.5–15). Three patients (2%) were older than 8 years old, (12, 13 and 15 years old respectively). All three patients presented with 5 or more days of fever, had bilateral conjunctival injection and oral mucosal changes. One patient presented with a rash, one with extremity changes and one with cervical lymph nodes. Therefore, all patients fulfilled clinical criteria of a complete KD. However, additional symptoms were frequent (arthralgia, respiratory and gastrointestinal symptoms) which lead to additional investigations. The mean time to diagnosis and treatment was 7 days (range 5–11). All three patients presented with coronary involvement, of which one patient presented with giant aneurysms affecting all three coronary arteries. They received high dose immunoglobulins and aspirin, with rapid resolution of fever. Follow up after 6 months confirmed complete regression of coronary artery abnormalities in all but one patient in whom a giant aneurysm persists on the circumflex artery.
Conclusion: Kawasaki disease is rare in the older child or adolescent. However, these patients are at higher risk of developing CAA. Diagnosis is often delayed due to prominent symptoms that are less frequently encountered in KD which can be misleading. KD should be excluded in any older child or adolescent presenting with persistent fever for more than 5 days.

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Acute intravascular hemolysis after high-dose intravenous immunoglobulin treatment in a 7-year-old children with Kawasaki disease

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Introduction: Intravenous immunoglobulin (IVIg) is the main treatment for Kawasaki disease. A rare adverse effect is IVIg-induced hemolysis, one of the possible mechanisms being the presence of anti-A and anti-B hemagglutinins in IVIg preparations. Some risk factors have been identified, i.e. high dose of IVIg, non-O blood group.
Case Summary: A 7-year-old male weighting 42.5 kg (BMI 25 kg/m^2) presented with continuous high fever for the last 5 days, unilateral lymphadenopathy, non purulent conjunctivitis, and cheilitis. Relevant laboratory data were: leucocytes 31.9 G/L, thrombocytes 771 G/L, sedimentation rate 170 mm/h. We diagnosed a Kawasaki disease and treated the patient with lysine acetylsalicylate and IVIg at 2 g/kg (Privigen®) that was repeated after 36h due to fever persistence. Less than 24h after this second infusion, the patient presented hematoglobinuria. His hemoglobin dropped from 130 g/L to 66 g/L. A G-6-PDH deficiency was excluded. After 72h of observation, he was discharged from the hospital with close hemoglobin controls.
Conclusion: IVIg most probably induced the observed hemolysis, as other medical causes were excluded. The cumulative prescribed dose was high (160 g), but followed Kawasaki's treatment guidelines. This raises the question if the dose should be adapted in case of obesity. The manufacturer of Privigen® doesn't specify such an adaptation, whereas some clinicians do in adults. The B blood group of the patient could have played a role in the event. Regarding Privigen® the anti-A and anti-B hemagglutinins titers are undetectable at 1:64 dilution, thus being conform to the European Pharmacopea's specification. Due to the severity of this adverse event, regular hemoglobin control should be recommended as routine management of patients treated with IVIg. Trials are still needed to elucidate the potential dose adjustment in obese children.

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Intravenous immunoglobulin treatment despite anaphylactic reaction in a child with Kawasaki disease

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Introduction: Early treatment with intravenous immunoglobulins (IVIG) reduces the risk of coronary artery aneurysm in children with Kawasaki disease (KD). However, although anaphylactic reactions to IVIG are not rare, there is no consensus about whether to continue or not the IVIG treatment in patients with KD who develop side effects from IVIG.
Case report: A previously healthy five-year-old boy, who was on oral penicillin 3x/d for suspected scarlet for the last 6 days, was admitted to our unit with persisting fever and reduced general condition over the last two days. On admission the child was in poor general condition with 39.9 °C, diffuse skin rash predominantly of the trunk, bilateral non-suppurative conjunctivitis, red lips and cheeks, strawberry tongue, pharyngitis, small cervical and axillary lymphadenopathies. Inflammatory markers and white blood count were high, liver function tests 2 to 3 fold. The diagnosis of KD was made and an IVIG treatment (Privigen®) was started at 30 mg/kg/h, and 30 minutes later increased to 60 mg/kg/h. The patient then developed itchiness, increased skin rash whole body pain, tachypnea and tachycardia. IVIG was discontinued and intravenous clemastin 0.1 mg/kg and methylprednisolone 1 mg/kg were given following which the patient's symptoms improved. After 8 hours the patient was given a second dose of clemastin 0.1 mg/kg and methylprednisolone 1 mg/kg and IVIG treatment was restarted at 30 mg/kg/h, and then increased to 60 mg/kg/h. As the patient got symptomatic again a few hours later, the decision was made to continue the IVIG at 30 mg/kg/h together with intravenous clemastin 0.1 mg/kg 3x/d and methylprednisolone 1 mg/kg 2x/d, so that the recommended total IVIG dose of 2 g/kg could be given over a total period of three days. The patient became apyrexial within 24 hours of treatment and an echocardiography at 3 weeks was found to be normal.
Discussion and conclusion: Because the outcome of patients with KD depends on early treatment with IVIG, the authors felt that the moderate recurrent anaphylactic reaction did not justify discontinuing the IGIV treatment. In this case the patient tolerated the IVIG so that the total dose of 2 g/kg could be achieved, once IVIG have been reduced to 30 mg/kg/h and given together with an antihistaminic drug and a steroid. Therefore the authors believe that cautious management of IVIG treatment may lead to an increased number of patients with KD tolerating IVIG in cases of moderate anaphylactic reactions.

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An increase in serum tryptase even below 11.4 ng/mL may indicate a mast cell-mediated hypersensitivity reaction: a prospective study in Hymenoptera venom allergic patients

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Background: During a systemic hypersensitivity reaction an increase in serum tryptase compared to the baseline value is an indicator of mast cell activation (often IgE-mediated). Until now only serum tryptase above normal value (11.4 ng/ml) are diagnosed pathologic. This study evaluates the relevance of an increase in serum tryptase below the upper normal value.
Method: Serum tryptase levels were measured in 35 patients with Hymenoptera venom hypersensitivity before and during venom exposure. Of these, 20 developed systemic reactions to stings or following venom injections during immunotherapy (reactors), while 15 tolerated reexposure to stings or venom injections without hypersensitivity reactions (non reactors). Serum tryptase was estimated at 2h, 5h and 24h after exposure and compared to a baseline value obtained before or at least 72 hours after exposure.

Results: Considering circadian variation of serum tryptase a relative increase to >135% of the baseline value was defined to indicate mast cell activation. Such an increase was observed in 17/20 reactors (85%), but in none of 15 non reactors. A serum tryptase of >11.4 ng/ml following venom exposure was observed in 8/20 reactors (40%) and 2 (13.3%) of the non reactors. Both of the two non reactors had an elevated baseline serum tryptase.
Conclusions: Serum tryptase value should be obtained during a suspected hypersensitivity reaction and must always be compared to a baseline value. A relative tryptase increase to >135% of the baseline value during a suspected hypersensitivity reaction indicates mast cell activation even below 11.4 ng/ml. (Clin Exp Allergy. 2011 Dec;41(12): 1777–83.)

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Torticollis in children: Red flags to potentially life-threatening causes

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Introduction: Torticollis, characterized by a lateral head tilt and chin rotation towards the opposite side, is a symptom frequently seen in the emergency department (incidence 0.3–2%). It may be present at birth (congenital or connatal) or acquired. According to the literature the acquired forms are usually associated with benign diseases, mostly spasms of the cervical muscles. But potentially life-threatening causes (e.g. tumor of the posterior fossa) need to be considered. The aim of this study was to identify possible red flags pointing towards these potentially fatal causes of torticollis.
Methods: We retrospectively analyzed the charts of all children with a diagnosis of torticollis presenting to our emergency department from January 2007 to January 2012 (5 years). Congenital forms of torticollis were excluded. As potentially life threatening causes we defined tumors of the posterior fossa, retropharyngeal abscesses, traumatic injuries and ocular paresis. We then tried to identify characteristics in presenting symptoms, history and physical examination unique or common to these causes.
Results: During this period 89 children with torticollis presented to our emergency department. 27 (= 30%) of them had an acquired form and their charts were further analyzed. Fourteen (52%) had potentially life threatening causes as per our definition. In five patients (18%) the torticollis was of ocular origin (three primary and two secondary to infection and tumor). The ocular symptoms were the main complaint and apparent in the initial physical examination. Traumatic injury (vertebral fractures and atlantoaxial subluxation) was the underlying cause in four children (15%). History revealed a significant trauma in all cases. In three patients (11%) a tumor of the posterior fossa was detected. All three showed additional neurological symptoms like ataxia or cranial nerve palsy. Two children (7.5%) presented with torticollis due to a retropharyngeal abscess. Both presented with fever and a sore throat in the absence of signs of respiratory infection.
Conclusions: Potentially life threatening causes of torticollis appear to be more common than previously reported. In our group of patients we were able to identify red flags to these causes. The following symptoms associated with torticollis should prompt further investigations: ocular symptoms like strabism or double vision, significant trauma, additional neurological findings and fever and a sore throat in the absence of signs of respiratory infection.

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Not your common gastroenteritis – systemic lupus erythematodes presenting with enteritis-like symptoms

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Introduction: Pediatric systemic lupus erythematodes (pSLE) is a rare systemic autoimmune disease characterized by the presence of autoantibodies and multiorgan involvement. About 20 to 30% experience gastrointestinal disease within the first year of diagnosis, but abdo-minal symptoms as the main initial presentation, indicating lupus enteropathy and pos-sible inflammatory peritonitis, are uncommon. Abdominal pain is most frequently pre-sent, followed by vomiting and diarrhea. All these symptoms are also hallmarks of com-mon gastroenteritis and can result in a delay of pSLE diagnosis. Here, we present the case of a boy with pSLE and repetitive episodes of gastroenteritic symptoms.
Case Report: A 12 years old boy was referred to the emergency department because of repetitive vomiting and watery diarrhea, associated with crampy abdominal pain. He had a past medical history of insuline dependent diabetes mellitus with absent islet-cell antibodies, two episodes of non-infectious bilateral parotitis and a campylobacter-associated arthritis. Eight and nineteen days earlier, he had been hospitalized with similar symptoms, and his brother was diagnosed simultaneously with a rotavirus-positive gastroenteritis. As the abdominal pain worsened and bowel sounds were diminished, radiographic evaluation showed the presence of hypomotile intestinal loops and thickened segments of the ileocolic wall. A gastro-duodenoscopy and colonoscopy were performed, showing unspecific intestinal changes not compatible with inflammatory bowel disease. Abdominal MRI and MRA were not further contributive. Considering the past medical history, rheumatological evaluation revealed high-titer anti-nuclear antibodies with strongly positive anti-ds-DNA, anti-SS-A and SS-B antibodies with C3 and C4 consumption. Together with further investigations, the diagnosis of pSLE was confirmed. Treatment with prednisone 1 mg/kg/day led to prompt clinical improvement and normalization of intestinal function.
Conclusions: Atypical courses of gastroenteritic symptoms should not only prompt surgical and gastroenterologic evaluation, but also take account of pSLE with predominant abdo-minal involvement, especially when preceeding symptoms, like arthritis, are present.

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Vomiting, lethargy and a peculiar smell: not just a common infectious gastroenteritis – a case report

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Background: Isovaleric acidemia is an autosomal recessive organic acidemia caused by a deficiency of the isovaleryl-CoA-dehydrogenase. Clinical presentation can be acute neonatal or chronic intermittent with manifestation later in life. Early diagnosis and treatment with a protein restricted diet and supplementation with carnitine are effective in promoting normal development.
Case report: The 4 year old boy presented to the paediatric emergency department because of persistent vomiting for almost 30 hours and noticeable sleepiness, without diarrhoea. He had been hospitalised for 'gastroenteritis' without vomiting several times before; two years earlier; he had been treated for a parainfectious encephalopathy with metabolic acidosis. Clinical examination revealed sleepiness, tachycardia, tachypnoea with hyperpnoea, and a peculiar smell. He was dehydrated with dry oral mucosa and tongue. Blood gas analysis showed metabolic acidosis (pH 7.26, pCO_2 1,6 kPa, bicarbonate 5.1 mmol/l, base excess –20.9 mmol/l). Glucose, lactate, electrolytes, and urea where within normal range; anion gap was markedly increased (25 mmol/l) and ammonia slightly elevated (92 µmol/l). Ketonuria was present. Treatment consisted of intravenous glucose administration and rehydration. Metabolic work-up including blood acylcarnitine profile and urine organic acids revealed isovaleric acidemia. Protein restricted diet and supplementation with carnitine was started.
Conclusion: Recurrent vomiting combined with metabolic acidosis and (mild) encephalopathy needs metabolic work-up. Recognition of a peculiar smell should raise suspicion of an inborn error of metabolism.

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Anisocoria: the culprit may be in the garden

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Introduction: Anisocoria always worries emergency doctors. Its sudden onset can cause great panic for the family and can be a diagnostic challenge in the emergency department. A thorough clinical history can guide towards a rapid diagnosis and avoid invasive or expensive investigations.
Case report: A 3-year old otherwise healthy boy was brought to our emergency department by his parents because of a dilated right pupil after playing with his friend in the garden. Half an hour before, he presented a brief crying episode, which the parents attributed to a fight between children. No fall, ocular trauma or commotion was reported. The right mydriasis was unresponsive to both papillary light reflex and accommodation reflex. The physical examination was otherwise normal, particularly no tachycardia was found. Finally a detailed history revealed that he had peeled an Angel's Trumpet (Datura) plant and then rubbed his right eye. After familly reassurance, the patient was discharged home and the mydriasis desappeared within 3 days without treatment.
Discussion: The cause of anisocoria can be central or peripheral, through trauma, tumoral, malformative, or toxic mechanisms. Angel's Trumpet, an ornamental plant increasingly found in our gardens and parks, contains parasympatholytic alkaloids: scopolamine, hyocyamine, atropine among others. In sudden, unilateral, non-reactive mydriasis in an otherwise healthy child, a toxic cause such as exposure to Angel's Trumpet should be searched. Moreover this plant can cause dangerous hallucinations, deliriums and hyperthermia. Severe intoxications may lead to convulsions, flaccid paralysis and death.
Conclusion: This report describes an accidental unilateral mydriasis caused by direct contact of the eye with parasympathicolytic (anticholinergic) alkaloids from Angel's Trumpet sap. Physicians, parents and gardeners must be alerted to the toxic effect of the accidental ocular contact with the sap of this widespread plant.

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Near fatal enema: beware of phosphate solution

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Introduction 1: Phosphate salts enemas are frequently used in paediatrics. In Switzerland, some of them are even sold over the counter (OTC). NASPGHAN guidelines state a minimal age of 2 years and maximal dose of 6 ml/kg or 135 ml. To our knowledge, there are no good human pharmacological studies about such enemas.
Case report: We describe a healthy 3 year old boy with a large rectal fecaloma who developped a nearly fatal hypocalcemia (ionized Ca 0.48 mmol/l) with a hyperphosphatemia (17.55 mmol/l) after rectal enema of 15 ml/kg of a ready-to-use sodium phosphate enema (Clyssie® (B- Braun, Melsungen, Germany)).
Introduction 2: This case led to an internal audit of enemas prescription in our 2 paediatric emergency units.
Methods: Retrospectively, all enemas prescriptions were retrieved from our billing system between January 1, 2010 to July 31, 2011. Anonymously, patients demographic data and details of enemas type, volume and side effects were compiled. Out of a total of 21296 visits, 105 enemas were billed to patients. Median (range) patient age was 54 months (3–186 m). Composition of 97/105 was known, out of which 61/97 (63%) contained phosphate salts. In this group, median patient age was 48 months (3–149 m), median dose was 7.5 ml/kg (1–20), 17/61 (28%) were ≤2 years. 44/61 (72%) recieved more than the recommended 6 ml/kg. No side effects were noticed.
Conclusions: Enemas are regularly used in our paediatric emergency units. Severe side effects of phosphate solutions are probably very rare but can be almost deadly. Apparently, we did not follow the paediatrics doses guidelines. Phosphate based enemas have been so far banned from our department. Phosphate based OTC paediatric enemas sales should probably be restricted as single units contain potentially too large volumes for small children (120/135 ml).

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Fomepizole Treatment of Severe Pediatric Ethylene Glycol Poisoning

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Introduction: Ethylene glycol (EG) is a well known cause of poisoning in children. Current Swiss guidelines consider hemodialysis with EG concentration above 50 mg/dL. We described the case of a toddler who was exclusively treated with fomepizole with EG concentration of 63.2 mg/dL.
Case Report: A healthy 30 month-old male gulped some EG stored in a bottle of orange juice. On arrival, the only sign of EG was a slight excitement. Fomepizole therapy was immediately initiated. Capillary blood gas was normal. The first measured serum EG concentration was 63.2 mg/dL. Without severe kidney injury and significant acidosis monotherapy was continued. Twenty-two hours after ingestion EG concentration was 11.1 mg/dL. No side-effects were reported.
Discussion: Due to its viscosity and thermal proprieties EG is a component of antifreeze. In Switzerland during 1997–2005 six severe intoxications are reported. Serious symptoms occur with a dose as low as 0.1 mg/kg and at admission laboratory data are not available on EG concentration. The main clinical features of EG poisoning are inebriation or alteration in consciousness, metabolic acidosis, hypocalcemia and acute renal failure. Formely treatment for EG poisoning required ethanol therapy with its attendant complications and not exceptionally hemodialysis
Conclusion: This case report shows that a child with severe EG poisoning was treated safely and cost effectively with fomepizole alone. Fomepizole treatment must be started immediately without waiting for EG concentration. Fomepizole has obviated the need of ethanol therapy. Hemodialysis should be limited to strictly selected cases.

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Detection of midazolam in children's hair after one dose for a procedure in anaesthesia

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Introduction: We had a child in our hospital where we had the suspicion that a person gave the child a sleeping drug. We contacted the institute for forensic medicine to ask how we could verify this suspicion. Because there aren't many data about the analysis of midazolam in children's hair we wanted to collect hair from children after they received a single dose of midazolam in our children's hospital. The aim of this study was to determine midazolam in these hair samples after a single dose of midazolam and to asses corresponding mechanisms of incorporation.
Methods: After having obtained informed consent from the parents and their children we collected hair from 12 children that needed an intervention in anaesthesia before they received any medication. We cut a thread fixed hair strand as close to the scalp as possible. As premedication every child received 0.5 mg/kg midazolam oral or rectal. We instructed the parents to cut a second hair strand 2–7 days after the intervention, and 7 parents sent us again an additional hair strand 6–10 weeks later. We wanted to examine if midazolam gets although through sweat in the hair so that we can detect it their after a few days and if we can trace midazolam after a single dose in the grown hair some weeks later. The hair was analysed in the institute for forensic medicine in Zürich. Segmental analysis of these hair strands was performed by standard procedure: decontamination of the hair, pulverization and extraction of the incorporated substances, analysis by LC-MS/MS (Shimadzu prominence XR, ABSciex 5500QTrap, Phenomenex Kinetex C18, 2.6 µm, 50/2.1, 5M Formate Buffer/5M NH4-Formate MeOH).
Results: We included 12 children (5 female and 7 male), mean age 5.6 (1–11). No child had midazolam in the hair before the intervention, 2–7 days after the intervention we found only in 7 cases a trace of midazolam. 6–10 weeks after the intervention we found in 6 of 7 cases midazolam in the hair.
Conclusion: Midazolam is traceable in the hair of children after a few weeks even if they received it only once. Through the sweat a tiny amount of the midazolam was found in some children's hair a few days after the exposure. Hair analysis is a powerful tool for retrospective monitoring of the ingestion or administration of licit or illicit drugs.

P 150

Traumatic aortic rupture treated by endovascular stent in an 11-year-old polytraumatized boy

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Introduction: Traumatic injury of the aorta is very rare in childhood. Only few case reports are found with no clear consensus concerning the optimal management.
Case Report: An 11 year-old boy was involved in a high speed car accident. He was a front-seat passenger wearing a 3-points seat belt. On arrival he was normotensive with tachycardia. GCS was 15 and the child complained about abdominal pain. His abdomen was tender with a large seat-belt sign. CT-scan showed intraperitoneal hemorrhage and abdominal aortic rupture. Laparotomy revealed massive intra-abdominal bleeding due to a mesenteric tear associated to multiple intestinal perforations. Haemostasis was done by arteric ligatures and a small intestine resection of 80 cm was performed. Complete aortic rupture was confirmed during the operation and an aortic endovascular stent was placed by the radiologist. No postoperative complications were noticed and the child was discharged after the 17th day. 3 months later, the boy is asymptomatic and no radiological complications have been noticed.
Discussion: Only 5% of aortic trauma in children concerns the abdominal part. The main cause of such trauma is high-speed car accidents. Due to its retroperitoneal protected position, the abdominal aorta is rarely injured alone. The most common associated injuries are small-bowel and lumbar spine injuries. In case of such lesions it's important to consider the risk of an aortic injury and to look for it. In adults, endovascular stent placement is the most appropriate alternative. In children, the situation isn't so clear. Recently, the use of endovascular stents appeared in the management of pediatric blunt aortic trauma. The results are encouraging but the long-term outcome is unknown.
Conclusion: In this situation, concerning a polytraumatized child, this endovascular procedure was efficient and simple. It prevented a contamination by the intestinal lesions and was less invasive than a traditional surgical approach. The results after 3 months are encouraging but the child will need a long term follow-up to assess the safety of this procedure.

P 151

Phenprocoumon intoxication and gross haematuria in an adolescent: The Broken Heart Syndrome

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Introduction: The case of a previously healthy adolescent boy presenting with monosymptomatic gross haematuria and non-measurable a-PTT and INR is reported.
Case report: A 16 year old boy was referred by his practitioner for gross haematuria and flank pain for one day, but no other symptoms. Haemorrhagic cystitis was suspected and antibiotic treatment begun. Gross haematuria persisted for 5 days and his mother took him again to hospital. Clinical examination was uneventful. Comprehensive haemostasiologic analysis showed very low levels of all vitamine K dependent coagulation factors.

	* below detection limit	normal values
a-PTT	not coagulating	29–41 s(econds)
International Normalized Ratio (INR)	not coagulating	1.0–1.2
Thrombin time	14.7 s	<21 s
F II	<10%*	75–125%
F VII	<10%*	52–148%
F X	<10%*	66–134%
Protein C	21%	78–150%
Protein S	12%	75–141%
Normal values: Factor V and VIII, vW-RICOF and -antigen, fibrinogen, PFA-ADP and PFA-epinephrin; no evidence of coagulation inhibitor (mixing study)		

The patient was treated with human coagulation factors (Beriplex®; single dose) and vitamine K (4 iv doses over 8 days). Coagulation parameters normalized after 10 days. In the mean time, high blood concentration of Phenprocoumon (T½ = 160 hrs) was revealed. Upon repeated interrogation the boy confessed to his mother having taken 69 mg of her Phenprocoumon tablets (she had stored away one year ago) 9 days before onset of haematuria. He had been feeling downcast as his girlfriend had left him.
Conclusion: This case highlights the importance of staying alert and critical towards the ambivalence of adolescent patients.

Free communications Young Researcher Day 2012

YRD 1

Impaired slow wave sleep downscaling in encephalopathy with status epilepticus during sleep (ESES)

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Introduction: "Encephalopathy related to electrical status epilepticus during sleep" (ESES) is characterised by the EEG-pattern of continuous spike waves during slow wave sleep (CSWS) and by variable neuropsychological impairments. Although spike waves are crucial for this progressive deterioration, the pathophysiological mechanisms are still unknown. The synaptic homeostasis hypothesis predicts that the strength of cortico-cortical synapses is decreasing during slow wave sleep. In the EEG this "downscaling" of synaptic strength is reflected by a decrease of the slope of slow waves. Therefore, we hypothesised that the overnight changes of the slope are altered in patients with ESES.
Methods: In a retrospective study, we analysed changes of the slope of slow waves (<2 Hz) from the first to the last hour of sleep in EEGs of 9 patients with ESES (age 3.4–11.1 years) and compared them to 9 age and gender matched healthy controls (age 3.0–12.3 years).
Results: As expected, in healthy controls the slope of slow waves declined significantly from the first to the last hour of sleep (17.2 % decrease, p <0.001). Patients instead showed no significant change in the slope across the night. In the last hour of sleep, the slope was significantly steeper in patients compared to controls (p <0.01).
Conclusion: The slope of slow waves in patients with ESES does not show the expected physiological decrease that is observed in healthy controls. This missing slope decrease may reflect a disruption of the downscaling process during sleep and could therefore be the basis for the developmental regression in these patients.

YRD 2

Fibroblast growth factor-7 sustains thymic expression of tissue-restricted antigens during experimental graft-vs.-host disease

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Introduction: Graft-versus-host disease (GVHD) impairs thymus-dependent T-cell regeneration and consequently contributes to immune deficiency after allogeneic hematopoietic stem cell transplantation (alloHSCT). Impaired thymopoiesis is due to an anti-host response directed against thymic epithelial cells (TECs) which normally deliver the signals required for T-cell development. The systemic administration of human fibroblast growth factor 7 (Fgf7; palifermin) can expand TEC numbers in mice. Here we tested whether Fgf7 protected number and function of medullary TEC (mTEC) during GVHD. These cells normally present to developing T cells an array of ectopic tissue-restricted antigens (TRAs) and are hence central to the process of thymic negative selection.
Methods: The effect of Fgf7 on mTEC-specific TRA expression was tested in a murine allogeneic transplantation model.
Results: Mature mTEC cell numbers were found to be progressively diminished in the course of GVHD which was paralleled by a lower than normal diversity of TRA expression. However, Fgf7 sustained a stable population of mTEC in allogeneically transplanted mice, even if total mTEC numbers remained lower than in age-matched controls. On a whole mTEC population level, Fgf7 therapy maintained in the long-term a much more diverse array of TRA expression than in untreated mice with acute GVHD.
Conclusions: Fgf7 conserved a crucial function of mTEC despite the continued existence of injurious donor T cells in the host thymus. Hence, a therapeutic strategy using Fgf7 may promote regeneration of a functionally competent T-cell adaptive immune system following alloHSCT.

YRD 3

Short term effects of chest physiotherapy in children with cystic fibrosis assessed by a new lung function test

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Background: Physiotherapeutic treatment (PT) and inhalation are standard of care in children with cystic fibrosis (CF). However no lung function test has been proven sensitive enough to detect short-term effects of PT. We recently developed a new and easy to perform tidal single-breath washout (SBW) using two tracer gases to measure ventilation inhomogeneity (VI) in small airways.
Aims: We assessed whether this new SBW test is able to measure short-term effects of PT and inhalation in CF patients.
Methods: Children with CF (n = 25) between 6 and 16 years performed lung-function assessments prior to and after inhalation and PT. Assessments consisted of a double tracer gas SBW (DTG-SBW) and spirometry. DTG contained sulfur hexafluoride (SF6) and helium (He), and was inhaled during tidal breathing. A side-stream ultrasonic flowmeter measured molar mass. DTG-SBW outcome was percentage of expired volume where expired molar mass equals inspired molar mass, reflecting inspired ratio of SF6 and He (IP_{DTG}).
Results: After intervention IP_{DTG} decreased from 66.5% (±25.8) to 59.7% (±25.4) resulting in a mean difference of –7.3% (95%CI –12.9 to –1.8). MEF_{25-75} from spirometry increased from 1.41 L/s to 1.62 L/s resulting in a mean difference of 0.19 L/s (95%CI 0.02 to 0.37). In a *post-hoc* subgroup analysis changes in small airway ventilation were detected with the DTG-SBW only in patients with mild CF lung disease (n = 14, FEV1 z-score >-2), whereas spirometry indexes increased only in patients with moderate CF lung disease (n=11, FEV1 z-score <-2).
Conclusion: The DTG-SBW is the first lung function test able to detect short-term effects on lung function following physiotherapy and inhalation in CF patients. This allows immediate and objective assessment of changes in therapeutic regimen.

YRD 4

The Unsolved Pathogenesis of Idiopathic Ketotic Hypoglycemia: Involvement of the Pyruvate Dehydrogenase Kinase Isoenzym 4 Gene?

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Introduction: Idiopathic ketotic hypoglycemia (IKH) is defined by hypoglycemia with high ketone levels in plasma and urine, provoked by periods of fasting often in combination with an intercurrent illness. The pathogenesis of IKH is not completely understood so far. The

hypothesis of this project is that variations of the Pyruvate Dehydrogenase Kinase isoenzyme 4 (PDK4), involved in glucose homeostasis, could be the causative genetic defect in some IKH patients.
Methods: The medical records of 10 IKH patients were reviewed to determine possible various clinical and biochemical phenotypes. DNA samples were collected from peripheral blood. The whole open reading frame of the PDK4 gene was sequenced. RT-PCR was then realized with RNA extracted from fibroblast of 4 patients to verify the effects of the observed gene alterations on the cDNA.
Results: In our cohort of 10 IKH patients we found an equal gender relation with a mean age at first crisis of 37.5 months. 88% of patients were <P50 for weight but only 57% <P50 for height. The majority of the changes found in the PDK4 sequence were polymorphisms. The other variations were mostly situated in introns, upstream the ATG translation start codon or downstream the translation stop codon. We could not find any pathogenic gene variation leading to changes on the cDNA.
Conclusion: The analysis of clinical data of our patients mostly confirmed the features of IKH reported in the literature. While a small height was only present in half of the patients we could confirm a weight under average as a common feature in IKH patients. No pathogenic changes in the open reading frame of PDK4 related to IKH were found in our cohort. IKH is the most common cause of hypoglycemia in children between 1 and 5 years of age among non-diabetic children and its pathogenesis remains poorly understood. We plan to perform whole genome sequencing in our cohort which might help us to identify the underlying genetic alterations in IKH patients.

YRD 5

Brain damage in methylmalonic aciduria and glutaric aciduria type I: Rat 3D primary reaggregated brain cell cultures elucidate the pathomechanisms

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Introduction: Neurological damage is a common feature in methylmalonic aciduria (MMA) and glutaric aciduria type I (GA-I). Cerebral accumulation of toxic metabolites upstream of the metabolic block is considered to be the main cause of neuronal damage, while the pathomechanism of neurodegeneration is still poorly understood. Both diseases manifest early in life. Cerebral maturation seems to play an important role in this age-dependant vulnerability.
Methods: We treated rat 3D primary reaggregated brain cell cultures with the metabolites accumulating in each disease and analyzed their effects on the biochemical profile in medium and the changes in morphology and viability of different cell types by immunohisto-chemistry. Experiments were performed at three different time points of the 3D cultures reflecting a time window between the neonatal period and childhood.
Results: 2-methylcitric acid treatment seemed to be the most toxic, with induction of hyperammonemia, cell swelling of astrocytes predominant in the most immaturely treated cultures and a general toxic effect on astrocytic fibers and oligodendrocytes independent from the age of culture. 3-hydroxyglutaric acid showed an important maturation-dependent toxicity on glial cells accompanied by hyperammonemia and astrocytic swelling. We did not observe any toxic effect on neurons. Interestingly, methylmalonic acid had a growth stimulating effect on all cell types at any age.
Conclusion: Our results reveal 2-methylcitrate and 3-hydroxglutaric acid as the most toxic metabolites in MMA and GA-I, respectively. The observed central hyperammonemia might not be visible in the periphery of patients. This finding may point to an additional pathomechanism and possible therapeutic target. We can confirm the clinical observation that toxicity seems to decrease with brain cell maturation. Investigations on respiratory chain function, metabolomics and gene expression profiling are ongoing and might help us to further determine the pathways involved in neurotoxicity.

YRD 7

Platelet apoptosis in paediatric immune thrombocytopenia is ameliorated by intravenous immunoglobulin

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To evaluate the role of intravenous immunoglobulin (IVIg) in platelet apoptosis in paediatric immune thrombocytopenia, we investigated platelets of paediatric patients with acute immune thrombocytopenia (ITP), before and after IVIg treatment. Markers of apoptosis, including activated caspase-3, -8 and -9, phosphatidylserine (PS) exposure, mitochondrial inner membrane potential $\Delta\psi m$, as well as platelet-derived microparticle formation, were analyzed by flow cytometry. After IVIg treatment, platelet counts increased to >20 x 10^9/L in all patients. As we have recently reported (Winkler et al. Br J Haematol 2012) ITP patients had significantly increased proportions of platelets with activated caspase-3, -8 and -9, with PS exposure, and with decreased mitochondrial inner membrane potential, and demonstrated increased microparticle formation. Except for $\Delta\psi m$, these markers for apoptosis were reduced by IVIg treatment. Platelets of children with thrombocytopenia after chemotherapy also demonstrated increased microparticle formation and decreased $\Delta\psi m$, but no activation of caspases 3, 8 and 9 or PS exposure. To understand these apoptotic events in platelets we started now to investigate systematically the apoptotic signalling in platelets. Preliminary findings show that besides caspases platelets also contain pro- and anti-apoptotic proteins such as FADD, Bax, Bad, Bcl-2, BclXL, Omi/HtrA2, Diablo/Smac and xIAP. In conclusion, platelet contain a complete apoptosis signalling cascade playing probably a role in healthy, but also in pediatric disease such as ITP.

YRD 8

Ten novel mutations in the *NR5A1* gene cause disordered sex development 1 in 46,XY and ovarian insufficiency in 46,XX individuals

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Introduction: Steroidogenic factor-1 (SF-1/*NR5A1*) is a nuclear receptor which regulates adrenal and reproductive development and function. *NR5A1* mutations have been detected in 46,XY individuals with disorders of sex development (DSD) but apparently normal adrenal function and in 46,XX women with normal sexual development yet primary ovarian insufficiency (POI). Our aim was to study a group of 100 46,XY DSD and 2 POI patients for *NR5A1* mutations and its impact.
Methods: Clinical, biochemical, histological, genetic and functional analyses were performed. Patients were referred from different centres in Spain (65 46,XY DSD), Switzerland (2 POI) and Turkey (35 46,XY DSD). Histologic and genetic studies were performed in Barcelona, Spain. *In vitro* studies were performed in Bern, Switzerland.
Results: Ten novel heterozygote *NR5A1* mutations were detected (5 missense, 1 nonsense, 3 frameshift mutations and 1 duplication). The novel *NR5A1* mutations were tested *in vitro* by promoter transactivation assays showing grossly reduced activity for mutations in the DNA binding domain and variably reduced activity for other mutations. We found high variability and thus no apparent genotype-structure-function-phenotype correlation. Histologic studies of testes revealed vacuolization of Leydig cells due to fat accumulation.
Conclusions: *NR5A1* mutations are frequently found in 46,XY DSD individuals (9%) and manifest with a broad phenotype. Testes histology is characteristic for fat accumulation and degeneration over time similar to findings observed in patients with lipoid congenital adrenal hyperplasia (due to StAR mutations). Genotype-structure-function-phenotype correlation remains elusive.

YRD 9

Involvement of autophagy in severe hypoxic-ischemic encephalopathy of newborn infants: an autopsy study

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Background: Hypoxic-ischemic encephalopathy (HIE) remains a major concern in neonatology. A more detailed understanding of neuronal cell death following hypoxia might lead to the development of neuroprotective strategies, which are lacking at the moment. Our and other groups have shown that autophagy is involvedneuronal cell death, and that its inhibition results in neuroprotection in rodent models of HIE.
Aims: To determine whether changes in autophagy can be observed following perinatal asphyxia in autoptic brains of human newborns.
Material and methods: Brain tissue samples (thalamus) conserved in paraffin blocks of human newborns (>36 GA) who died between 2004–2010 from perinatal asphyxia defined as (i) Apgar score of <5 at 5 min and (ii) arterial pH <7.00 at 1 h of life or a base deficit >12 mmol/l and (iii) clinical encephalopathy graded as Sarnat III. Neonates matched for gestational age and death from other conditions were selected as

controls. The presence of autophagy was investigated by using immunohistochemistry and confocal microscopy. LC3, a marker of autophagosomes, along with LAMP1 and cathepsin D, two markers of lysosomes were used. Similar investigations were done in parallel on a neonatal HIE rat model.
Results: The brains of 7 HIE cases and 5 control cases were analyzed. The number of positive dots per neuron for all 3 markers related to autophagy were significantly increased ($p < 0.001$, 7fold increase) in the thalamus of HIE cases compared to controls. LAMP1 and cathepsin D-positive dots were also larger than dots in control brains, suggesting an increased neuronal formation of autolysosomes. Finally, caspase-3 positive neurons were also strongly positive for autophagy markers. Similar results were obtained in dying thalamic neurons in the neonatal rat model of cerebral HI.
Conclusions: These results reveal a hitherto unknown upregulation of the autophagic flux in the thalamus of newborns with HIE, as observed in animal models, and suggests that autophagy could be involved in neuronal death. Autophagy seems to be a promising target for future neuroprotective approaches in combination with hypothermia.

YRD 10

Topical betablockers for infantile hemangiomas are effective but systemically absorbed

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Introduction: Systemic betablocker have become the first line treatment for complicated infantile hemangiomas (IH). A few reports have proposed the beneficial use of topical betablockers for the treatment of IH. However, the question, whether topical application of betablockers results in a solely topical or possibly systemic effect has not been investigated.
Methods: We treated 40 young infants with small proliferating IH with timolol gel 0.5% twice daily (no occlusion) and assessed systemic absorption by qualitative urine analysis and measurement of serum levels in a proportion of patients. The clinical response was evaluated by visual analogue scale (VAS) of photographs after 1, 2, 3 and 5 months.
Results: Fourty infants (median age 18 (2–35 weeks)) were included. Twentythree (58%) patients had a superficial IH and 17 (42%) a mixed-type IH. The median IH size was 3 cm^2 (0.1–15 cm^2). There was a significant improvement of the IH with a VAS of 4.9 (–4 to 9) and +5 (0 to 9) after 3 and 5 months, respectively. Thirtyfour IH (85%) showed regression, whereas 2 (5%) remained static and 4 (10%) deteriorated. Nine IH were ulcerated pre-treatment and healed completely within 14 days (6 to 18 days). In 24 children the urine was tested for the detection of timolol: in 20 (83%) the urine was positive but negative in 4 (17%) patients. In 4 infants serum levels of timolol were measured resulting in a median value of 0.16 ug/l (0.1–0.18).
Conclusions: Topical therapy with timolol seems to be effective in treating small IH. However, our data demonstrates that topically applied betablockers are systemically absorbed. The serum levels detected are lower compared to topical betablocker application for ocular therapy of glaucoma. This highlights the potential risk of extensive topical betablocker use particularly in very young infants and additional monitoring measures may need to be considered.

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