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

Lava S.A.G.1,2, Simonetti G.D.2, Ramelli G.P.1, Ferrari A.1, Bianchetti M.G.1
1Pediatria Bellinzona e Mendrisio, 2Kinderneuropathologie, Inselspital Bern

Introduction: In symptomatic fever management by pediatrians, there is often the need of 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 Swiss pediatrians. The survey was not commercially sponsored. Results: The questionnaire was answered by 322 (36%) pediatrians: 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 pediatrians 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-speaking (P < 0.001) respondents. 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 German-speaking region more frequently (P < 0.001) prescribe ibuprofen and paracetamol in a broad adult regimen with 2 drugs rather than German-speaking respondents. Finally, the stated occurrence of exaggerated fear of fever was higher (P < 0.001) among German- and Italian-speaking pediatrians. 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.

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

I. Iglowstein, C. Kahler, P. Drack, A. Niederer, B. Rodgo
Ostschweizer Kinderklinik

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 period, evidence-based guidelines and a standardised 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.

Comparison of pediatric emergency departments in Switzerland

Mascha Rochat1,2, Mario Gehri3, Eric Masserey4
1Department of Pediatrics, University Hospital of Lausanne, Lausanne, Switzerland; 2Public Health Department, Vaud, Switzerland

Introduction: The emergency department is an essential component of the medical care and everyday clinical practice. We were interested to see whether the 3 main linguistic regions of Switzerland differ in the management of fever.

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 (Immenschweiz). 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” pediatrians 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 number 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.

Interdisciplinarity and organisational structure of Pediatric Emergency Departments in Switzerland

J. Höffe, A. Duppenthaler, G. Staubli, I. Berger
1Notfallzentrum Kinder und Jugendliche, Universitätsklinik für Kinderchirurgie, Inselspital, Bern; 2Universitätsklinik für Kinderheilkunde, Inselspital Bern; 3Notfallstation, Universitäts-Kinderklinik Zürich

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 structure for triage and inpatient care. The aim was to analyze the interdisciplinarity of Pediatric Emergency Departments.

Results: 20 of 31 hospitals do have an interdisciplinary emergency department (65%). 5 of these 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-university children’s hospitals do run such a system. In 6 hospitals external pediatricians participate in these ambulatoires. 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 pediatric 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 and the role of 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).
Triage evaluation of all patients in the year 2010 at the emergency department of the children’s hospital Zurich
Schams D., Valk P., Staubli G.
Universitätskinderklinik Zürich

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 96% 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.

Minor head injury
Simma B., Luetsch J.
Kinder- und Jugendheilkunde, Akad. Lehrkrankenhaus, Feldkirch, Österreich

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 very low birth weight infants (VLBW, <1500 g). Only a few publications analyse changes of the perinatal 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 ≤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 increase in infants with potentially good outcome.
Neurodevelopmental Outcome in Extremely Premature Infants born in Switzerland between 2000 and 2008 – Preliminary Data of the Swiss Neonatal Network.

Schlapbach L.J.1, Adams M.2, Aebischer M.1, Latal B.3, Grunt S.4, Borradori-Tolsa C.3, Bickle Graz M.3, Bucher H.U.1, Natalucci G.3,3, Brisbane, Australia; 2Department of Neonatology, Zurich University Hospital Zurich; 3Child Development Center, Zurich University Children’s Hospital; 4Department of Neonatal Pediatrics, Bern University Children’s Hospital; 5Division of Development and Growth, Geneva University Children’s Hospital; 6Department of Child Development, CHUV, Lausanne.

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 mental (MDI) or psychomotor (PDI) development index of 55-70, or between 2000 and 2008 at 24 0/7 to 27 6/7 weeks gestational age.

Results: Among the 1147 extremely preterms born during the study period 303 (26%) died. Follow-up information was available in 684 (81%) of the remaining survivors. 133 (20%) showed normal development, 166 (24%) moderate ND, and 72 (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.

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

Gilles Duvoisin, Eric Giannoni
Service of Neonatology, Department of Pediatrics, CHUV, Lausanne

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 between October 2009 and September 2011 were compared to data from 4986 infants born between October 2009 and September 2011 (Period 1). 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 4 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.

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

Hauser N., Bucher HU, Fauchére J-C
Klinik für Neonatologie, Universitätsspital Zürich

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 (HCP) working in Swiss level III neonatal intensive care units (NICUs).

Methods: 224 Questionnaires were sent to neonatologists 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 neonatologists 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.

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 towards daily neonatal intensive care decision making, the importance of team debriefings and support under professional guidance cannot be stressed enough.

Natal / neonatal teeth – a real problem?

Buchter Hans Ulrich1, Spörri Carol2, Gnoinski Wanda3
Universitätsspital Zürich Klinik für Neonatologie1; Universität Zürich Zentrum für Zahnmedizin2

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. For that reason, we developed a new protocol for newborns with risk factors for EOS, where diagnostic tests were replaced by repeated clinical examination.

Objectives: 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 4986 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 4 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.

Breastfeeding? On enquiry, only 2 mothers mentioned pain related to the baby’s teeth while breastfeeding. With regular sucking, 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.
Incidental findings of mass lesions on neuroimages in children
PerretC.1, Boltshauser E.2, Scheer I.7, Kellenberger C.3, Grotzner M.4,
Departments of *Oncology; *Neurology and *Diagnostic Imaging, Kinderklinik, Zurich, Switzerland
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; and 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 ependymoma in another).
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 define optimal management strategies based on larger collections of natural histories, as well as to assess the true prevalence of incidental CNS mass lesions.

The development of atopic dermatitis according to age of onset and the interaction with early life exposures
Caroline Roduit, MD, MPH,1 Remo Frei, PhD,2 Georg Loss,3 Gisela Büchele, MPH,4 Juliane Weber, MD,5 MPH, Susanne Loeliger,1 Marie-Laure Dalphin, MD,6 Marjet Roponen, PhD,4 Anne Hyvärinen, PhD,7 Josef Riedler MD,1 Jean-Charles Dalphin, MD, PhD,8 Juha Peikanen, MD,6 Erika von Mutius, MD, MSc,9 Charlotte Braun-Fahrlander, MD,4 Roger Lausumer, MD,4 1University of Zurich, Children’s Hospital, and Christine Kühne-Center for Allergy Research and Education, Zurich, Switzerland; 2Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich and the Medical Clinic of Primary Care for Allergy Research and Education, Zurich, Switzerland; 3Swiss Tropical and Public Health Institute, Basel, Switzerland; 4University of Basel, Switzerland; 5Children’s allergy an Asthma Hospital, Hochgebärklinik, and Christine Kühne-Center for Allergy Research and Education, Davos, Switzerland; 6Institute of Epidemiology, University of Ulm, Germany; 7University Children’s Hospital Munich, Germany; 8Department of Pediatrics, University Hospital of Basançon, France; 9Department of Environmental Science, University of Eastern Finland, Kuopio, Finland; 10Department of Environment Health, National Institute for Health and Welfare, Kuopio, Finland; 11Department of Respiratory Disease, UMR/CNRS 6249 Chrono-environnement, University Hospital of Basançon, France
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 atopy 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.

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
Eva Brack, MD1, 2, Nicole Bodmer, MD,1 Arne Simon, MD,1 Kurt Leibundgut, MD1, 2, Thomas Kühne, MD1, Felix K. Niggli, MD2, Roland A. Ammann, MD3,4 Department of Pediatrics, University of Bern; 5Department of Pediatrics, Kantonsspital Aarau; 6Department of Pediatrics, University of Zürich; 7Department of Pediatrics, University of Bonn; 8University Children’s Hospital Basel
Background: In children with malignancies, the standard treatment of fever in chemotherapy-induced neutropenia (FN) includes emergency hospitalization and empirical intravenous antimicrobial therapy. 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 change 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.
Acute Poisoning in Children – Looking at Iron Poisoning:
What should be done?

 ubierto H.1, Iglowstein I.2, Marx G.3
1 Department of Pediatric Hematology and Oncology, 2 Emergency Unit and 3 Department of Pediatric Gastroenterology, Ochsner Children’s Hospital, New Orleans, LA, USA

Introduction: In 2016, 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 Ochsner Children’s Hospital in St. Galen 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 among children, 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 by different approaches 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 poisoning. 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 or decontamination 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.

Psoriasis Distress in Adolescent Survivors of Childhood Cancer

M.E. Gianiazzi1, C.S. Rueegg1, L. Wengenroth1, E. Bergstrasser2, J. Rischewski3, R.A. Ammann2, C.E. Kuehni1, G. Michel3
1 Institute of Social and Preventive Medicine, University of Bern, Switzerland; 2 Children’s Hospital Zurich, Switzerland; 3 Department of Pediatric Gastroenterology, Ostschweizer Krankenanstalten, Switzerland

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.

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

J. Barben1, R. Fingeruth1, S. Gallati2, M.H.Schönen3, C.E. Kuehni1, M. Baumgartner4, T. Torresan1, and the Swiss CF screening group*
1 Division of Pediatric Pulmonology, Children’s Hospital, St. Gallen; 2 Swiss Newborn Screening, Children’s Hospital, Zürich; 3 Department of Pediatrics, University of Berne; 4 Institute of Social and Preventive Medicine University of Berne

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 immuno-reactive 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 cases referred to a CF center 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 1.286/100,000 (29/21,938).

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 1.286/100,000 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. Confirmed diagnoses by CFTR gene analysis

Gallati S., Torresani T., Schönli M., Baumgartner M., Barben J., and the Swiss CF screening group*
1 Department of Pediatrics, University of Berne; 2 Swiss Newborn Screening, University Children’s Hospital, Zürich; 3 Division of Paediatric Pulmonology, Children’s Hospital, St. Gallen

Introduction: Cystic fibrosis (CF) is the second most common life threatening autosomal disorder and the most common life threatening autosomal disorder in the Caucasian population. A recent study on the basis of 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 analysis.

Methods: From 01.11.11 to 27.01.12 EDTA blood or buccal cell samples from 31 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 the 32 most common CFTR mutations using the CF-OLA Kit (ABDOS). 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 (MRCL Holland).

Results: In 28 out of 31 newborns (89.7%) we identified two CFTR mutations confirming the diagnosis of a classic CF in 23 (82%) newborns, 14 of them being F508del homzygous. 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, 47 different mutations were found in 33% of the patients (G486E) 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.

C. Barazzone, C. Casaulta, A. Mornand, P. Eng, G. Hafen, J. Hammer, A. Moller, D. Muller, N. Regamey, R. Spinas, J. Spalinger
Newborn screening for cystic fibrosis in Switzerland – Comparison of Nanoduct versus Macroduct sweat test in the diagnosis of CF

J. Barben1, C.S. Rueegg2, S. Gallati3, C.E. Kuehn3,2, M. Baumgartner2, T. Torresani1, M.H.Schoeni2 and the Swiss CF screening group* 1Institute of Social and Preventive Medicine, University of Bern, Switzerland; 2Department of Paediatric Pulmonology, Children’s Hospital, St. Gallen, Switzerland; 3Swiss Newborn Screening, University Children’s Hospital, Zurich, Switzerland

Background: Newborn screening (NBS) for cystic fibrosis (CF), based on immuno reactive 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 65 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 possible; with 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.

*C. Barazzone, C. Casaulta, A. Mondan, P. Eng, G. Hafen, J. Hammer, A. Möller, D. Müller, N. Regamey, R. Spinas, J. Spalinger

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

T. Torresani1, R. Fingerhut1, S. Gallati2, M.H. Schoeni2, C.E. Kuehn2, M. Baumgartner2, J. Barben1 and the Swiss CF screening group* 1Swiss Newborn Screening, University Children’s Hospital, Zürich; 2Department of Pediatrics, University of Berne; *Institute of Social and Preventive Medicine University of Bern; 3Division of Paediatric Pulmonology, Children’s Hospital, St. Gallen

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 for the final CF diagnosis. All children referred to a CF center, 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 majority of parents (91%, 39/43) felt satisfied with the information received in the CF centre was, although 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, independent of the final CF diagnosis, were glad that the screening tests had been performed.


Free communications SGP/SSP

Newborn screening for cystic fibrosis in Switzerland – Feedback from parents

C.S. Rueegg1, J. Barben2, T. Torresani3, M. Baumgartner4, C.E. Kuehn3, for the Swiss CF Screening Group* 1Institute of Social and Preventive Medicine, University of Bern, Switzerland; 2Division of Paediatric Pulmonology, Children’s Hospital St. Gallen, Switzerland; 3Swiss Newborn Screening, University Children’s Hospital Zurich, Switzerland

Background: In January 2011, Switzerland started a pilot study on newborn screening (NBS) for cystic fibrosis (CF) as part of the Guthrie test. For final confirmation 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 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 (28/39). 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) felt 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.


Newborn screening for cystic fibrosis in Switzerland – How do patterns of wheeze change over the first 14 years of life?

Anina Pescatore1, Marie-Pierre Strippoli1, Ben Spycher1, Caroline Beardsmore2, Erol Gaillard3, Claudia Kuehn1, 1Institute of Social and Preventive Medicine, University of Bern, Switzerland; 2Department of Infection, Immunity & Inflammation, University of Leicester, United Kingdom

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 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 information on indicators of severity in the preceding 12 months (number of wheezing attacks, shortness of breath, sleep disturbance and activity disturbance due to wheeze), wheeze 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 became more frequent with age: time-related of breath (increasing from 54% at age 1 to 88% 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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Fourteen years of regional experience with respiratory syncytial virus in hospitalized children at the University Children's Hospital Bern, Switzerland
Philipp Aygemen1,2, Maria Teresa Barbani2, Christoph Aebi1,2, Andrea Duppenthermal1
1Department of Pediatrics, University of Bern; 2Institute for Infectious Diseases, University of Bern
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 variable predictability, influenced by local climatic 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.

Methods: Single center observational study of retrospectively (1997-2000) and prospectively collected data (2000–2011) on all pediatric hospitalizations due to RSV infections ≥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 (N = 323 vs. N = 292, p < 0.001). Infants younger (median age 4.5 months [IQR 1.7–11.7] vs. 5.6 months [IQR 2.2–8.9], p < 0.001) and infants born with 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.

Impact of prenatal diagnosis of congenital heart disease on neonatal outcome in a regional case controlled study (Canton of Vaud, Switzerland)
Marie-Claude Rossier, Alice Tornay-Alvarez, Karine Lepigeon, Yvan Mivelaz, Nicole Sekarski, Marie-Claude Addor, Yvan Vial, Erik Jan Meijboom
CHUV, Lausanne
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), 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 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) required 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 = TOP in 10 cases (all associated with chromosomal/ syndromal anomalies or other malformations), 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 chromosome/syndromal/other anomalies.

The Swiss Growth Registry: aims, methods and first results
Sommer G.1, Kuehni C.1, Karabulut F.1, Stettler C.1, Mullis P.E.2, for the Swiss Association for Paediatric Endocrinology and Diabetology*
1Institute of Social and Preventive Medicine, University of Bern, Switzerland; 2Children’s Hospital Berne, Switzerland
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 ± 6.75D (12.1–42.2). 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), diaphyseal dwarfism in 5% (N = 37) and other indications in 2% (N = 19). In total, only 2% (N = 17) of these patients are reported to have died.
Conclusions: 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.
Funding: Swiss Cancer League (KLS-02586-02-2010); EU-FP7 (call HEALTH-2007-3.1-5)

Neonatal Arterial Ischemic Stroke in Switzerland
Sebastian Grunt1, Lea Mazenauer2, Eugen Bolthausen2, Luca Remonda2, Kevin Wingierbe1, Andrea Capone Monti1, Möi Flüss2, Daniëlle Gubser-Mercart4, Elmar Keller5, Oliver Maier6, Claudia Poloni7, Gian-Paolo Ramelli8, Thomas Schmitt-Meche1, Peter Weber1, Maja Steinlin9,10
1Dep. of Neuropaediatrics, University Children’s Hospital, Berne; 2Dep. of Neuropaediatrics, University Children’s Hospital, Zurich; 3Dep. of Neuroradiology, Cantonal Hospital, Aarau; 4Dep. of Neuropaediatrics, Children’s Hospital, Zurich; 5Dep. of Neurology, University Children’s Hospital, Lausanne; 7Dep. of Paediatric Surgery, University Children’s Hospital, Geneva; 8Champagnayres 4, Neuchâtel; 9Dep. of Neuropaediatrics, Children’s Hospital, St. Gallen; 10Dep. of Neuroradiology, University Children’s Hospital, Basel
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 network of all participating physicians in Switzerland was performed by two experienced investigators. Clinical follow-up assessments were performed. Predictors of poor outcome (including symptoms, infant 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 other obstetric 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% resulted in anticonvulsive medication. Nonrespiratory 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 most likely due to the multifactorial etiology and pathophysiology of neonatal stroke. As a result larger scale multicenter case-control studies are mandatory.

The Swiss national registry of primary immunodeficiency diseases

**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 age at diagnosis is estimated to be 1–10 years, 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 PIDs 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 15,000 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 those 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 Swiss PIDs patients (80/177) 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 there are 89 documenting centres in Europe that have registered over 15,000 subjects since 2004, the Swiss National PID Registry can provide a basis for both national and international investigations and activities that aim to raise physicians' awareness of PID, allow better knowledge of the Swiss PID Registry Working Group University Children's Hospital Zürich, Zürich.

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

**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 antipporter) with an estimated overall incidence of 1:8,000. Patients 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 protocol for PIDs in neonatal and 1:1000, care 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 several European countries and 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 reviewed by external specialist consultants, unrelated authorities in the field of UCDs and practicing paediatricians in training.

**Results:** Although the evidence degree did not exceed level C (evidence from non-analytical studies like case reports and series), it was useful to set a sound basis and clear indications. This resulted in 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 studies.

**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.
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 (70–85) among those with score 3, 80–95% CI (78–85) among those with score 4 and 93–95% CI (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.

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


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, Phd, PhhE, LytB and PcpA), viral serology, nasopharyngeal culture and PCR for P. aeruginosa, 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 84.4 % for 3.15 ng/ml and 91.0% 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; 78/83% for high PCT/CRP combined with a positive urinary test and 88% for high PCT/CRP combined with virus negative.

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.

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

Thiongane A.1, Gehri M.1
Hôpital de l’Enfance, DMCP, CHUV, 1011 Lausanne

Introduction: Delayed diagnosis of community acquired pneumonia (CAP) potentially leads to increased mortality (developing countries) or morbidity (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 and 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 from 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.

Results: 20 patients included (median age 32 months), 3 with a severe pleural effusion, all immunized (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 mentioned by mothers and/or written in the medical report. Initial 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 mentioned by the mother; 2. Unnecessary diagnostic delays were potentially caused by

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

Anastaze Stelle K.1, Blanchon S.1, Monnard A.1, Ruchonnet-Metrailler I.1, Guindan S.1, Vidal I.2, Barazzago Argirocco C.3
1Pneumologie pédiatrique; 2Chirurgie pédiatrique, Hôpital Cantonal de Genève

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, antibiotic, oxygenotherapy and duration of hospitalization) and outcome.

Results: Sixteen children with a median age of 3.89 y (0.05–10) were included. 8/16 were previously vaccinated with Prevenar®. Main symptoms were fever (n = 15), cough (12), rash (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 findings (2) and clinical suspicions (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 thoracotomy (8). Pathogens were identified in 13/16 children: streptococcus pneumonia (n = 11), staphylococcus aureus (2) and others (3), including 2 co-infections. Intravenous antibiotic was given for a duration of 10 d (4–64): amoxicillin (n = 3), amoxicillin-clavulanate (9) and ceftriaxone (7). Total hospital stay was 10 d (5–120), 15/16 treated by intravenous antibiotic, 6 had a prolonged duration of 28 d (7–35). 3/16 patients had complicated outcome: right superficial lobectomy for persistent pneumothorax and pulmonary collapse, prolonged chest tube for broncho-pleural fistula, and prolonged hospitalization on mechanical 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 sequel of lung lost.

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

Ceroni D.1, Dubois Ferrière V.1, Anderson de la Llana R.1, Renzi G.2, Cherkoua A.2, Schrenzel J.3,4
1Pediatric Orthopedic Service, University Hospitals of Geneva, CH-1211 Geneva 14, Switzerland; 2Clinical Microbiology Laboratory, Service of Infectious Diseases, University Hospitals of Geneva, CH-1211 Geneva 14, Switzerland; 3Genomic Research Laboratory, Service of Infectious Diseases, University Hospitals of Geneva, CH-1211 Geneva 14, Switzerland; 4Institute of Microbiology, University of Bern, Switzerland

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 oropharyngeal 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. Oropharyngeal specimens were tested with a PCR assay specific for K. kingae.

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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 (79%) swabs from 74 other patients, were positive. The sensitivity, specificity, positive predictive value, and negative predictive value of the oropharyngeal swab PCR assay for K. kingae were 100%, 89.2%, 77.1%, and 100%, respectively.

Conclusions: Detection of K. kingae DNA in the oropharyngeal 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.

High Birth Weight: a Major Risk Factor for Developmental Dysplasia of the Hip
M. Schams
Division of Neonatology, Hirslanden Clinic, Zürich, Switzerland

The aim of this retrospective study was to investigate the influence of birth weight on the incidence of developmental dysplasia of the hip (DDH).

Methods: Between 1993 and 2003, ultrasonography (US) of the hips was performed in 7477 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 159 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 found in the highest morbidity factor requiring treatment (15.6%), followed by normal birth weight and breech presentation (76%), 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.

Optimizing radiographic control of gastric feeding tube placement in neonates
Quandt Daniel1, MeyerSchiffer Philipp2, Brouns Egle1, Schranner Thomas1, Bucher Hans Ulrich1, Arletzki Mieth Romaine1,2
1Clinic for Neonatology, University Hospital, Zurich, Switzerland; 2Department of Diagnostic Imaging, Children’s Hospital, Zurich, Switzerland

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: Neonates were given negative radiography with injection of 1 ml of air via lying gastric 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. Presence of correct and incorrect 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.

Bilateral thalamic lesions in a preterm female, incidental finding on routine cerebral ultrasound at first day of life
Liamlahi R.1, Landolt B.1, Scheer I.1, Das-Kundu S.1, Tomaske M.1
1Klinik für Kinder und Jugendliche, Städtische Klinik, Zürich, Switzerland; 2Klinik für Neonatologie, Universitätsspital Zürich

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 accompanied by 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 hypoplasic 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.
Cauliflower in a preterm brain

Daeoster C.1, Arlettaz R.1
1Clinic of Neonatology, University Hospital, Zurich

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 meningococcaemia, often with a fatal course. The diagnosis is made by the culture of blood and cerebrospinal fluid, but also by the typical and unique cauliflower-like pattern on cerebral ultrasound.

Discussion: Severe hemorrhagic pulmonary edema is associated with a high mortality rates in extremely preterm infants. If patients cannot be stabilized with conventional management, rFF may be an effective additional treatment option that should be discussed early.

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Neonatal distress syndrome due to congenital vocal cords paralysis

Département médico-chirurgical de pédiatrie, Hôpital du Valais, CHCVs, Sion

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.

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

Schätzle S.1, Berger T.M.1, Rischewski J.2
1Pediatric Hemato/Oncology and Neonatology, 2Children's Hospital Lucerne

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 results 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 (rFF7) 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, rFF7 may be an effective additional treatment option that should be discussed early.

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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

Denvraud V., Wildhaber J., Kaczala G.W.
Hôpital Fribourgeois, Service de Pédiatrie

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 corticosteroid shortening, 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 HNA-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.

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EXIT procedure for massive cervical lymphangioma

Gubler D.1, Berger T.M.1, Jöhr M.2, Winiker H.1, Hodel M.1
1NeolPS, 2Kinderkardiologie, Kinderchirurgie, Kinderpulmologen, Luzern, Switzerland

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 with potential upper airway obstruction. 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.

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 clamped 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. Local aspiration and sclerotherapy 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 extraterine life in patients with large neck masses that could otherwise lead to life-threatening upper airway obstruction immediately after conventional delivery.
A premature born girl and her inflammamson: why neonatologists and pediatrices must know CINCA? Eva Witz, P. Haberstich, H. Köhler, G. Berthet Klinik für Kinder und Jugendliche, Aarau

Background: Chronic infantile neurologic cutaneous articular (CINCA) syndrome is a rare chronic inflammatory disease characterized by neurologic-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 five the newborn developed arthritis of both knee and 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 Eculizumab (an IL-1 receptor antagonist) an antenataly on day 35, the inflammatory markers normalized, urticaria-like rash disappeared, arthritis improved and weight gain was appropriate.

Conclusion: Neonatologists and pediactrians should be aware of because CINCA might lead to severe deforming arthropathy, mental retardation, loss of peripheral vision, hearing loss, systemic arthritis improved and weight gain was appropriate.

Cow’s milk protein allergy in a premature baby: pitfalls in therapy
Sommer J., Martinez M., Paccoud D., Diebold P.
Hôpital du Châble, 1860 Aigle

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 cow’s milk protein and soy protein, there was a continuous worsening of anemia and the minimal Hb 87 g/L at 17 days of life and an increasing hematocritemia. 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 exclusion of cow’s milk proteins in the maternal diet was explained by the supplementation of maternal milk with FM85 that contains lactosomus 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 breastfeeding baby, enrichment with FM85 should be stopped.

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

Held-Egli K. 1 Glanzmann R., 1 Huemer M., 2 Filges I., 1 Schulze S. Departments of 1Neonatology, 2Metabolism, and 3 Medical Genetics, University Children’s Hospital Basel (UKBB)

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 “floppsy 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 mitochondrial enzyme 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 of 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 delay. 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: Floppsy 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, neuropaediatrics, geneticists, neonatologists and paediatricians is helpful in order to diagnose PDHCD. Given the severity of disease, ethical considerations are vital once diagnosis is established.

Coarctatio aortae in a neonate: dramatic presentation and positive outcome
Bellardi D., Nobile L., Pancaldi R., Castiglioni A., Facchini M., Buetti L.
Ospedale “La Carità”

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 arms, severe metabolic abnormalities, no respiratory distress or fever. His condition deteriorated quickly with progressive centralisation, diminished O2 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 cardiac-arrest that recovered within one minute under intubation and ventilation, brief cardiac massage and Adrenalin. The clinical suspicion of a ductus dependent congenital heart 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 with a coarctatio 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 murmur with peak femoral pulses or/a diastolic cyanosis) are often not detectable until the ductus is patent; closing of the ductus generally results in a cardio-vascular collapse. Neonates with left heart obstructive lesions frequent present with profound metabolic acidosis and shock, but can be resuscitated successfully with persistent organ system collaboration, the rule rather than the exception.

Failed neonatal resuscitation: the importance of post-mortem examinations
S. Angwardt, S. Hürlimann, T.M. Berger
Children’s Hospital of Lucerne and *LUKSS

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 rupture premature rupture of membranes at a 37-year-old G7/P1. A left-sided congenital diaphragmatic hernia had been diagnosed antenatally, but based on a

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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 esophageo-tracheal or esophageo-bronchial fistula was therefore suspected and an ETT was adventitiously 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.

**Posteri SGP/SSP – Neonatologie**

**Long term outcome after prenatal diagnosis of CAKUT**

Samuel Nef1, Thomas J. Neuhaus2, Giuseppina Sparrà3, Ritt Gotb5, Ulrich Willi4, Guido F. Laube8

1Universitätskinderspital Zürich; 2Kinderspital Luzern

**Background:** Congenital anomalies of the kidney and urinary tract (CAKUT) are 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 diagnosis of pregnancy duration, amniotic fluid, complications, fetal interventions dilatation >10 mm, calix dilatation or hydronephrosis. 2) “High risk” with bilateral (bil.) isolated pelvic dilatation with normal amniotic fluid: US within the first 2 days and prophylactic antibiotics immediately after birth, no chest excursions, the ETT was removed and bag-mask ventilation of life, she was intubated without apparent difficulties. However, when chest compressions were started and epinephrine was administered. Additional attempts at intubation and ventilation through the ETT were unsuccessful. Tracheal agenesis with an esophageo-tracheal or esophageo-bronchial fistula was therefore suspected and an ETT was adventitiously 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.

**Poster 16**

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


**Case report:** Baby, born by caesarean section, with Kristeller’s maneuver. Due to lupus anticoagulant Ab and a history of fetal loss, the aspirin was treated with multivitamin 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 cisterna 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. hematomata 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 antplatelet 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 antplatelet 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 maneuvers 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**

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

Chehade H., Cachat F., Faouzi M., Bardy D., Moug D., Meyrat J.B., Gao A., Girardi E.

Centre Hospitalier Universitaire Vaudois, Lausanne

The most widely used formula for estimating glomerular filtration rate (eGFR) in children is the Schwartz formula. It was revised in 2009 using ioheol clearance with measured GFR (mGFR) ranging between 15 and 75 ml/min x 1.73 m². 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 m² and is significantly less accurate for a GFR >103 ml/min x 1.73 m². 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 m² (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.
Renal Function Follow-up Evaluation Using Cystatin C in Neonates Prenatally Diagnosed for Congenital Anomalies of the Kidney and Urinary Tract

Parvex P.1, Combescure C.2, Birraux J.3, Rodriguez M.4, Wilhelms-Bals A.1, Girardin E.1
Pediatric nephrology unit 1, Division of clinical epidemiology 1, pediatric research platform 1, University hospital, Geneva, Switzerland

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 reparable as follow: 12 pelvic dilatations >10 mm; 5 hypo- dysplastic or ectopic kidney (2 with TCF2 mutation); 3 urethral valves; 1 uretherocoele; 1 megablabder. One of pts was start on dialysis 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%) <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 = 0.003). 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.

Development of Nephrocalcinosis in Preterm Infants

Das-Kundu S.1, Göttler S.1, Vehar S.1, Schraner T.1, Adams M.1, Bucher H.U.1
1Clinic for Neonatology, University Hospital Zürich; 2Department of Radiology, Childrens Hospital Zürich

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. 114 infants were recruited, 48 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 12 weeks. 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.

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

Kottanattu L.1, Bucher B.1, Tschumi S.1, Stritt A.1, Steinmann M.1, von Steiger N.2, Stephan R.3, Haechter H.3, Simonetti G.D.1
1Universitätssklinik für Kinderheilkunde, Inselspital, Bern; 2Institut für Infektionskrankheiten, Universität Bern; 3Institute for Food Safety and Hygiene, National Centre for Enteropathogenic Bacteria and Listeria, University of Zurich

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 *109/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 sterile 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.

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

Eberhardt Kati, Heininger Ulrich, Rudin Christoph
Universitäts-Kinderklinik beider Basel

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

Boksberger K., Rischewski J., Caduff J., Neuhaus T.J.
Kinderspital Luzern

Introduction: Children with idiopathic nephrotic syndrome (INS) are at increased risk of thromboembolic complications. Contributing factors include a high red blood cell count, hypervolaemia, 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 withheld 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-mer 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 antibodies against 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 eruptions and 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.

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

Liamthia R., Konrad M. 2, Schlingmann K.P. 2, Goetschel P. 1
1 Department of Pediatrics, Triemli Hospital Zurich; 2 University Children’s Hospital, Pediatric Nephrology, Münster, Germany.

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. This enzyme is responsible for renal male infant hypercalcaemia. 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 first 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. 1,25-(OH)2-D3 in the upper normal range. Nephrocalcinosis persisted, symptomatic nephrolithiasis occurred for the first time at the age of three years.

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Conclusion: Patients with INS are at risk of thromboembolic complications, in particular during a severe relapse, but also at the beginning of eruptions and 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.

Pseudohypoaldosteronism: A rare cause of failure to thrive in infancy

Sauteur M., Tonella P., Neuhaus T.J.
Kinderspital Luzern

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 hypoplasia, 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 diarrhoea and less appetite, had drank more frequently smaller portions, but had neither fever nor signs neither fever nor signs. 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 pyelo-ureteric junction obstruction (pyelonephritis 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 (10.2 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 CFU/ml). Intravenous therapy with ceftriaxone and amoxicillin, 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 (>2000 ng/ml) 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 an 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) and other bacteria. Tubular unresponsiveness to aldosterone with natriuresis is caused by combined action of cytokines in obstructive uropathy and bacterial endotoxins.

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

Heinrich B., Tomasse M., Goetschel P., Ambühl J.
Department of Paediatrics, Triemli Hospital Zurich

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 infection erythromelalgia, macrocytic polynucleocytes with signs of 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-haemolytic 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 (8470 mU/L, norm: 5–47) and high aldosterone (16312 ng/l, norm: 29–182). 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 substitution for urinary infection was stopped at 5 month. Micturating cystourethrogram 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: (Atebrile) 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 results in secondary pseudohypoaldosteronism. Urine diagnosis is crucial. Prompt clinical improvement occurred with antibiotic therapy and oral salt supplements. Miliaria rubra reinforces the diagnosis.
from a peripheral hospital with vomiting, dehydration, failure to thrive
A one month old female infant was transferred as it leads untreated to life-threatening electrolyte imbalance.

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 concentration was the mid-range for newborns with 2314 pmol/l (277–4995). 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 fludrocortisone 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 hyponatraemia and hyperkalaemia hypoaldosteronism should be promptly considered, since in this age group the salt-water homeostasis depends almost entirely on mineralocorticoids and their synthesis defect of aldosterone. It is relevant in newborns and infants with this rare disease, this ratio seems to be a reliable diagnostic parameter in this age group as well.

Molecular analysis of the 21-hydroxylase encoding gene CYP21A2 in patients with congenital adrenal hyperplasia
Saller E1, Filges F1, Dutly F1
1IMD, Institut für medizinische & molekulare Diagnostik, Rautistrasse 13, 8047 Zürich; 2Medizinische Genetik, Universitäts-Kinderklinik beider Basel, Felix Platter-Spital, Haus J, Burgfelderstr 101, 4012 Basel

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 1:15'000 newborns and depending on the mutation causes a classic CAH form with severe virilisation 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 pseudogene 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 newborns 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 this specific point 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.

Concomitant Blepharophimosis-Postis-Epicanthus Inversus Syndrome (BPEIS) and Congenital Adrenal Hyperplasia (CAH) in a young girl
M. Decarli1, D. Isenes1, M.-C. Addor1, S. Stoppa1, F. Phan-Hug1, N. Pitteloud1, M. Hauschild1
1Unite d’endocrinologie-diabetologie pediaetrique; 2Gene+etique medicale, CHUV, Lausanne

Introduction: The Blepharophimosis-Postis-Epicanthus Inversus Syndrome (BPEIS) 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 mmol/l, N <3.5). Adrenocorticotropin stimulation-test confirmed the diagnosis of CAH (17-OH-P max 141 mmol/l). Genetic testing demonstrated an inherited heterozygous compound form with a gene conversion in the intron 2 (1685G>T) in exon7 of the CYP21 gene, consistent with CAH (simple virilisation). 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.

Not a coincidence: Diabetes mellitus in patients with renal, genital and other abnormalities (MODY 5)
Scheidegger UA, Laux R, Marx G, Kluckert Ch., L’Allemand D.
Ostschweizer Kinderspital

Background: HNF1α is a transcription factor involved in the development of pancreas, kidney, gut, liver, lung, neural tube, and internal genital structures. A defect in HNF1α causes structural and functional renal abnormalities as well as diabetes mellitus due to pancreatic malformations (Renal Cyst and Diabetes Syndrome, MODY 5).

Case reports: Case 1 is a 10 year old girl with history of bilateral multicystic 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 agenesia of pancreas tail. Gene sequencing confirmed the suspected diagnosis of HNF1α 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 small 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/gluicosuria should be sought in patients with otherwise unexplained structural or functional kidney abnormalities, as HNF1α mutations account for 14% of renal abnormalities, around half of which also cause diabetes mellitus. – The combination of diabetes mellitus and kidney or pancreatic abnormalities as should raise suspicion of 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 hypoglycaemic agents are mostly ineffective.

Five years follow-up of a patient with severe congenital hyperinsulinism
T. Cortiglano1, M. Bickle Grazi1, M. Roth-Kleiner1, F. Phan-Hug1, N. Stoppa-Vaucher1, M. Hauschild1
1Endocrinologie-diabetologie pediatrique; 2Unité de Développement, Service de Néonatologie, CHUV Lausanne

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 macromosaic (4640 gr (>90)) female newborn was delivered at term after uneventful pregnancy by cesarean 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 unexplained insulin (45.4 mU/L; N <2.8) in the absence of ketone bodies confirming the diagnosis of congenital hyperinsulinism. Initial treatment with subcutaneous 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 pathogenic c.530>T; c.888C>G on gene ABCC8). A 18F-DOPA PET-scan performed at 1½ years of age couldn't accurately differentiate between focal and diffuse type of the disease. The evolution was excellent with normalization of 18F-DOPA uptake 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.

Poster SGP/SSP – Nephrology – Endocrinology – Diabetology

Severe Acne Conglobata after Treatment of Constitutionally Tall Stature

Fluri S, Perruchoud D², Rossi C¹, Roten H¹, Kernill D²
1. Abteilung für Pädiatrie, Departement Frau&Kind, Spitalzentrum Oberwallis, Spital Wallis, 3930 Visp; 2. Universitätsklinik für Dermatologie, Inselspital, 3010 Bern

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 which was treated successfully in Oxford, 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, hypertrichosis. Onset of puberty, growth spurt and pubic hair growth is psychologocal 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 was demonstrated in our cases.

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.
excluding implausible values. Multiple regressions analyzed disease predictions 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 disprove the level of overweight, suggesting that Pediatric Emergency Services could be excellent "sentinel sites" for obesity-malnutrition surveillance.

Acute changes in secretion of the hormone amylin following a meal challenge in lean and obese adolescents
S. Beglinger, S. Graf, C. Beglinger, U. Zumsteg
Clinical Research Centre, Department of Biomedicine and Division of Gastroenterology, University Children’s Hospital and University Hospital Basel, Switzerland

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/m²) and 16 were obese (6 males, 8 females; mean age = 13 years, BMI range = 31–41 kg/m²). 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.

Quality of life of young adults treated with Recombinant Growth Hormone during childhood
Karabulut F.1, Sommer G.1, Mullis P.-E.2, Kuehni C.E.3
1Institute of Social and Preventive Medicine, Bern; 2Children’s Hospital, Inselspital Bern

Introduction: Recombinant human Growth Hormone (rGH) 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 rGH. 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 rGH 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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New Genetic Tests: What is the impact in patients with mental retardation with/unwithout dysmorphic traits from the southern part of Switzerland
S. Capobianco S.1, A. Ferrarini A1., N. Dukanak N1., Pifferini R.1, Martinet D.1, Ramelli GP1
1Servizio di Pediatria, 6500 Bellinzona; 2Service de génétique, CHUV, 1011 Lausanne.

Introduction: Children with mental retardation are commonly encountered in child clinics and establishing an etiological diagnosis is a challenge for pediatricians. The new ARRY Array based Comparative Genomic Hybridization (array-CGH) is a revolutionary approach which 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.

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.

When 36 is bigger than 63: Numbers in the brain of children with developmental dyscalculia
Karin Kucian1,2, Ernst Martin1,2, Ruth O’Gorman1,2, Michael von Aster1,2,3
1Center for MR-Research, University Children’s Hospital Zurich; 2Children’s Research Center, University Children’s Hospital Zurich; 3Center for Integrative Human Physiology, University of Zurich; 4Department of Child and Adolescent Psychiatry, German Red-Cross Hospitals Westend Berlin, Germany

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 dyscalcic 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 dyscalcic 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 neuronal plasticity learning efforts in affected children and further enhance the prospects of linking changes in brain structure to educational experimental manipulations.  


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

S. Prader1, T. M. Berger2, D. Morgillo2, J. Caduff3, T. Schmitt-Mechelke1
1Division of Neuropediatrics, “Neonatal and Pediatric Intensive Care Unit, Division of Radiology, Children’s Hospital of Lucerne.

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 1996 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 27.37 weeks (range 23.67 – 32.97 weeks) with a median birth weight of 1063 g (range 560 – 1950 g). Median age at the end of followup was 5.6 years (range 12 months – 10 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 neurosensorimotor 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 PVHI.

Myotonic dystrophies – analysis of incidence, age of presentation and primary symptoms of myotonic dystrophy population of the central part of Switzerland from 1995–2010

Ronald Jager1, Petra Kolditz1, Thomas Schmitt-Mechelke1
1Kinderspital Luzern

Introduction: Myotonic dystrophy type 1 (DM 1, M. Curschmann-Steinert) is a complex multisystem disorder caused by a dynamic mutation of the DMPP-gene on chromosome 19. In the pediatric population, it manifests with neuromuscular, cognitive, gastrointestinal or unspecified 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 severe muscular hypotonia/ respiratory insufficiency and/or feeding difficulties. The remaining children were diagnosed around 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 deformities (n = 1), and other symptoms (n = 1). The mean age for diagnosis after the neonatal period was 3.6 years (range 0.6–7.3). In 3 cases, the diagnosis was made sympathetically. For the last follow-up, all patients confirmed 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 counselling, myotonic dystrophy should be considered in children with psychomotor retardation, “mystaphic” facies, skeletal muscle weakness, incontinence, unexplained feet deformity or gastrointestinal symptoms.

isolated neonatal bilateral palsy of the n. radialis

Böhringer E, Weber P. Neuropädiatrie UKBB, Basel

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 radial 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 radial 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 few cases of bilateral radial palsies 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 for aspiration or ecchymosis at the time of the 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.

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

Ch. Zegg1, E. Giger1, M. Lori2, B. Heiland3, R. Wirth4, R.I. Hassink1
1Center of Developmental Advancement and Paediatric Neurorehabilitation of the Wildenmüh Forest Foundation, C.D.N. Biet, Switzerland

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: To assess 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 eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) and ω-6 fatty acid (γ-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.
Mutism in Adeno-/Rhinovirus Encephalopathy with a Reversible Splenial Lesion: A Case Report

Andrea Pauli1,2, Thomas Joder1, Margrit Balbi1, Thomas Schmid-Melin1,2
1Medical Faculty of Bern, University of Bern; 2Neuropediatric Department, Childrens Hospital Lucerne; 3Radiological Department, Cantonal Hospital Lucerne; 4Developmental Psychology/Neuropsychology, Childrens Hospital Lucerne

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 a 3-day history of fever (Glasgow Scale 0), 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 callosum 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 day, 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.

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

Perron E.1, Strozzi S.1, Tschumi S.1, Gerull R.3, Bingell R.4, Gralla J.1, Grunt S.1
1Departments of Paediatric Neurology; 2Paediatric Nephrology, and 3Paediatric Intensive Care, University Children’s Hospital, Berne; 4Clinic for Neurosurgery and 5Department for Diagnostic and Interventional Neuroradiology, University Hospital Berne

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 hypertension (P 180/110 mmHg) and urinary retention. laboratory examination revealed a pulmonary infiltrate. Suspected pneumonia was treated with intravenous rehydration and antibiotics. Additional severe hyponatraemia, mild metabolic acidosis and renal failure were ascribed to dehydration. Because of persisting somnolence, dystonia, hyperthermia, hyponatremia 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 10 days with supportive therapy. Treatment of 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 dystonia 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 (idiopathic) treatment. Early diagnosis and prompt recognition has important therapeutic consequences.
Familial macrocephaly – not always harmless
K. Zimmermann, T. Schnitt-Mechelke, J. Rischewski, B. Steiner
Kinderspital Luzern, Pädiatrische Klinik

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 macrocephaly. We report a case of familial macrocephaly, which, combined with other clinical signs, led to an 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 multiple cancers.

Case report: A boy, born at term after an inconstant 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 postures. Physical therapy 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 enhanced tumour of the 4. ventricle with mild ventricular dilatation due to occlusive hydrocephalus. The boy underwent complete resection of the tumour which was classified histologically as a WHO IV megdulloblastoma 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 PTC121-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 megaloblastoma, cranial MRI should be performed in infants at risk.

Headache, unilateral facial nerve palsy and arterial hypertension: atypical presentation of an otherwise well known neurological disease
Sandra Waldmeier, Florence Martin, Eva Brack, Karin Baumgartner, Andrea Capone Mori
Klinik für Kinder und Jugendliche, Kantonsspital Aarau

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 a 15-year-old girl with a history of unexplained neurologic symptoms. On admission his clinical examination was nearly normal. A repeated brain MRI showed 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 neurological syndrome. Our patient was classified on the basis of a new phenotype characterized by attacks of facial, unilateral peripheral facial nerve palsy and arterial hypertension. This report adds to the phenotype of the syndrome and performs a literature review on this topic.

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 eye deviation, brisk deep tendon reflexes and bilateral Babinski sign. Lumbar puncture was hemorrhagic, and blood sample showed: PCT 50 mcg/l, WBC 6.9G/l. Intravenous antibiotherapy and acyclovir was administered. After 72h the patient was transferred to the ICU with artificial ventilation for 5 days and received high dose methylprednisolone for 10 days. His persistent headache, a newly occurred unilateral peripheral facial nerve palsy, areflexia and ataxia was seen on the follow-up after 4 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: ACE is a potentially fatal acute encephalopathy characterized by rapid alteration of consciousness ± epileptic seizures after viral illnesses (Influenza, ...). 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 thalamai with variable involvement of the white matter, basal ganglia, brainstem or cerebellum. Rapid recognition can allow a good outcome by initiating corticotherapy immediately. 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.

Acute encephalopathy with fever: look at the thalami!
M. Jacquier-Goetschmann1, E. Roulet Perez2, C. Polon2, AS. Knoepfli3, S. Lebon2
1Service de pédiatrie, CHUV; 2Service de neuro-pédiatrie, CHUV; 3Service de radiodiagnostic et radiologie interventionnelle, CHUV

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 eye deviation, brisk deep tendon reflexes and bilateral Babinski sign. Lumbar puncture was hemorrhagic, and blood sample showed: PCT 50 mcg/l, WBC 6.9G/l. Intravenous antibiotherapy and acyclovir was administered. After 72h the patient was transferred to the ICU with artificial ventilation for 5 days and received high dose methylprednisolone for 10 days. His persistent headache, a newly occurred unilateral peripheral facial nerve palsy, areflexia and ataxia was seen on the follow-up after 4 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.

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A complicated rota-story
Annette Roggen1, Marc Effeney2, Ilkbel El-Faleh3, Danielle Gubser-Mercat3, Christian Weisstanner3, Barbara Goeggel Simonetti4, AS. Knoepfli3, S. Lebon2
1Department of Paediatrics, Inselspital, University of Berne; 2Department of Paediatrics and 3Paediatric Neurology, Hôpital Pourtalès, Neuchâtel; 4Department of Diagnostic and Interventional Neuroradiology, and 5Division of Paediatric Neurology, Inselspital, University of Berne, Switzerland

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

Refractory epilepsy and ring chromosome 20 syndrome
N. Grunauer1, M. Kurian1, C. Menacher, C. Korff1, J. Fluss2, HUG1, Clinicne Grangette2

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 an 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 controlled 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 atonic seizures, a karyotype was performed that confirmed the diagnosis of ring chromosome 20.

Discussion: Ring chromosome 20 epilepsy syndrome is a rare and possibly underdiagnosed neurological 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.
comparisons, due to both direct infection and immune-mediated neuronal dysfunction, are considered to be rare with seizures occurring in 4% and meningoencephalitis 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 they 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, evolving the differential diagnosis of an encephalitis or 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 cystic area in the mesial temporal lobe.

**Conclusion:** The role 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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**Acute psychotic disorder – what else matters?**

**Jakob D., Cavegn R., Stelmini M., Bürki S.**

**Kinderklinik Bern, Abteilung für Neuropädiatrie**

**und Kinder- und Jugendpsychiatrie**

**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 described 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 months short episode, 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, ataxic dyskinesia and autonomic instability. Lumbar puncture test results were unsppecific 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 anti-epileptic propofol were initiated, with continued clinical outcome is highly dependent on an early diagnosis and timely immunotherapy without delay.

**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 for the differential diagnosis of first-episode psychosis. Timely diagnosis and adequately treated outcome can be expected to be good.
Fetal cholelithiasis – prenatal findings and postnatal outcome
Schlueckerb1, D., McLin1 V. Département de l’enfant et de l’adolescent Unité de Gastroentérologie pédiatrique1, HUG Genève

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%.

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.

Laboratory investigations: There was no significant perturbation in serum aminotransferase levels or conjugated bilirubin levels.

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 be necessary until resolution is demonstrated by abdominal ultrasound.

Non-resolution by 3 months of age should lead to work up for underlying choledocal cyst, newborn hepatitis, and congenital hypothyroidism in familial brain-lung-thyroid syndrome
Graf S., Bösch N., Zumsteg U., Heinimann K., Szinnai G. Paediatric Endocrinology and Medical Genetics, University Children’s Hospital Basel UKBB

Background: Brain-lung-thyroid syndrome is characterized by the combination of congenital hypothyroidism (CH), benign hereditary choledochal disease, and surfactant deficiency at birth. It is caused by mutations in the homeobox containing transcription factor NK homeobox 2 (HBCD). Two clinical presentations of 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 and neonatal hyperbilirubinemia. Choledochal cyst is an associated finding in 40% of patients.

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 athyrosis. LT4 was started at day 6 of life. Despite good compliance and normal TSH and FT4 under LT4, he developed progressive hypothyponia during the first year of life, evolving to severe cholecystoatrophic 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 wheelchair dependent. The combination of hypochoeosthenosis 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 choledochal disease is pathognomonic for the syndrome. 2. Hypothyroidism of NKX2-1 may result in autosomal dominantly inherited brain-lung-thyroid syndrome. 3. Unexplained unfavorable neurological outcome in patients with CH despite adequate substitutive therapy may be due to NKX2-1 gene defects.

Gowers’ sign in a 3-year-old boy
Barbara Kuehling1, Sergio Stocker2, Andrea Klein2, Rotraud Saurenmann2
1Kinderarztpraxis Dr. Sergio Stocker, Schaffhausen; 2Department of Paediatric Neurology and 2Department of Rheumatology, University Children’s Hospital, Zurich

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: – the 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.

Infliximab induced dermatologic complications in Adolescents with Crohn’s Disease: A report of 3 cases
Grunder F., Kentland K.1, Spalinger H.1,2, Kayawak N.2, Bissig D.1, Schibli S.1
1Medizinische Kinderklinik Inselspital; 2Kinderklinik Luzern; 3Dermatologische Klinik Inselspital

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 adalimumab. 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-year-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-year-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 seborrheic 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.

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**Eosinophilic colitis as a risk factor for protein – losing enteropathy**

**Bregy J.1, Röthlin-Hotz R.1, Vosbek J.1, Spalinger J.1**

1Pathologisches Institut LUKS

**Background:** A subset of patients with eosinophilic enteropathy develops hypoaibuminemia 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 always present. The diagnosis is confirmed by the finding of increased faecal concentrations of alpha-1-antitrypsin (α-1AT).

**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 was 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/ml). No proteinuria or haematuria was found. stool test was negative for bacterial or viral infections, but an elevated serum calprotectin. Patients suspected for a CD should undergo digestive panendoscopy to confirm diagnosis.

**Conclusion:** Acute symptoms with high fever and elevated CRP do not exclude CD, neither do so young age, absence of aphthous stomatitis or perianal disease, normal ESR or elevated fecal calprotectin. Patients suspected for a CD should undergo digestive panendoscopy to confirm diagnosis.

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**Giardiasis with protein losing enteropathy**

**Menhem M., Marczo J.-P., Cheseaux J.-J., Lor J., Taib A.**

Département de pédiatrie – CHUV, Lausanne

**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 hypoaibuminemia.

**Case Report:** A 2 y old boy 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 anaemia (Hb 98 g/l) with normal ESR, and hypoaibuminemia (42.3 g/l). Hepatic, renal and cardiac causes 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 hypoaibuminemia. 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**

**Vieten H.-K.1, Braegger C.P.2, Kropp B.2, Bühler P.2, Prim J.3, Tomaszke M.1**

1Klinik für Kinder und Jugendliche und 3. Institut für Radiologie Stadtpalast Triemli, Zürich; 2Abt. für Gastroenterologie & Ernährung, Universitäts-Kinderklinik Zürich

**Introduction:** In the pediatric emergency department vomiting is a common symptom, mainly related to acute gastroenteritis. However, if distress, fever and vomiting, a variety of entities need to be considered. Gastrointestinal (GI) obstruction due to a bezoar resulting from accumulating nonabsorbable 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. 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, lack of previous GI obstruction, and food intolerance. 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 pathophysiological process. Available treatment methods include chemical dissolution, endoscopy or surgery.
Intussusception following appendectomy: a case report

Haddon J., Panchard M.A., Ramseyer P.
Service de pédiatrie, hôpital du Samaritain, Vevey, Suisse

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 uneventful 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 GI, CRP 34 mg/l and 1379 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 pyocolical dilatation 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 emedematous 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.

Multiple Magnet Ingestion in Children

D. Cholewa, R. Fierling, S. Berger, J. Hoeffe
Department of Pediatric Surgery University Bern, 3010 Inselspital Bern

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.

Discussion: 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 the health-care providers to have a high degree of suspicion for potential foreign body ingestion in any child with persistent unspecified abdominal symptoms, such as isolated vomiting or unspecified 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.

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.

Magnet Ingestion: A Dangerous Attraction

Mapelli E., Rahal E., Van Wingham J., Reinhard L., Wildhaber B.E., Lacroix L.
Hôpitaux Universitaires de Genève; Hôpital de La Tour, Genève

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 the health-care providers to have a high degree of suspicion for potential foreign body ingestion in any child with persistent unspecified abdominal symptoms, such as isolated vomiting or unspecified 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.

Results: From January 1st to December 31st 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.

Arterial switch: medium-term outcome of neoaortic root and peripheral pulmonary arteries
Sekarski N.1, Nebel C.1, Mivelaz Y.1, Di Bernardo S.1, Département de pédiatrie, CHUV Lausanne

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 switch 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 and years postop. PPS: The normal range 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.

Conclusion: Neoaortic root dilatation and PPS are common problems after arterial switch operation and need close follow-up in these patients.

Cardiogene: an innovative multidisciplinary consultation for genetic arrhythmias
Sekarski N.1, Schlaper J.2, Di Bernardo S.1, Boulos T.1, Mivelaz Y.1, Michael K.1, Bhujian Z.2, Failmann F.1, Département de pédiatrie1, Service de cardiologie2, Institut de médecine légale2, Service de génétique1 CHUV Lausanne

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), catecholaminergic 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 in 1 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 promises 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.

Scimitar Syndrome – clinical presentation, management and outcome
Hoop R., Oxenius A., Greutmann M., Valsangiacomo Büchel E.1, Universitäts-Kinderklinik Zürich, Universitätsspital Zürich

Introduction: Scimitar syndrome (SS) is defined by a partial or complete anomalous pulmonary venous drainage of the right lung into the inferior vena cava with various additional cardiovascular 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.

Methods: 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 (5–30 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 operated pts (50%) significant obstruction or 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.

The Swinging Heart
Cavigelli-Brunner A.1, Hoop R.1, Pachlkonj J.2, Dave H.2, Güngör T.1, Kretschmar O.1
1Kardiologie, 2Immunologie, 3Kardiochirurgie, Universitäts-Kinderklinik Zürich

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.

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An exceptional cause of sudden death in infants: histiocytoïd cardiomyopathy

Sekarski N.1, Di Bernardo S.1, Schlaffer J.2, Mivelaz Y.2, Barras N.1, Boulou T.1, Cotting J.1, Perez Marie-Hélène1
Département de pédiatrie1, Service de cardiologie2, SMUR3, CHUV Lausanne

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 adrenaline she regained sinus rhythm. Upon arrival at the hospital lactate was 14. She recovered rapidly without neurological sequelae. 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-Purkinje tachycardia. Intravenous betablockers were introduced without recurrences of arrhythmias. However 48h later she presented extensive ischemic bowel disorder, sepseis 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 heart disease and right ventricle (RV) compression of the right atrium (RA) and right ventricle (RV). 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. 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

Theodoropoulou A.1, Gallardo C.1, Panchard M.A.1, Cachat F.1, Mivelaz Y.2, Di Bernardo S.2
Department of pediatrics, Hôpital Riviera, Vevey1; Department of pediatric cardiology, CHUV, Lausanne2

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, cyanotic and in severe respiratory distress, with evidence of fluid overload and signs of cardiogenic shock. Blood pressure was 90/60 mmHg and pulse pressure 30 mmHg. Laboratory tests revealed leukocytosis (13.000/mm3) and elevation of cardiac enzymes (cardiac troponin 53 ng/l, creatine kinase MB 96 ng/l). ECG showed atrial flutter with a rapid ventricular response and signs of ventricular hypertrophy. Given the clinical severity, a pericardiocentesis was performed, which revealed 1500 ml of hemorrhagic-serous fluid.

Conclusion: Cardiogenic shock due to myopericarditis as a presentation of H1N1 influenza A virus infection 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.
Comparison of different brushing techniques to obtain nasal epithelial cells from human subjects
A. Stokes1,2, E. Kieninger1,2, B. S. Kopf1,2, C. Casaulta1, N. Regamey2, M. P. Alves1,2
1Division of Paediatric Respiratory Medicine, University Children’s Hospital, Bern, Switzerland; 2Department of Clinical Research, University of Bern, Bern, Switzerland

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 ±0.0001) than by swabs (5.4 ±0.0001) and curettes (1.3 ±0.0001). Viability was higher for cells obtained using curettes (54 ±29–68%) and swabs (54 ±16–69%) compared to brushes (42 ±15–70%). Cell counts determined by brushes grew fastest (6 ±0.0001), followed by cells obtained by curettes (11 ±0.0001) and swabs (19 ±0.0001). Success rate in establishing primary cell cultures (100% confluent cell layers within 21 days in a 12.5 cm² cell culture flask) was 85% 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 technique is the nasal brush.

Arterial stiffness in asthmatic children
Steinmann M, Regamey N, Casaulta C, Latzin P, Abbas C, Singer F, Simonetti G.D.
Division of pediatric pneumology and Division of pediatric nephrology, University Children’s Hospital Bern, Inselspital, Bern, Switzerland

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 4.5–15 years, mean FEV1 86.4% predicted) and 35 healthy children (10 female, median age 11, range 4.5–15 years, mean FEV1 103.4% predicted). PWV was inversely related to FEV1 (R² = 0.23, p = 0.003) and to MMEF 25–75 (R² = 0.17, p = 0.01), but was not related to FeNO. Age, gender and FEV1 remained significantly associated with PWV in multivariable regression analysis adjusting for possible confounders including body mass index, blood pressure and gender 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.

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 function which may lead to cardiogenic shock requiring inotropic support. In our case the presentation was atypical with early symptoms of cardiac involvement (3rd day), absence of fever and no significant ECG abnormalities. This case reminds us 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.

Arterial stiffness in asthmatic children

Diagnostic value of nasal NO measurement using the NIOX MINO device
Selina Sommermatter1, Christian Geidel1, Alexander Möller1, Günter Menz2, Roger Lauener3, Andreas Jung1, 2, 3
1Christine Kühne – Center for Allergy Research and Education (CK-CARE); 2Hochgebirgsklinik Davos, Zentrum für Kinder und Jugendliche; 3Kinderspital Zürich, Abteilung für Pädiatrische Pneumologie

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 nitric oxide (nNO). However, no data on accuracy and quality of the measurements are

Arterial stiffness in asthmatic children

Diagnostic value of nasal NO measurement using the NIOX MINO device

Poster SGP/SSP – Pulmonology

Poster SGP/SSP – Cardiology
available. This study aimed to compare nNO measurement with the NIOX MINO to the NIOX FLEX gold standard device. 

Methods: Nasal nNO 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 test with subjects holding their breath (BH), followed by a test 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 healthy children (age 54, 16–68 yrs) were included, 42 of them had both a valid BH and TB NIOX FLEX test. No optical quality control (nNO, CO2 or air flow curve) was available for the NIOX MINO. A BH test with the NIOX MINO requires a breath hold of 45s, which often results in breath hold inability (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 (quantiles) nNO levels were 861 (670, 1147) ppb for NIOX FLEX vs. 657 (445, 780) ppb for NIOX MINO, whereas median nNO values for the TB technique were 867 (692, 1187) ppb vs. 687 (537, 865) ppb.

Conclusion: Nasal nNO values in healthy subjects are generally lower when the NIOX MINO is used, compliant 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.
acid gastro-oesophageal 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 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.

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**Educational problems in school-aged childhood cancer survivors and siblings**

Laura Wengenroth1, Corina Rueegg1, Micòl Gianinazzi1, Gisela Michél1, Eva Bergstraesser2, Nicolas von der Weid3, Claudia Kuehn3

*1Institut of Social and Preventive Medicine, University Bern; 2University Children’s Hospital, Zurich; 3Children’s University Hospital, University Lausanne

**Objectives:** Diagnosis and treatment of childhood cancer often occurs during school years and the patients may encounter educational problems. So far, little is known how 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 weeks before 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.

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**

Mattielo V., Larigaldie S., Zarra S., Ceroni D., DeCoulon G., Gumy-Pause F., Ansari M., Ozsahin H

*Department of Pediatrics, University Hospital of Geneva (HUG): 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 (spondylophytosis, 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 following: Hb at baseline >150 g/L, uncontrolled hypertension or

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

Gisela Michél1, Stefan Essagi1, Nicolas von der Weid1, Claudia Kuehn1

1Schweizer Kinderkrebsregister, Institut für Sozial- und Präventivmedizin, Universität Bern, Schweiz; 2Centre Hospitalier Universitaire Vaudois, Pediatric Hematology-Oncology Unit, Lausanne, Schweiz

**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

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**Bleeding Disorders in Noonan Syndrome**

S. Prader1, S. Kroiss2, W. Knirsch2, O. Speer1,2, M. Schmugge1

*Division of Haematology, Division of Cardiology, University Children’s Hospital Zurich; 2Children’s Research Center, University of Zurich

**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 comorbidities. 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.
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 about 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 specialties. Most respondents reported to use guidelines (89%) Activities were according to guidelines, but required 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 programme).

**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 up programmes according to needs of countries, institutions and survivors. Funded by SNF-Ambizione-grant PZ00P3_121682/1.

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

Müller D., Bergsträsser E., Gobel R., Schweigmann G., Sennhauser F.H.

Kinderspital Zürich, Universitäts-Kinderkliniken

**Introduction:** Ewing’s sarcoma (ES) is a rare however well-known 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 of ES arising in the renal area.

**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 health. Elevated C-reactive protein (180 mg/l) and micro-haematuria with a positive coagulation test were found. Ultrasound revealed two lesions of the right kidney (largest diameter 4 and 2.6 cm), both with small fluid filled cysts and faint vascularity. Further diagnostic including computed tomography of the abdomen revealed discrete contrast enhancement of one of these intralesional 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. The lesions remained unaltered 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 extraskeletal ES. Adjuvant chemotherapy to nephrectomy 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.

**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 appendix. 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 the right femur in association with bone. MRI revealed a 2.8 x 2.7 x 3.5 cm measuring tumor in the region of brachialis and fector digitorum superficialis muscles with involvement of the medine nerve. A marked reduction of the lesion was achieved. Complete surgical removal avoiding injury to the medine 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 is unclear. Innovative therapeutic trials are warranted to demonstrate progress in this field of medicine and to confirm results which have been achieved in our patient.

**Poster SGP/SSP – Oncology – Haematology**

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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)

Jager R1, Kremer Hoffing J.A.1, Rischewski J.1
1Pediatric Hemato-/Oncology, Children’s Hospital Lucerne; 2University Clinic of Hematology and Central Hematology Laboratory, University Hospital Bern

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-oligomers in the plasma (defining “2A”) and a specifically aberrant pattern of multimer (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 treated during the last five months and suffered from epistaxis 3–5x a week since the age of 15 months. There was no other history or signs of bleeding. A blood test in May 2011 showed a severe iron deficiency (Hb 56 g/l). A history of recurrent epistaxis was referred. A variety of blood counts showed recurrent epistaxis in the father during childhood. Clinically he was a 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 vWShield-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 of 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 anaemia was corrected and the epistaxis disappeared. Newborn K. had a minor decrease in laboratory parameters, however the parents had a follow up visit after the first birthday and therapy was interrupted. K. does not suffer from epistaxis any more. He is 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. begins 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 decompensation combined with lower thoracic laminectomy and placement of a syringostabaknoid 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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Basal ganglia germinoma in a 6-year-old boy – a diagnostic challenge

S. Prader1, J. Rischewski1, K. Kothbauer2, I. Steurer2, L. Marian1, C. Ares1, T. Schmitt-Mehrelke1
1Children’s Hospital Lucerne; 2Division of Neurosurgery; 3Radiological Department Cantonal Hospital Lucerne; 4Neurosurgery Children’s Hospital Basel; 5Center for Proton Therapy, Paul Scherrer Institute, Villigen

Background: Basal ganglia germinoma are very rare malignant CNS tumours almost exclusively observed in South East Asia. Due to the lack of diagnostic features on neurological examination a correct 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 off the left hemisphere and a small malformation of the corpus callosum as well as slight abnormalities of the left basal ganglia. A cranial CT scan revealed calcification of the lesion. Cerebral 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. Decisive chemotherapy and fractioned cranial 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 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

S. Prader1, N. Gerber, U. Mühler1, C. Kellenberger1, M. Grotzer2
1Division of Oncology, 2Department of Paediatric Surgery, 3Department of Diagnostic Imaging, University Children’s Hospital Zurich

Purpose: To describe symptoms, diagnostic features, treatment and outcome of pneumatisis intestinalis (PI) in a child being treated for acute lymphoblastic leukaemia (ALL).

Case report: After being diagnosed with acute lymphoblastic leukaemia (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 intraperitoneal gas in the venous gasous vein 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 small intestine. 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, abdominal sonography revealed intraperitoneal gas in the venous gasous vein 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 small intestine. 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.
Fatal hyperammonemia following autologous hematopoietic stem cell transplantation

Alexander Laemmle, Matthias Gautschi, Giacomo Simonetti, Sarah Bürki, Bendicht Wagner, Sonja Lüer, Jean-Marc Nuoffer, Kurt Leibundgut

Department of Pediatrics, University of Bern, Bern, Switzerland

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.

Hyperleukocytosis and its role in the Pediatric Emergency Department

Dr Lynda Vandertuin¹, Dr Laurence Lacroix¹, Dr Elisa Mapelli¹, Dr Hulya Ozsahin¹, Dr Marc Ansari¹, Pr Alan Gervaix¹
¹Service d'Accueil et d'Urgences Pédiatiques, Hôpitaux Universitaires de Genève

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 fresh frozen plasma. Patient II had double-volume ET (160 ml/kg) and 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.

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

Dr Diane Schaller, Dr Laurence Lacroix, Dr Lynda Vanderput, Pr Alan Gervaix
Service d’Accueil et d’Urgences Pédiatiques, Hôpitaux Universitaires de Genève

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 O2 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 leukocytes) 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.

Consumptive hypothyroidism due to infantile hemangioendothelioma

Sarah Felber Appiagyei¹, Gabor Szinnai¹, Barbara E. Wildhaber¹, Alexandra Schifferli¹, Tamara Diesch¹, Thomas Kühne¹
¹University Children’s Hospital Basel; ²L’Hôpital des enfants HUG

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 hemangioendothelioma and clinical consumptive hypothyroidism due to excessive inactivation of thyroid hormones suggesting type 3 thyroglobulin (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 x10⁹/l and leukocytes of 7.27 x10⁹/l. PTT was 28 sec and PT 77%. Further radiologic investigations including sonography of the abdomen following MRI revealed a giant panhepatic multifocal infantile hemangioendothelioma and clinical consumptive hypothyroidism due to excessive inactivation of thyroid hormones suggesting type 3 thyroglobulin (D3) hyperactivity. After giving beta-blocker there was a considerable decrease in size of the liver tumor.

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

Manzano S.1, Bailey B.2, Lacroix L.1, Galetto A.1, Gervaix A.1
1Service d’Accueil et d’Urgences Pédiatriques, Hôpital des Enfants HUG, Genève; 2Division de l’Urgence, Dpt de Pédiatrie, CHU Sainte-Justine, Montréal, Canada

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. Positive and negative predictive value were 60% (95% CI 53, 65) and 0.75, 0.84). The lab-Score AUC was statistically superior to the AUC of procalcitonin (PCT), PCT and 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.

Methods: A prospective cohort study was conducted on a convenience sample that took place in a tertiary pediatric hospital emergency department in children included 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 PCT and CRP. The Lab-score had a sensitivity of 0.99 (95% CI 0.74, 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.

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

Buetcher M.1, Ayegy P.1, Tschumi S.1, Droz S.1, Duppenthaler A.1
1Kinderheilkunde; 2Institut für Infektionskrankheiten, Inselspital Bern

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 regimen 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 Children’s 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 47(71%) Cefotaxime sensitivity, respectively. Ceftriaxone sensitivity was detected in 18 (37%) 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 Cefotaxime, respectively, and all were sensitive to Ceftriaxone.

Conclusion: Starting with a third generation cephalosporin empirically is the safest option to avoid treatment failure. Particularly Cefotaxim and possibly also Amox/Clav are not sufficient as first choice to cover for E. coli febrile urinary tract infection at our centre.

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

Pauchard J.Y.1, Verga M.E.1, Bersier J.2, Prod’Hom3, Galetto A.1, Gervaix A.1
1Unité d’infectiologie et de Vaccinologie-DMCP-CHUV; 2Laboratoire-HEL-CHUV; 3Bactériologie-CHUV; 4Unité d’infection et de Vaccinologie-DMCP-CHUV

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 occurrence of facial nodules. The ages of children were treated with ocular antibiotics and steroids. Four patients with rather new and fluctuating facial nodules were treated with systemic antibiotics (azithromycin, metronidazole) for 4 weeks resulting in gradual improvement. For all facial nodules zink containing creams were applied until full recovery.

Idiopathic facial aseptic granuloma:
high frequency of ocular involvement

Scheer H.1, Weibel L.2
1University Children’s Hospital Zurich; 2Dermatology Department University Hospital Zurich

Introduction: Idiopatich 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 occurrence of facial nodules. The ages of children were treated with ocular antibiotics and steroids. Four patients with rather new and fluctuating facial nodules were treated with systemic antibiotics (azithromycin, metronidazole) 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.

Atypical skin complications of Mycoplasma Pneumoniae

Rock N., Bajwa N. Hôpitaux Universitaires Genève

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.

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

Gabriel Geiges1, Stefan Schneider2, Christoph Stüssi3, Peter Safléld4

1Klinik für Kinder und Jugendliche, Kantonsspital Münsterlingen; 2Praxis Dr. Schneider, Kreuzlingen

Introduction: The overall number of invasive pneumococcal disease (IPD) is reduced by 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 critically 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 control of children in an inpatient 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 series the suspicion of pneumococci type 3 as the causative agent pneumococci antigen in the pleural effusion is regarded superior (1).

Conclusion: 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.

Cluster of severe group A beta-haemolytic streptococcal infections

Marco Patrick Lurà1, K. Eberhardt2, Ulrich Heininger2, Nicole Ritz2, Daniel Trachsel2

1Division of Intensive Care and Pulmonology, and 2Division of Infectious Diseases, UKBB, Basel

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 on 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.

Table 1

<table>
<thead>
<tr>
<th>Description</th>
<th>Diagnosis</th>
<th>Skin Lesions</th>
<th>Treatment and Outcome</th>
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<tr>
<td>12-yr-old boy with fever, cough, rales, skin lesions, conjunctivitis, mucositis</td>
<td>Positive Mycoplasma PCR Chest x-ray confirmed pneumonia</td>
<td>Bullous Erythema Multiforme</td>
<td>Macrolide Complete resolution after 2 weeks</td>
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<tr>
<td>11-yr-old boy with fever, cough, rales, skin lesions, conjunctivitis, and mucositis</td>
<td>Positive Mycoplasma PCR Chest x-ray confirmed pneumonia</td>
<td>Bullous Erythema Multiforme</td>
<td>Macrolide Corticosteroids Complete resolution after 3 weeks</td>
</tr>
<tr>
<td>15-yr-old girl with fever, cough, rales, skin lesions, conjunctivitis, and mucositis</td>
<td>Positive Mycoplasma PCR Chest x-ray confirmed pneumonia</td>
<td>Bullous Erythema Multiforme</td>
<td>Macrolide Corticosteroids Complete resolution after 2 1/2 weeks</td>
</tr>
<tr>
<td>15-yr-old boy with fever, cough, skin lesions, conjunctivitis, mucositis</td>
<td>Positive Mycoplasma PCR</td>
<td>MP-associated mucositis</td>
<td>Corticosteroids Complete resolution after 2 weeks</td>
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Meropenem-associated agranulocytosis in an infant with brain abscess

Marie-Anne Burckhardt¹, Elvire Ettel¹, Gurli Baer¹; Manuel Haschke¹, Alexander Rätz Bravo², Ulrich Heininger¹, Nicole Ritz²

¹Neonatology Unit, University Children’s Hospital Basel, Switzerland; ²Paediatric Infectious Diseases Unit, University Children’s Hospital Basel, Switzerland; ³Division of Clinical Pharmacology & Toxicology and Regional Pharmacovigilance Center, University Hospital Basel, Switzerland

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 under three months of age. 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, it 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 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 leucopenia or agranulocytosis.

Cytomegalovirus associated polyradiculitis mimics meningitis in a boy with medulloblastoma

Paionı P.¹, Schmitt-Mechelke Th.², Rischewski J.¹

¹Department of Paediatric Haemat-/Oncology and Neurology, Lucerne Children’s Hospital, Switzerland

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 privilege 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 opthalmoplegia. Bladder and bowel control were not affected.

Cerebrospinal fluid (CSF) examination showed cytolytic dissociation. Cytomegalovirus 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 improvement and no relapse of symptoms.

Conclusion: Cytomegalovirus infection as a treatable cause of neurologic symptoms should be suspected in immunocompromised individuals presenting with neurological symptoms.

Osteoarticular tuberculosis of the wrist – a case report

Manon Janach, Daniela Kaiser

Luzeiren Kantonsospital (LUKS), Pädiatrie

Background: The incidence of tuberculosis is generally rising due to rising cases of HIV- patients and the emergence of multidrug-resistant mycobacteria. Musculoskeletal manifestations of tuberculosis (TB) are rare (2–3%) and its occurrence mainly consists of TB located in the spine (tuberculous spondylitis). Extrapleural musculoskeletal involvement is among the least common manifestations of TB. We present our experience of a patient with a tuberculosiis 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 affectation of the wrist was confirmed in the biopsy specimen, which recommended for people >6 years who live or travel in endemic areas. 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 5 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. Influenza virus antibodies 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 care and hydration 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?

Does tick-borne encephalitis cross the borders?

S. Stalder, M. Cegieliski, C.-A. Mayor, A. Zemmouri

Service de pédiatrie, CHUV, Morges

Introduction: Tick-borne encephalitis is a well known cause of encephalitis in Switzerland and in endemic areas. Long-term consequences are numerous and can be severe. Vaccination is
revealed a granulomatous epithelio-gigantocellular 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 hilar regions. A large 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 is vital in order to prevent irreversible osteoarticular destruction and function, differential diagnosis of a painful swollen joint should include TB, especially if the patient does not respond to a anti-inflammatory therapy.

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

Gräni K.1, Röthlin R.1, Güngör T.2, Rischewski J.1

1Kinderklinik Luzern; 2Kinderklinik Zürich

**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 rhinits 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 Trimethoprim-Sulfamethoxazol, amphotericin B, and meropenem, stabilized on a therapy with meropenem, and intravenous immunoglobulin/PJP prophylaxis should be started. Allogeneic HSCT is the only available cure of the otherwise fatal condition.

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

Caroline Berkeimeier1, Mike Half1, Georg Holländer2, Universitätskinderklinik beider Basel1, Universitätsspital Basel2

**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 are able 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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**Parinaud ocuoluglandular syndrome – an atypical presentation of Bartonella henselae infection**

P. Haberstich, H. Höhler, G. Berthet

Klinik für Kinder und Jugendliche, Kantonsspital Aarau

**Background:** Parinaud ocuoluglandular 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 reflect being scratched in the eye nor fever. Her, antibiotics treat with intravenously presoifed acic agel without any effect. Her left eye was mildly injected with moderate subbursal papille 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:** Knowledge of Parinaud ocuoluglandular 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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**Regeneration of a functional thymus from adult murine thymic epithelial cells**

Thomas Barthlott2, Caroline Berkeimeier1, Elea Piccinini2, Stefan Heiler1, Marita Bosticardo1, Chiara Belin1, David Wendt1, Ivan Martín1, Georg Holländer2, Universitätsspital beider Basel1, Universitätsspital Basel2

**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 dual role. On the one hand, TEC exert 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 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 and cultured TEC retain their capacity 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.
DEEP look into Thymic Epithelial Cell Transcriptome
Shikama-Dorn N.1, Nusspamer G.1, Balwierz P.2, Peter A.1, Christen E.1, Holländer G.A.1
1UKBB, Uni. Basel

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 (APECED) 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 bioinformatic tools.

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
Bosch A.1, Barblott T.1, Zuklys S.1, Holländer G.A.2
1Pediatric Immunology, Department of Biomedicine, University of Basel and Basel University Children’s Hospital (UKBB), Basel, Switzerland; 2Department of Paediatrics, University of Oxford, Oxford, United Kingdom

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
Mayer C.1, Zuklys S.1, Zhanybekova S.1, Nusspamer G.1, Chappaz S.1, Pascual-Montano A.2, Finke D.1, Holländer G.1,3
1Universitäts-Kinderklinik beider Basel (UKBB); 2Universidad Autónoma de Madrid; 3University of Oxford

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 TEC relate to altered expression of 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
Gretel Nusspamer, Simon Bornschein, Noniko Shikama, Saulius Zuklys, Werner Krenger, Thomas Barthlott and Georg Holländer UKBB

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 IIhigh) 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 diphtheria 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 locally replaced by fibroblasts but also concurrently resulted in a decrease in mTEC with an immature (i.e. MHC class IIhigh) 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.
Collaboration between the “Centre Médico-Chirurgical Pédiatrique Persis” (CMCPP, Ouahigouya, Burkina Faso) and the Departments of Pediatrics of the CHCVs and CHC, Switzerland

Tabin R.1, Zala L.2, Melvaz B.3, Diebold P.1, Cheseaux JJ.1, Llor J.1, Frick M.4

1CHCVs, Sion; 2CMCPP, Ouahigouya, Burkina Faso; 3Association Persis Valais, Trient; 4CHC, Aigle

Introduction: The Centre Médico-Chirurgical Pédiatrique Persis (CMCPP) in Ouahigouya/Burkina Faso is a private medical center for social purposes. It was founded 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 mortality and malnutrition.

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 a high level 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 go to CMCPP for a 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 CMCCP. 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 an improvement of the quality of the medical care in Ouahigouya, Burkina Faso, 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.

Paediatric Partnership Program Zurich – Yerevan (Armenia)

Leumann E.1, Steinnmann B.1, Sarkissian A.2, Babloyan A.2

1Kinderspital Zurich; 2MC Arabkit, Yerevan, Armenia

Introduction: An acute relief operation (haemodialysis for the crush injuries in the outpatients department) in the CMCPP 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 between swiss and burkinabé physicians, to promote mutual education and exchange 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 go to CMCPP for a 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.

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Conclusion: The collaboration between the CMCPP and CHCVs+CHC has already achieved many goals, and should be further developed.

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

Lava S.A.G.1,2, Simonetti G.D.3, Ramelli G.P.3, Tsuchimi S.1, Bianchetti M.G.1

1Department of Pediatrics, CHUV, 1011 Lausanne; 2Department of Psychology, UNIL, 1000 Lausanne

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 exactely 300 members (72% of the Swiss board-certified Pediatricians) of the regional societies of Pediatrics from 13 Swiss cantons (86% 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 antipyretics 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

Vonbach P., Caduff Good A., Glienzmann C., Thoma R., Division of Pharmacy, University Children’s Hospital, Switzerland

Introduction: Drug doses for children seem to challenge paediatricians 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. Most users in an electronic version 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.

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

Claudia Zaugg1, Jessica Behringer1, Michael Walther2, Richard Egger1, Henrik Köhler3
Spitalapotheke; 1Klinik für Kinder und Jugendliche Kantonsspital Aarau

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"). 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 questionnaire 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 antinfective 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 questionnaires 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 market information of older substances, or the need of a national database for drug use and dosage in children.


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

Dr L. Lacroix, Dr S. Manzano, Dr E. Mapelli, Dr A. Gervais, Dr L. Larribau, Dr L. Suppan, Dr M. Niquille
Hôpitaux Universitaires de Genève

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 exist 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 outcomes. 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 10.1%, intubation in 19%, IV cannulation in 17.7% and intravenous 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.

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

Dolci M.1, Gaillard T.1, Carron P.N.2, Lutz N.3
Service d’Anesthésiologie,1, des Urgences2 et de Chirurgie Pédiatrique3, CHUV, Lausanne

Objective: Assess inter-hospital transportation of paediatric life threatening emergencies received by Emergency Medical Dispatch Centre in our single urban setting, in order to better define dispatch criteria.

Methods: Retrospective analysis of data collected by the pre-hospital transportation and paediatric resuscitation quality control teams between May 2005 and 2011 regarding the patient transferred to the resuscitation room of the University Hospital of Lausanne (CHUV) from another institution.

Results: 208 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 238 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.

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

Mascha Rochat1, Mario Gehri1, Eric Masserey2
1Department of Pediatrics, University Hospital of Lausanne, Lausanne, Switzerland; 2Public Health Department, Vaud, Switzerland

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

Beaud S.1, Racine L.1,2, Gehri M.2, Laubscher B.1,2
1Department of Paediatrics, Hôpital neuchâtelois; Switzerland; 2Department of Paediatrics, Lausanne University Hospital (CHUV); Switzerland

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 Pourtales (HNE, patients age 0–16 years) and Hôpital de l’Enfance HEL (HNE/Hel, patients age 0–18 years), cases were 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 2 178/337 (3.4/2.6%), ATS 3 2 767/2387 (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 was 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 11/29 and 2/29.

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.
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 the team in managing 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 if at an event (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).

Cand. med. Annina Ruffini; Dr. med. Renate Hürlimann
Universitätshôpital Zürich

Background: Since 2005 the Childrens Hospital of Zuerich has an interdisciplinary emergency department (ED). To assess the 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 (laceration, 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%) had hematoma, 34 (26%) abrasions, 28 (22%) disrupted communications. 20% (40) girls 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 (64%) 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 80% of SA in 17 yrs with AGT (lacerations, abrasion, bruising) including sexual abuse (SA).

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 Spanish et al in Ped. Emerg. Care 2008: 63% of AGT and 80% of sexual abuse (SA) were unexplained. Sexual abuse in girls involves 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.
Kawasaki disease in adolescents
Boulos Ksontini, Di Bernardo S, Mivelaz Y, Sekarsi N. Unité de cardiologie pédiatrique, DMCOP, CHUV, Lausanne
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 is difficult because presentation may be incomplete or atypical leading to delay in diagnosis and treatment.
Methods: Prospective 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. Median age at presentation was 2 years old (range 0.5–15), Three patients (2%) were older than 8 years old (12, 13 and 16 years respectively). All 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 lymphadenopathy. 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 prompting 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.

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 doesn’t specify 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 manufacturer’s pharmacokinetics. However, 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.

Intravenous immunoglobulin treatment despite anaphylactic reaction in a child with Kawasaki disease
Jacquier David, Gehrke Thomas
1Service de Pédiatrie, Hôpital du Chablais – Aigle
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 prednisolone 3x/d for the previous 5 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 and bilateral lymphadenopathy, 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 a thrombotic dose. The cumulative prescribed dose of clemastin 0.1 mg/kg and methylprednisolone 1 mg/kg was given following which the patient’s symptoms improved. However, 6 hours later the patient 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 prompting 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.

Acute intravascular hemolysis after high-dose intravenous immunoglobulin treatment in a 7-year-old child with Kawasaki disease
Pereira Alexandre, Kirchofer Laila, Mayor Claude-André, Challet Corinne, Zemmouri Abdelaziz
Service de Pédiatrie – Hôpital de Morges
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. Anti-B hemagglutinins in IVIG preparations. Some risk factors have been identified, i.e. high dose of IVIG, non-O blood group. 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/m²) had recurrent anaphylactic reactions to IVIG (Privigen®) that was repeated after 38h due to fever persistence. Less than 24h after this second infusion, the patient presented hemoglobinuria. 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: 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
1Allergie-Fachklinik, ABB, Allergologie, Universitätsspital Bern, Switzerland; 2Allergiepoliklinik, Klinik für Rheumatologie, Immunologie und Allergologie, Universitätsspital Bern, Switzerland
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 (11.4 ng/mL).
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 (reactions), while 15 tolerated reexposure to stings or venom injections without hypersensitivity reactions (non reactions). 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 venous puncture was observed in 9/20 reactors (45%) 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 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.)

Vomiting, lethargy and a peculiar smell: not just a common infectious gastroenteritis – a case report
Renata M. Baggenstos-Clement1, Thomas Schmitt-Mechehle1, Johannes Häberle1, Florian Dietrich1
1Kinderklinik Luzern; 2Universitätskinderklinik Zürich

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 manifestations later in life such as vomiting and 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 due to 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, pCO2 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.

Discussion: 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.

Torticollis in children: Red flags to potentially life-threatening causes
Nather C., Garcia D., Grunder E.
Kinderklinik Zürich

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 torticollis) or develop afterwards (infantile torticollis). The lateral neck deformity is caused by myofascial contracture of the sternocleidomastoid muscle, often caused by obstetric trauma. As the neck is frequently examined by emergency department staff and the associated symptoms usually resolve within a short period of time, torticollis is often not fully evaluated. In the absence of defined criteria for evaluating torticollis, the risk of potentially life-threatening causes is underestimated.

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 or cranial nerve palsies were excluded. As potentially life-threatening causes we defined tumors of the posterior fossa, retropharyngeal abscesses, traumatic injuries and ocular paraesthesia. 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 and 13 (48%) were able to identify red flags to these causes. The following symptoms associated with torticollis should prompt further investigations: ocular symptoms like strabismus or double vision, significant trauma, additional neurological findings 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. Many of our patients were able to identify red flags to these causes. The following symptoms associated with torticollis should prompt further investigations: ocular symptoms like strabismus or double vision, significant trauma, additional neurological findings and a sore throat in the absence of signs of respiratory infection.

Not your common gastroenteritis – systemic lupus erythematoses presenting with enteritis-like symptoms
Woerner A.*, Cayr S.*, Bonhoeffer J.*, Daiker E.*
1Department of Pediatrics, University Children’s Hospital Basel; 2Department of Rheumatology, University Hospital Basel

Introduction: Pediatric systemic lupus erythematoses (pSLE) is a rare systemic autoimmune disease characterized by the presence of autoantibodies and multorgan involvement. About 30 to 30% experience gastrointestinal disease within the first year of diagnosis, but abdo-minal symptoms as the main initial presentation, indicating systemic autoimmune disease characterized by the presence of gastroenteritic symptoms. As the abdominal pain worsened and bowel sounds were diminished, radiographic evaluation showed the presence of hypomotile intestinal loops and thickened segments of the ileocecal wall. A gastro-duodenoscopy and colonoscopy were performed, showing unspicific intestinal changes not compatible with inflammatory bowel disease. Abdominal MRI and MRA were not further contributive. Considered the past medical history, rheumatological evaluation revealed high-titer anti-nuclear antibodies with strongly positive anti-ds-DNA disease, 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 patient workup but also take account of pSLE with predominant abdo-minal involvement, especially when preceeding symptoms, like arthritis, are present.

Anisocoria: the culprit may be in the garden
Vunda A., Alcoba G., Gervaix A.
Service d’Accueil et d’Urgences Pédiatriques, Hôpitaux Universitaires de Genève

Introduction: Anisocoria 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 family reassurance, the patient was noted that he had peeled an Angel’s Trumpet (Datura) plant and then rubbed his right eye. After family 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, hyoscymine, atropine and hyoscymine. In our patient, the right pupil 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.

Conclusions: 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.
Near fatal enema: beware of phosphate solution
Rosato L.¹, Reynaud S.¹, Laubscher B.¹,², Racine L.¹,²
¹Department of Paediatrics, Hôpital neuchâtelois; Switzerland; ²Department of Paediatrics, Lausanne University Hospital (CHUV); Switzerland

Introduction: 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 a 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), and ≤2 years. 44/61 (72%) received more than the recommended 6 ml/kg. No side effects were reported.

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 guidelines. Phosphate based enemas have been so far banned but can be almost deadly. Apparently, we did not follow the paediatrics guidelines. Phosphate based enemas have been so far banned in these conditions. LC-MS/MS (Shimadzu prominence XR, ABSciex 5500QTrap, Applied Biosystems) was performed by standard procedure: decontamination of the hair, pretreatment with NH4-Formate MeOH). 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, 5 M Formate Buffer/5 M NH4HCO3 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.

Phenprocoumon intoxication and gross haematuria in an adolescent: The Broken Heart Syndrome
Donas A.¹, Baggenstos R.¹, Trindler M.¹, Gährer A.², Rischedewi J.¹
¹Kinderklinik Luzern; ²Hämatoonkologie LUKS Luzern

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 anemia for that duration. On admission the boy complained about abdominal pain. His abdomen was tender with guarding and rebound tenderness. On arrival he was normotensive with tachycardia. GCS was 15 and the child was breathing rapidly. Capillary blood gas was normal. The first measured serum 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 were 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 if we can trace midazolam after a single dose in the grown hair 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, 5 M Formate Buffer/5 M NH4HCO3 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.
Impaired slow wave sleep downscaling in encephalopathy with status epilepticus during sleep (ESES)

Bigna K. Bölsterli Heinzle1, Bernhard Schmitt1, Thomas Bast2, Hanne Critelli1, Jakob Heinzle3, Oskar G. Jenni4, Reto Huber1
1Division of Clinical Neurophysiology, University Children’s Hospital Zurich; 2Department of Paediatric Neurology, University Children’s Hospital, Heidelberg (D); 3Epilepsy Centre Kork, Kehl-Kork (D); 4Bernstein Center for Computational Neuroscience, Charité – Universitätsmedizin Berlin (D); Child Development Centre, University Children’s Hospital Zurich

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.

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

Derschning S.1, Nusspauer G.1, Holländer G.A.2, Krenger W.1
1Department of Biomedicine, University of Basel and Basel University Children’s Hospital (UKBB), Basel, 4031, Switzerland; 2Department of Biomedicine, University of Basel, Basel, Switzerland

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 developmental regression in these patients.

Methods: The effect of Fgf7 on mTEC-specific TRA expression was tested in a murine allogeneic transplantation model. Results: Mature mTEC cells 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.

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

Chiara Abbas1 MD, Florian Singer1 MD, Carmen Casaula1 MD, Philipp Latzin1 MD, PhD
1Division of Respiratory Medicine, Department of Pediatrics, University Hospital of Bern, Switzerland

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 (IPDTG).

Results: As expected, in healthy controls the slope of slow waves decreased (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.

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

Thanh Hong Phuc Cung, Luisa Bonafè, Diana Ballhausen
Pédiatrie Moléculaire, CHUV, Lausanne

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

Jafari P.,1 Braissant O.2, Henry H.2, Bonafé L.1, 3, Balhauzen D.1 1Div Mol Ped, CHUV, Lausanne, 2Biomédecine, CHUV, Lausanne

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 this 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-dependent 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 immunohistochemistry. 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-hydroxylglutaric 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 revealed 2-methylcitrate and 3-hydroxylglutaric 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 possibly 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.

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Platelet apoptosis in paediatric immune thrombocytopenia is ameliorated by intravenous immunoglobulin

Jeanine Winkler1,2,3, Sabine Kroiss1,2, Margaret L. Rand1, Oliver Speer1,2,3, Markus Schmugge1,2,3 1Division of Haematology, University Children’s Hospital Zürich; 2Zurich Center for Integrated Human Physiology, University of Zürich; 3Children’s Research Center, University of Zurich, Switzerland

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 ∆ψm, 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 ∆ψm, these markers for apoptosis were reduced by IVig. Platelets of children with thrombocytopenia after chemotherapy also demonstrated increased microparticle formation and decreased ∆ψm, 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.

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

Camats N.1,2, Pandey A.V.,3 Fernández-Cancio M.,1 Andaluz P.,1 Janner M.,3 Torán N.,4 Mullis P.E.1, Carrascosa A.1, Audi L.1, Flück C.E.1 1Pediatric Endocrinology Research Unit. VHIR. Hospital Universitari Vall d’Hebron (HUHV). Barcelona, Spain; 2Department of Pediatrics and Clinical Research; 3Division for Paediatric Endocrinology, University Children’s Hospital Bern. Switzerland; 4Pathology Department. HUVH. Barcelona, Spain

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 on neurodevelopment.

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,XX 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-correlation. Histologic studies and functional tests 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 this phenotype. Functional studies revealed reduction of Leydig cells due to fat accumulation and are thus similar to findings observed in patients with lipid congenital adrenal hyperplasia (due to STAR mutations). Genotype-structure-function-phenotype correlation remains elusive.
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.

**Topical betablockers for infantile hemangiomas are effective but systemically absorbed**

L. Weibel1,2, H.S. Scheer1, M. Barysch1, I. König3, U. Subotic3, D. Müller4, C. Schiestl3, K. Rentsch4

1Dermatology Department and 3Plastic Surgery Department, University Children’s Hospital Zurich; 2Dermatology Department and 4Institute for Clinical Chemistry, University Hospital Zurich

**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:** Forty infants (median age 18 (2–35 weeks)) were included. Twenty-three (58%) patients had a superficial IH and 17 (42%) a mixed-type IH. The median IH size was 3 cm² (0.1–15 cm²). 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. Thirty-four 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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