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WILEY-BLACKWELL
O-001 Concordance between the Child Self-Report and Parent-Proxy Reports for the PedsQLTM Generic Core Scales 4.0 amongst Malaysian Paediatric Leukaemic Population.

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Background: To determine the concordance in the Health-Related Quality of Life (HRQOL) scores between child self-reports and parent-proxy reports in children on maintenance chemotherapy and those who have completed chemotherapy.

Methodology: Seventy seven children with leukaemia were consecutively enrolled, of which 22 were on maintenance chemotherapy and the rest had completed treatment. HRQOL scores were assessed using the Pediatric Quality of Life Inventory (PedsQL™) Generic Core Scales Ver. 4.0, which yielded total, physical and psychosocial health summary scores as well as domain scores in emotion, school and social functioning. Concordance between child and parent ratings on each of the PedsQL subscales and total scores were judged according to guidelines established by Cohen & Holliday.

Results: Concordance was good between child self-report and parent-proxy report for children on maintenance chemotherapy (r=0.583-0.770) except for the school (r=0.229) and social domain (r=0.248). For children who had completed chemotherapy, there was only moderate concordance between child and parent in the domains of school, physical health scores, psychosocial health scores and total scores (r=0.414-0.494) whereas emotion domain showed strong concordance (r=0.589) and poor concordance in social domain (r=0.116).

Conclusion: In general, the strong concordance in the chemotherapy group showed that Malaysian parents are perceptive to their children’s needs and problems. This perception wanes somewhat when their children have completed chemotherapy as evidenced by poorer concordance in the maintenance chemotherapy group.

O-002 Acute Pancreatitis in Children with Acute Lymphoblastic Leukemia following Chemotherapy

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Background: Acute lymphoblastic leukemia (ALL) is a common malignancy in children. The etiology of acute pancreatitis (AP) in ALL children receiving chemotherapy is unknown but has often been reported associated with L-asparaginase therapy. Objectives: To determine the incidence, risk factors, clinical data, outcome and mortality of AP in ALL children.

Patients and Methods: Retrospective cohort study was conducted by reviewing the data of total 192 pediatric ALL patients from Pediatric Oncology Registry at Ramathibodi Hospital from 2000 to 2006 to assess incidence, clinical data, outcome and mortality of AP. Then, we conducted a nested case-control study to identify potential risk factors for AP by recruiting all AP patients as cases (n=16), and randomly selected patients without AP to serve as controls up to four controls per case with the total of 68 controls. Results: The incidence of AP in ALL children in this study was 8.3%. Seven of the 16 patients with AP (43.8%) died. The mortality rate of AP group was significantly higher than the group of patients without AP (43.8% VS 19.3%, p=0.02). Having AP and receiving standard/high risk chemotherapy protocol were associated with high mortality, with the hazard ratio of 5.1 (95%CI 2.2, 12), and 2.8 (95%CI 1.4, 5.8), respectively. Multivariate analysis identified the high risk chemotherapy protocol was the only risk factor for AP. Conclusion: High risk chemotherapy protocol is a risk factor for pancreatitis in ALL patients. Factors associated with high mortality in ALL children were having pancreatitis and receiving standard/high risk chemotherapy protocol.

O-003 Review on childhood astrocytoma: The Hong Kong Paediatric Haematology / Oncology Study Group (HKPHOSG) Experience (1994 to 2006)

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Background: Astrocytoma is the commonest brain tumor in both adult and childhood with a diverse clinical behavior. We reviewed our local experience in this tumor. Materials & Methods: Local children (<18yrs) with brain tumor diagnosed. Astrocytoma account for 117/343(34%) which is lower than Western countries. Low risk chemotherapy protocol.

Objective: Although calcium (Ca) is an essential mineral for bones, little is known about its effect on inflammatory or oxidative regulation. We evaluate the role of Ca on production of reactive oxygen species (ROS) and nitric oxide (NO) from polymorphonuclear leukocytes (PMN).

Methods: Using flow cytometry, we compared the ROS and NO production from PMNs after the stimulation by S. aureus or phorbol myristate acetate (PMA) (25 µg/ml). PMNs taken from the 3 groups of mice were analyzed: C57BL/6 wild type mice (Group C), low Ca diet fed for 2 weeks mice (Group Low Ca), and low magnesium (Mg) diet fed for 2 weeks (Group Low Mg). Animals did not differ in PMN counts.

Results: ROS production at basal in the Group Low Ca was lowest among the groups. There was no significant difference among the groups.

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Results: ROS production at basal in the Group Low Ca was lowest among the groups. There was no significant difference among the groups.

Conclusions: Low Ca diet increases the radical production of polymorphonuclear leukocytes from mice.

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O-005 Prevalence of Hb H Disease among Newborn Infants with Jaundice or Anemia

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Background: Thalassemia is the most commonly found genetic blood disorder in Thailand. Hb H disease can be diagnosed in newborn infants with jaundice or anemia. Objective: To determine the prevalence of Hb H disease among newborn infants with jaundice or anemia. Methods and materials: Eligible cases were newborn infants with gestational age ≥35 weeks, who presented with jaundice and/or anemia born at Ramathibodi Hospital between January-December 2005. Results: A total of 209 newborns were enrolled in the study. Most common cause of neonatal jaundice was inconclusive jaundice (78.7%), and for anemia was unspecified cause (59.9%). Three infants with Hb H disease were identified. Conclusion: Hb H disease is not a cause of neonatal jaundice but among unspecified anemia newborns is common. Therefore, hemoglobin typing should be considered among newborn with unspecified cause of anemia. All infants with Hb H disease had low MCV and positive inclusion bodies.

O-006 Frequencies of Polymorphisms Associated with VKORC1 Gene in Thai People and in Patients receiving Warfarin

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Background: High variability in drug response complicate warfarin administration. Objectives: This study is to determine the frequencies of polymorphisms of VKORC1 among Thai people and in patients receiving warfarin. Methods: Patients receiving warfarin and healthy blood donor were enrolled in this study. Warfarin dosage and clinical information were collected. VKORC1 polymorphisms were determined by standard DNA amplification followed by restriction enzyme digestion. Results: 314 blood donors (218 males, 96 females) and 112 patients (48 male, 74 females) were enrolled. The mean age of blood donors and patients were 39.1 and 49.4 years, respectively. Implication: DNA analysis of VKORC1 before starting warfarin treatment is suggested in order to prevent bleeding complication.
O-009 Oligonucleotide tiling array based genome-wide detection of epigenetic abnormalities in neuroblastoma

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Neuroblastoma is the most common solid tumors in childhood. Although a number of genetic and epigenetic alterations have been reported, the etiology of neuroblastoma has not been fully understood. Recently, it is becoming clear that epigenetic abnormalities play important role in oncogenesis. However, genome-wide and detailed epigenetic analysis of neuroblastoma has not been reported due to limitation of conventional techniques. In this study, focusing the role of epigenetic abnormalities in neuroblastoma, we performed genome-wide methylation analysis of neuroblastoma samples using methylated DNA immunoprecipitation (MeDIP) method and oligonucleotide tiling array. In this assay, genomic DNA from samples is fragmented by sonication, and immunoprecipitated using anti-methyl-cytosine antibody, followed by PCR amplification of the precipitated DNA. Amplified DNA was subjected to hybridization to high-density tiling arrays (MeDIP-on-chip). Using MeDIP-on-chip assay, we revealed genome-wide methylation patterns of neuroblastoma, showing a number of common methylation sites among different samples, which were subsequently verified by bisulfate sequencing. Our results demonstrated that MeDIP-on-chip assay is a robust tool for comprehensive analysis of DNA methylation, providing a new insight into the role of epigenetic changes in the pathogenesis of neuroblastoma.

O-010 The Niche Regulation of Quiescent Hematopoietic Stem Cells through Thrombopoietin/Mpl Signaling

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Hematopoietic stem cells (HSCs) self-renew and differentiate to develop blood hierarchy throughout individual’s life. Maintenance of HSCs is supported by microenvironment called niche, which is located at trabecular bone area in the bone marrow. Interaction of HSCs and the niche regulate the balance between quiescent and active form of HSCs. Recent findings suggest that cancer cells also require a special microenvironment to maintain cancer stem cells and to support cancer growth. Clarification of mechanisms underlying beyond HSC-niche interaction is indispensable not only for the achievement of efficient therapy such as HSC expansion, but also for understanding pathophysiology of leukemia.

We demonstrated that thrombopoietin (Tpo)/Mpl signaling between osteoblastic niche and HSCs plays a crucial role in regulating HSC quiescence and self-renewal ability. Inhibition and stimulation of Tpo/Mpl pathway by treatments with an anti-Mpl neutralizing antibody, AMM2, and Tpo showed reciprocal regulation of HSC quiescence in mice bone marrow. AMM2 treatment suppressed the quiescence and HSC-niche interaction, resulting in the creation of the vacant niche to allow exogenous HSC engraftment. By contrast, exogenous Tpo transiently promoted quiescence, and subsequently induced transient HSC proliferation with side-population and CD34+ profiles in vivo. Moreover, Tpo up-regulates p15Ink4a and p21Cip1, and down-regulates c-Myc in Mpl+ fraction in CD34+ HSCs in vitro. These observations indicate that Tpo/Mpl signaling is a novel niche component that plays a critical role in the regulations of not only self-renewal but also maintenance of quiescence of HSCs in osteoblastic niche.

O-011 Clinical outcomes of cardiac complications associated with chronic activated Epstein-Barr virus infection

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Objective: To clarify the clinical aspects and outcomes of cardiac complication associated with chronic activated Epstein-Barr virus infection (CAEBV).

Patients and methods: Fifteen patients (8 females) with CAEBV were studied. Median age at the onset of CAEBV was 6.3 (1.2 -17.8) years. All patients fulfilled the diagnostic criteria of CAEBV. Serial studies of echocardiography were performed to evaluate cardiac complications in all the patients. Median follow-up period was 8 years (2-20).

Results: Nine patients (60%) had cardiac complications including coronary arterial lesion (CAL) in 4 (27%), decreased left ventricular ejection fraction and pericardial effusion in 3 (20%) and complete atrioventricular block in one. Median age of the initial detection of cardiac complication was 6.1 (0-12.5) years. In 4 patients with CAL, median duration from the clinical onset and the first detection of CAL was 3.4 (1.8-8.6) years. Coronary arterial lesions were detected in both coronary arteries in one and left coronary artery in 3. The mean maximum diameter of CALs was 4.4 (4.0-5.0) mm. In 2 patients who had CAL survived after successful hematopoietic cell transplantation, CALs were regressed in the normal size. No cardiac event has occurred in all the survived patients. Nine (60%) in 15 patients died during the follow-up period due to multiple organ failure or transplantation related events (N=1) and sudden cardiac arrest after CHOP chemotherapy (N=1).

Conclusions: CAL was the most common cardiac complication in patients with CAEBV. It appeared that the successful managements of CAEBV lead to regression of CALs in patients with CAEBV.

O-012 Central nervous system reactivation of Epstein-Barr virus (EBV) in chronic active EBV infection and EBV-associated encephalitis

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[Backgrounds&Objectives] EBV usually induces asymptomatic infection or acute infectious mononucleosis (IM) in susceptible persons. Chronic active EBV infection (CAEBV) is a rare chronic mononucleosis syndrome characterized by persistent IM-like symptoms along with coronary artery and central nervous system (CNS) diseases. Neurological manifestations occur in 1–5% of acute IM patients. EBV-associated CNS disease alone could occur in previously healthy individuals. To assess the role of EBV in CNS disease, CSF EBV load was quantified in patients with CAEBV or EBV-associated encephalitis. [Methods] EBV DNA was quantified by real-time PCR in peripheral blood (PB) and cerebrospinal fluid (CSF) of 9 CAEBV patients with or without neurological manifestation, and 2 EBV-associated encephalitis. [Results] Four CAEBV patients had neurologic abnormality, and 5 had not it. All 9 patients showed non-pyocytic CSF that contained unremarkable protein and glucose levels. Despite the high viral load in PB, CSF EBV copy number was >200/ml in 3 of 4 patients with neurologic abnormality, and 1 of 5 patients without it. One patient with seizure showed higher CSF EBV level (5000/ml) than the PB level (800/ml). On the other hand, EBV DNA was detected in CSF but not in PB of 2 patients with EBV-associated meningoencephalitis. Both showed serologically positive for EBNA. EBV DNA was undetectable in 10 pyocytic CSF and 5 paired sera obtained from aseptic meningitis patients. [Conclusions] Intrathecal reactivation of EBV could occur in patients with CAEBV or EBV-associated encephalitis. CSF EBV load may predict the development of EBV-associated CNS disease.
Immunizations using live-attenuated vaccines are difficult to perform in children after living-donor liver transplantation (LDLT), as the seroconversion rate can be lower, and theoretical risks of serious adverse effects and rejection exist. Criteria and immunization schedules for live-attenuated vaccine application for those children who have undergone LDLT have not been established. In consideration of above risk factors, we have established criteria for administering live-attenuated vaccines after LDLT as shown below. 1) At least 2 years after LDLT, 2) Underlying liver disease well-controlled with normal liver function tests, 3) No graft rejection in the last 6 months, 4)No gamma-globulin or steroid therapy in the past 6 months, 5) Normal cell-mediated immunity, 6) Low serum concentration of immune suppressant (tacrolimus, or cyclosporin), 7) Written informed consent obtained. We have immunized 12 children after LDLT against measles, rubella, varicella and mumps. All of the patients fulfilled the criteria and had negative antibody titer against each disease. A total of 47 immunizations were performed with each separated by at least 4 weeks. No serious adverse events were observed. Seroconversion rates were high for measles (100%, 11/11), rubella (100%, 10/10) and varicella (82%, 9/11). Seroconversion rate was low (43%, 3/7) for mumps Torii strain, but higher for Hoshino strain (88%, 7/8). Some patients had to be immunized more than twice, especially for mumps Torii strain. The criteria and schedules for the post-LDLT immunizations should be modified for each strain with special attention to the timing and the number of immunizations.

O-015 CLINICAL PROFILE OF DENGUE PATIENTS GIVEN AND NOT GIVEN CARBAZOCROME SODIUM SULFONATE (ADENOGEN) ADMITTED AT DE LA SALLE UNIVERSITY MEDICAL CENTER,DASMARINAS, CAVITE, PHILIPPINES, FROM JANUARY TO DECEMBER 2004

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All throughout the year, dengue fever has always been present in pediatric census in different hospitals in our country. It still has been a health problem. Despite supportive treatment has always been the conventional management in dengue. For some pediatricians, the incorporation of Carbazochrome sodium sulfonate or Adenogen has been part of their management in dengue cases. But there are no studies yet to prove the efficacy of it in dengue. This is a descriptive study of pediatric dengue patients admitted at De La Salle University-Medical Center from January-December 2004 given and not given Adenogen. There were 249 pediatric patients diagnosed with dengue fever/dengue hemorrhagic fever admitted. Nineteen had other concomitant illness, thus were excluded in the study. A total of 230 pediatric patients were included in the study, and 83 of which were given Adenogen and the rest were subjected to conventional dengue management. For dengue patients given Adenogen, most of them live in Dasmarinas, Cavite and were female aged 6-9 years old. Out of 83 patients, only 7 developed complication (8.4%), all of which had hemoconcentration, and no morbidity or mortalities were noted among them. Compared with the group who were not given Adenogen, 17.0% had complications such as pleural effusion, hemoconcentration, bleeding and mortalities.

O-016 ASSESSMENT OF INFLUENZA VACCINE EFFECTIVENESS IN SCHOOLCHILDREN USING RAPID TEST RESULTS OBTAINED FROM A QUESTIONNAIRE SURVEY

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Background: Virtually all the Japanese schoolchildren who developed a sudden onset of high fever during the influenza epidemic season are taken to a clinic and most of them are tested with an influenza rapid test. Such a circumstance has enabled us to estimate the vaccine effectiveness (VE) without conducting an expensive study. Methods: Prospective cohort study. All the pupils in 4 primary schools in Tsuchiura city, Ibaraki, Japan were included in the study (n=2607). A questionnaire for baseline survey was sent to the parents in January 2007, which inquired about several risk factors to influenza including vaccination status. When a child was diagnosed as influenza with a rapid test during the winter in 2006/2007, the parent was asked to submit an influenza reporting form to the school administration. Adjusted VE was calculated with a logistic regression model. Results: Vaccination rate was 44.8% in total. Incidence of influenza A and B was 5.2% and 11.7%, respectively. The epidemics began in late February 2007, which was markedly delayed compared to other years. The crude VE for influenza A and B was 20% (95%CI: 11 to 43%) and 2% (-21 to 21%), while adjusted VE for influenza A and B was 52.4% (23.1 to 70.7%) and 6.8% (-34.0 to 35.2%), respectively. Disease history of influenza A in the previous year seemed protective to the development of influenza A in the current season (Odds ratio: 0.27, 0.07 to 1.09). Conclusions: Results of rapid tests could be utilized to assess influenza VE without much cost.
O-017  Milk Whey or Milk-Derived Sialyl Lactose Enhances Susceptibility of Neonatal Lymphocytes to HIV-1 and HTLV-I, Milk-Borne Human Retroviruses

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Background: HIV-1 and human T-cell leukemia virus type-I (HTLV-I) are transmitted from mother to child via breastfeeding. Milk whey (MW) or milk-derived sialyl lactose (SL) have been shown to enhance HIV-1 and HTLV-I infection of cell culture systems.

Methods: Neonatal mononuclear cells (NMC) were propagated in RPMI1640/10%FBS/IL-2 (100 U/ml) with or without MW or SL. Cells were infected with HIV-1 (titer 10^3 TCID50/ml) or HTLV-I (titer 10^3 infectious units/ml) for 24 hours and the number of infected cells was determined by p24 antigenemia.

Results: MW- or SL-exposed NMC infected with HIV-1 more efficiently than control cells. Similarly, MW- or SL-exposed NMC infected with HTLV-I more efficiently than control cells.

Discussion: The enhanced infection of NMC by MW and SL may be due to the presence of proinflammatory cytokines or the inhibition of the innate immune response.

O-018  Molecular diversity of viral gastroenteritis in a day care center in Japan

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Background: Influenza virus is an important respiratory pathogen in children of Taiwan. We collected <18 year-old cases with positive influenza cultures isolation from March 1999 to February 2006. We analyzed their clinical history.

Methods: We collected 899 episodes of influenza infections in the study period and a hospitalization rate of 37.7%. Among the cases requiring hospitalization, one third had underlying medical conditions and one half aged below three years old. One-fourth of the total cases developed lower respiratory tract infections. Twenty cases (2.2%) were complicated with encephalitis or encephalopathy.

Results: There were 899 episodes of influenza infections in the study period with a hospitalization rate of 37.7%. Among the cases requiring hospitalization, one third had underlying medical conditions and one half aged below three years old. One-fourth of the total cases developed lower respiratory tract infections. Twenty cases (2.2%) were complicated with encephalitis or encephalopathy.

Conclusion: Influenza A carried a higher hospitalization rate than influenza B in Taiwan. The majority of cases requiring hospitalization were previously healthy children, especially those under three years old.

O-019  Using clinical scores for diagnosing tuberculosis in children of developing countries

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The diagnosis of childhood TB is difficult because the disease produces non-specific clinical manifestations. We evaluated two clinical scoring systems - the modified Kenneth-Jones score (KJS) and the WHO-recommended TB score (TBS) for diagnosing TB in children. The KJS is based on age, nutritional status, non-response to therapy (failure to thrive, pneumonia not responding to treatment), history of contact, etc. The TBS considers a good clinical history, physical examination and Mantoux test, etc.

We applied both the scores to 389 children with features suggestive of TB. A total of 102 children had positive KJS or TBS or both and were treated for TB. Markers including AFB smear, culture (both Lowenstein-Jenssen (LJ) medium and MGIT), PCR using IS6110 and rpoB primers were done on gastric aspirates of children with positive scores and 31 children with negative scores.

The median age of children who had positive TB was 15 months and 55% of 102 children diagnosed to have TB, 46% had positive KJS, 94% had positive TBS while both scores were positive in 32% children. Gastric aspirate for AFB smear, LJ and MGIT cultures were positive in 11%, 17% and 13% respectively of children with TB diagnosed by either or both scores. PCR using IS6110 or rpoB were positive in 62% and 9% of children with TB compared to 38% and 3% respectively in children without TB (p<0.02 for IS6110). The modified KJS is less dependent on clinical history and can be used in the diagnosis of childhood TB in developing countries.
O-021 ACCURACY OF BROSELOW TAPE IN EMERGENCY DRUG CALCULATIONS AND SELECTION OF APPROPRIATE TRACHEAL TUBE SIZE IN SELECTED FILIPINO CHILDREN

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Background: Broselow tape, a length-based tool of weight estimation, enables us to estimate drug dosages and tracheal tube sizes from patient’s body length. However, its reliability and accuracy has not yet been fully recognized.

Methods: This is a cross-sectional study involving 1143 children ages <10 years old with weights <34 kilograms, and heights <143cm with a mean age of 4.17 years (± 2.8 years). Accuracy of Broselow tape in weight and tracheal tube size estimation, and drug dosage calculation was measured by obtaining the difference between Broselow (recumbent length) and actual values (using calibrated weighing scale and standard measuring stick).

Results: Results revealed high association between Broselow and standard reference values for weight, dose and ET size, r =1.004 (95 % CI 0.992, 1.017), 1.000 (95 % CI 0.988, 1.013) and 1.08 (95 % CI 1.054, 1.109) respectively. The difference between Broselow and actual values for weight, mean 0.468 (95 % CI 0.3, 0.5) dose, 0.154 (95 % CI 0.06, 0.12) ET Size, 0.164 (95 % CI -0.03, 0.03). Tape overestimated weight and dose by 0.4 kg and 0.13 mg, and underestimated 0.3, 0.5) dose, 0.134 (95 % CI 0.06, 0.12) ET Size, 0.164 (95 % CI -0.03, 0.03).

Conclusion: Broselow tape can be recommended as a reliable tool in providing rapid and accurate method of estimating weight, drug dosage and ET tube size.

Keywords: Accuracy, weight, dosage, tracheal tube size

O-022 Toxocara seropositivity in Sri Lankan children: association with asthma

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Background: Toxocariasis is the clinical term applied to infection in the human host either with Toxocara canis or Toxocara cati, nematode parasites of dogs and cats respectively. The relationship between toxocariasis and asthma is complex. As asthma is a major public health problem in Sri Lanka this study investigates Toxocara seropositivity and its association with asthma.

Methods: Two groups of children were studied: group 1 included 100 children with bronchial asthma; group 2 included 96 children who did not have asthma or upper respiratory tract infection, but was attending for treatment of non respiratory conditions. Diagnosis of Toxocara seropositivity was based on IgG Toxocara Microwell Serum Elisa Kits. The ELISA test was regarded as positive if 0.3 Optical Density Units or above. Stool samples were examined for helmhnt ov and protozoan cysts.

Results: Toxocara seropositivity in children with asthma was 29% and this was significantly more than Toxocara seropositivity among non asthmatic children (p<0.001). Toxocara seropositivity was identified as a significant risk factor of asthma in a multivariate model. Eosinophilia was seen in a significantly higher proportion of non asthmatic and asthmatic children who were Toxocara seropositive indicating an active parasitic infection. However, Toxocara seropositivity was not identified as a significant risk factor in a multivariate model.

Conclusions: The analysis confirmed previously identified risk factors for asthma but there was no association between toxocariasis and bronchial asthma in children. The high eosinophil count in the non asthmatics and asthmatics with toxocariasis indicates an active parasitic infection.

O-023 Computerized-Database Model for Pediatric Injury

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Background: Injury is one the leading causes of death found in children. It is a high cost management due to its complication. Objectives: A computerized database model for pediatric injury was created. The Pediatric Trauma Score (PTS) and the Revised Trauma Score (RTS) from Advanced Trauma Life Support (ATLS) Guideline were also included. Methods: A computerized data collection system for pediatric injury was used at the emergency room. It consisted of demographic data and clinical data including triage level, chief complaint, injury types, disposition, PTS and RTS. Results: 1082 injured child (679 males, 403 females), attended the emergency service at Ramathibodi Hospital between Jan 2003-Dec 2004, were retrospectively studied. Their mean age was 7 year with the high prevalence at an aged-group of 0-4 years. Pediatric injury encountered 4% of emergency visits and 60.4% of them presented at the evening shift of the emergency service (16.00-24.00 p.m.). 64.8% were triage level 2 and the five top ranks of injury involved animal bite or string, struck by against, fall, traffic accident and cut wound. Most of the pediatric injuries were defined as minor trauma while only 5.8% of patients with more serious injury required hospitalization. The PTS was more accurate and effective compared to those of the RTS for the evaluation and management at the emergency room.

Conclusions: The created computerized database model is essential for injury surveillance and holistic approach for the injury prevention. RTS is a useful tool for the management of pediatric injury at the emergency room.

O-024 Endoscopic study of intranasal injuries in newborn infants on nasal CPAP therapy

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Continuous positive airway pressure (CPAP) is conveniently and effectively delivered via nasal prongs. External deformation and skin injuries have been reported.

Objectives: This study aimed to determine the incidence and types of intranasal injuries associated with nasal CPAP (nCPAP).

Methods: Ten infants admitted to the neonatal intensive care unit with respiratory distress requiring nCPAP were examined endoscopically just before commencement of nCPAP. Endoscopic examination was repeated just before nCPAP therapy was terminated.

Results: The mean birthweight of the infants were 2385 g (SD=525). Median age of infants was 2 days when nCPAP therapy was commenced. The median age when endoscope examination was repeated was 7.5 days. Except for two infants with mild redness at the rim of their noses before onset of nCPAP, no other injuries were detected before commencement of nCPAP. After being on nCPAP, repeat endoscopic examination showed all infants had some degree of injuries, ranging from redness, swelling of the nasal mucosa, narrowing of the nasal passage, excoriation to obvious ulceration.

Conclusion: nCPAP can cause intranasal injuries in newborn infants.
O-025  Eosinophil-related T helper 2 (Th2) cytokines associated with the protection of coronary artery lesions in Kawasaki disease
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OBJECTIVE: Kawasaki disease (KD) is a febrile disease with systemic vasculitis, especially coronary artery involvement. Eosinophilia has been found in our and other studies in KD. This study has further investigated whether eosinophil related T helper 2 (Th2) cytokines or eosinophil activation mediator (eosinophil cationic protein, ECP) involved in the KD with coronary artery lesions (CAL).

PATIENTS AND METHODS: A total of 95 KD patients were enrolled for this study. Plasma samples were subjected to measurement of interleukin-4 (IL-4), IL-5 and tryptase by Luminex-Bedalyte multiplex beadmates system and to measurement of ECP by fluorimunnoassay. CAL was defined as internal diameter greater than 3 mm of coronary artery.

RESULTS: Patients with KD had higher C-reactive protein (CRP) and eosinophils than febrile controls. Eosinophil-related mediators: IL-4, IL-5, eosinophils and ECP levels were also higher in KD patients than controls before intravenous immunoglobulin (IVIG) treatment. After IVIG treatment, ECP levels decreased but IL-4, IL-5, and eosinophil increased significantly. The higher the IL-5 and eosinophil levels after IVIG treatment, the lower rate of CAL was found in KD patients. Changes of eosinophils after IVIG treatment were positively correlated to changes of IL-5 levels but not the ECP levels.

CONCLUSIONS: The eosinophilia associated with higher Th2 mediator (IL-5) but not ECP level after IVIG treatment was associated with protection of CAL formation.

O-026  IL-10 gene polymorphism, but not TGF-β1 cytokine gene polymorphisms, is associated with food allergy in a Japanese population.
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Introduction: IL-10 and TGF-β1 cytokine gene SNPs (single nucleotide polymorphisms) have been associated with allergic diseases in different populations. However, no associations between IL-10 and TGF-β1 gene SNPs and food allergy (FA) in Japanese children have been evaluated so far. To clarify the relationship of SNPs of these 2 regulatory cytokine genes with FA, not atopy itself, polymorphisms IL-10 A–1082G, C–819T, C–627A and TGF-β1 T+869C, G+915C, C–509T in FA patients were compared with those in non-FA atopic controls.

Methods: 111 childhood FA patients with a mean 7.6+/−4.0 years of age and 115 atopic control children without FA (mean = 8.2+/−1.5 years of age) were recruited. Most of FA patients and atopic controls were sensitized with house dust mite. DNA samples from these subjects were genotyped by using PCR.

Results: The odds ratio (OR) of IL-10 A–1082AA genotype was 2.5 (95%CI, 1.0 - 6.4) for FA risk when compared with atopic control subjects (p = 0.03). This study had a power of 80% to achieve significance at the 0.05 level for IL-10–1082A allele when OR is greater than 2.3. Our OR value was 2.4; therefore, we consider this association had enough statistical power to support our finding. There were no significative differences in the other SNPs between both groups.

Conclusion: This result indicates that IL-10 A–1082G gene SNP is associated with FA in atopic Japanese children. Our findings should encourage further studies to elucidate the functional relationship of IL-10 A–1082G gene polymorphism in FA.

O-027  16 cases of Food-dependent exercise-induced anaphylaxis (FEIAn) successfully diagnosed by provocation test
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(Background) Provocation test is required for the diagnosis and identification of food allergens in FEIAn patients. However, provocation tests often fails to provoke symptoms. (Methods) For the diagnosis of 21 patients with FEIAn (17 males and 4 females; 7 to 18 years old), RAST, skin prick test (SPT), and provocation test on the treadmill were performed. Also we measured blood histamine, tryptase, eosinophil cationic protein (ECP), leukotrieneB4 (LTB4) and LTC4,D4,E4 levels during provocation test. (Results) Implicated food was identified in 16 patients. Among these 16 patients, eleven patients had more than two suspected food allergens. RAST for all implicated food demonstrated above class 1 in seven patients, negative in four. SPT turned positive in nine patients, negative in four. Both RAST and SPT were negative in three patients. Provocation test was positive in nine patients, negative in seven. There was no significant increase of tryptase and ECP during the tests. (Conclusion) The diagnosis of FEIAn was made by the elevated plasma histamine levels on provocation test in three patients whose RAST, SPT and the symptoms on provocation test were all negative. For clarifying implicated allergen in FEIAn patients, repeated provocation tests with several conditions are required.

O-028  The Analysis of 178 Patients with Systemic Lupus Erythematosus in Chinese Children
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Background: JSLE is a systemic involvement disease and difficulty to treatment. We summarized the patients to analysis the clinical characteristics and the treatment experience of JSLE patients. Methods: Patients hospitalized in our Hospital from 2003 to 2006. They all fulfilled the ACR criteria for SLE in 1997 year. We retrospectively analyzed the clinical features, therapy and the outcome. Results: There were 178 patients with JSLE. The gender was male 32 and female 146. The age of onset was from 3 to 16 years old. The clinical manifestations: The mild SLE patients were 44 cases with rashes, joint symptoms and fever, or some with slight anemia, leukopenia and thrombocytopenia. The neuropsychiatric SLE was 45 cases with headache, psychosis, seizures or stroke. The lupus nephritis were 116 cases with proteuria or hematuria. There were 62 cases with pulmonary manifestations and pleurisy. The cardiac and hematologic manifestations were 38% and 42% respectively. The lab test: all patients were ANA positive, the anti-dsDNA positive, anti-SM positive, anti-SSA positive and anti-SSB positive were 46%, 20%, 36% and 25% respectively. All patients represented a decreased complement level. The main treatment was steroid pulsed CTX. The fellow up periods was 6 months to 3 years. The outcome was remission 82%, repeated relapse17% and died 1 case by renal failure. Conclusion: SLE in childhood is more common in adolescent age female. Most patients are multisystem involvement. And also most patients could get remission in the near future with regularly treatment and periodic follow up.
O-029  Infection and Risk Factors of Fatal Infection in Children with Lupus Nephritis Treated with Intravenous Cyclophosphamide

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To determine the microbial etiology and risks factors of fatal infection in children with lupus nephritis treated with intravenous cyclophosphamide we retrospectively reviewed the medical records of patients <16 years between January 1996 and April 2006 in Songklanagarind Hospital, Thailand. Of 84 patients, there were 32 (38.1%) with 64 infection episodes. Patients had pneumonia, skin and soft tissue infection, infected peritoneal dialysis, gastroenteritis, and urinary tract infection in 22, 14, 13, 9, and 7 episodes, respectively. Microbiological documented infection were documented in 42/64 (65.6%) episodes isolated from blood, urine, stool, pus, and other sites in 56 specimens. Of the 44 bacteria isolated, Gram-negative bacteria were found in 32 (72.7%), Salmonella spp., K. pneumoniae, E. coli, A. baumannii, Enterobacter spp., and S. aureus were commonly found organisms. Opportunistic infection determined by fungal infection, Nocardiosis, Strongyloidesis, and Mycobacteria spp were found in 7, 3, 2, and 2 patients, respectively. Fatal infection were found in 13/32 (40.6%) patients. In the univariate analysis, factors associated with fatal infection were renal failure, opportunistic infection, previously received pulse methylprednisolone, platelet < 100,000/mm³, and hemoglobin < 10 g/dl. In the multivariable analysis, factors associated with fatal infection included renal failure (odds ratio, 21.4; 95% CI, 1.9-238.8) and opportunistic infection (odds ratio, 14.1; 95% CI, 1.8-110.2). One-third of lupus nephritis patients treated with intravenous cyclophosphamide had an infection average of two episodes per case. Of these, 40% had fatal infection. Renal failure and opportunistic infection were significant risk factors of fatality.

O-030  Cleft Lip and/or Palate: Study in Southern Thailand

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Background: Cleft lip and/or palate (CL/P) is the most common craniofacial anomaly. The incidence of CL/P in Thailand has been reported to be 1.22: 1,000.

Objective: To study the clinical characteristics of pediatric patients with CL/P.

Methods: Children with CL/P who were seen at Songkanagarind Hospital between January 1997 and December 2006 were reviewed. Data collection included age, sex, types of cleft, associated anomalies, weight, height, age at clefts, and the growth parameters. However, the children with syndromic clefts were significantly lighter at birth, and had grown up with significantly shorter, lighter, and smaller head circumference.

Conclusions: The prevalence of CL/P is high in children who had family history of cleft. Chromosomal abnormalities were commonly found in children with syndromic clefts. Children with syndromic clefts were significantly lighter at birth, had high mortality rate, and those who survived would be grown up with shorter, lighter, and smaller head size compared to those with non-syndromic cleft.

O-031  Maternal Genetic Susceptibility, Pro-oxidant Lifestyle Factors and Congenital Heart Defects (CHDs)

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Background: Congenital heart defects (CHDs) are the most common birth defects. Women with CHD-affected pregnancies may be genetically susceptible to alterations in folate-dependent metabolic pathways and these susceptibilities may be modified by maternal pro-oxidant lifestyle factors.

Methods: We conducted a population-based case-control study of 620 women who had pregnancies affected by nonsyndromic congenital heart defects, and 391 women without such a history. All pregnancies ended between January 1, 1999 and March 1, 2005. Maternal interviews were conducted on cases and controls to determine lifestyle factors such as smoking and alcohol intake. The Genomic DNA was extracted from maternal buffy cell samples. Using ABI PRISM 7900HT Sequence Detection System, DNA was genotyped for methylenetetrahydrofolate reductase (MTHFR) 677 C>T, transcobalamin II (TCII) 776 C>G, and betaine homocysteine methyltransferase (BHMT) 742 G>A polymorphisms.

Results: Women who smoked or consumed alcohol periconceptionally had high risk of CHD-affected pregnancies. Renal failure and opportunistic infection were significant risk factors of fatality.

O-032  Genetic Factors Associated Neonatal Hyperbilirubinemia

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Background: Polymorphisms of the UGT1A1 or OATP-2 gene have been reported to increase risk for significant hyperbilirubinemia in East-Asian infants. In Glucose-6-phosphate dehydrogenase (G6PD) deficiency subgroup, polymorphisms of UGT1A1 were also associated with severe hyperbilirubinemia. Since G6PD deficiency is common in Thailand, but polymorphisms of these genes have never been studied before.

Objectives: To determine whether the polymorphisms of UGT1A1 and OATP-2 genes play a role in neonatal hyperbilirubinemia and to determine their association with G6PD enzyme activity.

Methods: The subjects consisted of 91 infants with microbilirubin <95th percentile (jaundice group) and 86 controls with microbilirubin <40th percentile, respectively. The PCR-restrictive fragment length polymorphism was applied to detect the variants. G6PD enzyme activity was performed according to the WHO-standard test.

Results: Prevalence of G6PD deficiency was 21.2% in jaundice group compared to 4.8% in controls, p=0.02. Gene frequency of UGT1A1 (211G->A) was 0.15% compared to 0.04% in controls, p<0.01, no significant difference in OATP-2 (388G->A) between groups. Multivariate analysis showed only G6PD deficiency and polymorphisms of UGT1A1 (211G->A) were the significant factors for significant hyperbilirubinemia with odds ratio (ORs) of 6.29 (95% CI 1.33-29.75; p=0.02), and 4.73 (95% CI 1.80-12.38; p=0.002) respectively. The relationship of G6PD deficiency and polymorphisms of UGT1A1 (211G->A) could not be determined due to low frequency of UGT1A1 (211G->A) gene.

Conclusions: In this study, the polymorphism at the UGT1A1 (211G->A) and G6PD deficiency are the significant factors for hyperbilirubinemia in Thai neonates.
O-033 Caudal regression following adriamycin exposure: A novel animal model
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[Background] Caudal regression represents a pattern of malformation defined by hypoplasia of the caudal end of the embryo: aplasia or hypoplasia of the spinal cord, vertebrae, the urogenital system, the hindgut, and the lower extremities. It has been hypothesized that pathogenesis of caudal regression is associated with abnormality within the primitive streak. However, direct evidences for the hypothesis have been lacking. [Methods] Increasing amount of adriamycin was injected in the yolk of 2-day old embryo. The distribution of the adriamycin within the embryonic body was monitored by detecting fluorescence from adriamycin and morphological changes of the embryo were followed in a serial manner. [Results] When 5 μg of adriamycin was injected at stage 10-11, signal from adriamycin was detected most intensely in the caudal eminence 6 hours after injection. Twenty-four hours after injection, cells at the level of upper limb bud underwent massive cell death. Caudal regression was evident 48 hours after injection. Administration of 2 μg lead to caudal regression whereas that of 1 μg did not. Administration of 2-5 μg at stage 13 did not lead to caudal regression. [Discussion] We have developed a novel animal model of caudal regression. The induction of caudal regression was developmental stage- and dose- dependent. Adriamycin was accumulated to caudal eminence, a structure that evolves from primitive streak. We speculate that the primitive streak, a tissue consisting of expanding population of pluripotent cells, is vulnerable to adriamycin which brings about massive cell death. Adriamycin accumulation to caudal eminence, a structure that evolves from primitive streak. We speculate that the primitive streak, a tissue consisting of expanding population of pluripotent cells, is vulnerable to adriamycin which brings about massive cell death.

O-034 Transcriptome analysis of Down syndrome and the discovery of perturbagen patterns in the developing fetus.
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BACKGROUND: Down syndrome (DS) is a model of genomic dosage imbalance. The aim is to investigate the transcriptome difference between DS and euploid from fetal amniotic fluid (AF). The perturbagen pattern means possible treatment for genomic imbalance. METHODS: Amniocytes cultures were collected from fetuses between 16-22 weeks pregnancy. Gene expression was obtained using oligonucleotide chips (22,572 probes). Significant gene expression was analyzed by two-sample t test, Welch’s test and Significance Analysis of Microarrays (SAM), and combination by score and rank function. CMAP-based discretization by up/down tags of genes revealed candidate perturbagens in forms of agonists and antagonists. Perturbagens pattern was plotted by CMAP score versus ATC code (Anatomical Therapeutic Chemical classification), calculated permutation p values. RESULTS: AF were collected from 6 pregnancies with DS fetuses and 6 with normal. One of the DS was partial trisomy. Among 22,572 gene probes investigated, 29 genes were significantly up-regulated by all three tests. Eighteen (63%) of them were on chromosome 21. In data fusion exercises, we found combination of rank scorings was more effective than any single. Using discretization by CMAP, there were 158 agonists and 63 antagonists as candidate perturbagens. Among agonists, ATC-L (immunosuppressive agents) was the most frequent occurrence and two were significant by p value. Among antagonists, ATC-A (oral glucose lowering drugs) were the most frequent, but none was significant. CONCLUSIONS: Our microarray analysis determined expressions of 29 genes potentially important in DS and found immunosuppressive as significant agonist for DS in developing fetus. It is necessary for further study.

O-035 The Leu544Ile Polymorphism of the Growth Hormone Receptor Gene Affects the Serum Cholesterol Levels during GH treatment in Children with GH Deficiency
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Objective: The biological effects on cells by growth hormone (GH) are mediated directly through the interaction between GH and GH receptor (GHR). We investigated the association between the polymorphisms in the GHR gene and changes in height standard deviation scores (SDSs), or the lipid metabolism during GH treatment for GH deficient children.

Design: A one-year study: determining the growth rate and the lipid metabolism under GH treatment.

Patients: Eighty-three children (61 boys and 22 girls) with the GH deficiency were treated with GH for one year after the diagnosis.

Intervention: The patients were treated with recombinant human GH (0.19 mg/kg/week) for at least one year after the diagnosis. The growth rates and biochemical parameters for lipid metabolism were measured both before and during the treatment. The four types of SNPs in the GHR gene, Cys440Phe, Pro495Thr, Leu544Ile and Pro579Thr, and exon 3 deletion polymorphisms were genotyped by direct-sequencing and multiplex PCR.

Results: We found no significant association between the GHR polymorphisms and changes in the height SDSs during GH treatment. The total cholesterol levels of the GH deficient boys with Ile/Ile at codon 544 showed significantly higher cholesterol levels before GH treatment and then maintained those the high levels during the GH treatment than those with other genotypes. No other polymorphisms seemed to have any apparent effects on the lipid metabolism.

Conclusion: The Leu544Ile mutation of the GHR gene was therefore associated with the cholesterol levels in boys with GH deficiency.

O-036 Plasma adiponectin level and sleep structures in children with Prader-Willi syndrome
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Context: Adiponectin, an adipose tissue-derived hormone, has been negatively related to obstructive sleep apnea syndrome (OSA) in obese population. In addition to OSA, children with Prader-Willi syndrome (PWS) suffer from excessive daytime sleepiness and the abnormality of rapid eye movement (REM) sleep. Objective: To determine if the sleep stages are related to the plasma level of adiponectin, and whether these relationships are influenced after controlling for age, obesity and insulin resistance. Design: The sleep structures in 26 PWS children and 18 controls were compared, and the correlations between the sleep stages and the adiponectin levels were then analyzed. Setting: All subjects were admitted to the Samsung Medical Center. Interventions: Overnight polysomnography was performed and the plasma levels of adiponectin were measured. Main Outcome Measures: The relationships between the sleep stages and adiponectin levels. Results: Higher fasting plasma adiponectin levels were found in the PWS children than in the normal obese controls (P=0.006). Adiponectin levels were correlated with total sleep time (r=0.399, P=0.022) and REM sleep % (r=0.675, P=0.0001). Moreover, the correlation between adiponectin and REM sleep % remained significant after controlling for age, obesity (fat %), insulin resistance (HOMA-IR) and the apnea-hypopnea index (r=0.570, P=0.005). However, these sleep related correlations were not observed in control. Conclusions: In PWS children, elevated levels of plasma adiponectin are independently associated with the REM sleep %, which is not observed in control. These results suggest potential influence of elevated adiponectin level on the sleep structure in PWS.
O-037  Type 2 diabetic children and adolescents are not necessarily obese in Japanese and Asian populations
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Background: Type 2 diabetes (T2DM) is often erroneously considered as simply resulting from obesity. We aim to demonstrate that Japanese and Asian T2DM is, to some extent, non-obese.

Methods: Recent four studies for childhood T2DM in Japanese and Asian populations were evaluated; T2DM surveys by the IDF WPR and by the Japanese Society for Pediatric Endocrinology (JSPE), a report according to the Urine Glucose Screening and a study of hyperbolic relationship between acute phase insulin resistance (AIR) and insulin sensitivity (SI) in obese T2DM Japanese adolescents after normoglycemia.

Results: According to the IDF WPR study, non-obese T2DM adolescents ranged 14 to 35 % of the total T2DM in each country, 27 % in the WPR as a whole. The JSPE study revealed again 30.6 % were non-obese, showing the near-normal distribution without any skewed distribution to the severer obesity. Recently incidence of T2DM screened by urine glucose has not been increased in Tokyo, speculating that life style might be improved there. Regarding the hyperbolic relationship, Japanese obese T2DM adolescents revealed significantly more depressed AIR to SI in comparison with simple obese subjects showing almost the same SI.

Conclusions: We have demonstrated that non-obese T2DM children are not unusual in Japanese and Asian populations, whereas most of adolescent T2DM in African American, Hispanic and Caucasian White populations are reportedly obese. We may thus regard that Japanese and Asian populations are more susceptible to insulin secretory failure, resulting in high incidence of T2DM even with mild decrease in SI during adolescence.

O-038  Relationship between life-style related matters and very low density lipoprotein-triglyceride in children’s metabolic syndrome
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Background: Concept of metabolic syndrome (MetS) in children has been growing in recent Japan, but the studies of the pathogenesis are still very rare.

Purpose: The aim of this study is to investigate the formation of visceral fat accumulation in obese children, which is considered one of the most important mechanisms in MetS.

Subjects and Methods: Seventy three (male 36 and female 37) junior high school children aged 12.5 years at one city in Shizuoka prefecture were subjected. Waist circumference (W) was measured for the index of visceral fat accumulation. Adiponectin, serum lipids, IRI and glucose were determined, and HOMA-R was calculated. Very low density lipoprotein-triglyceride (VLDL-TG) was determined by HPLC. Life-style related questionnaire have been completed by their parents.

Results: 1) Only one male satisfied the criteria derived from Health and Labour Sciences Research. Six (male 3 and female 3) showed abdominal obesity (AB), which was defined that W was equal or over than 80 cm. 2) Comparison of non-AB group, AB group revealed significantly higher systolic blood pressure, IRI and HOMA-R, and significantly lower adiponectin levels. 3) VLDL-TG was significantly higher in AB group compared to non-AB group (p < 0.01). 4) VLDL-TG was positively correlated with W, IRI and HOMA-R. 5) Consequence of the questionnaire, physical inactivity was strongly correlated with VLDL-TG and abdominal obesity.

Conclusions: Increased hepatic lipogenesis strongly associated with scarce physical activity. These results indicated that daily physical activity must be activated for prevention and management of MetS in early teens.

O-039  Maple Syrup Urine Disease: Mutation analysis in Filipino patients using the COPPER plate system
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[BACKGROUND] Maple Syrup Urine Disease (MSUD) is a recessive metabolic disorder caused by defective function of the branched chain α-ketoacid dehydrogenase complex (BCKD). Mutation analysis of the dihydrolipoyl transacetylase (E2), the alpha and beta subunits of the branched chain α-ketoacid dehydrogenase complex was done in 33 Filipino patients. [METHODS] A quick but highly sensitive and specific mutation scanning method, called the COPPER (Condition-Oriented-PCR–primer–Embedded-Reactor) plate system, to analyze the entire coding regions of the E1α, E1β and E2 genes was used. The coding regions were amplified using 31 primer pairs, all with the same cycling conditions, and aliquoted on a 96-well format polymerase chain reaction (PCR) plate. This method allowed simultaneous amplification of all coding regions of the 3 genes using a single block in a thermal cycler. [RESULTS] Using this method, 7 novel mutations were identified, 2 missense mutations (G132S, M348K) in the E2 gene, 1 missense mutation (S339L) in the E1β gene and 2 nonsense mutations (Q157X, Q190X) in the E1α gene. We also identified an A to G nucleotide substitution changing the start codon ATG to GTG in the E1β gene. Another novel deletion involving nt 788-790 (TCT) was identified in exon 6 of the E1α gene. [CONCLUSIONS] These findings show that the COPPER plate system is an ideal tool for mutation analysis. This study also provides the molecular basis for understanding this genetic disorder among Filipino MSUD patients.

O-040  In vivo dilatation of the neonatal and fetal ductus arteriosus by inhibition of Rho-Kinase in rats
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Background: Rho-kinase activation is an additional mechanism that sustains duc tus arteriosus (DA) constriction.

Objectives: To clarify the ductus-dilating effects of Rho-Kinase inhibitor in near-term neonatal and fetal rat, in in-vivo studies.

Methods: The in vivo ductal diameter of neonatal and fetal rats was measured using a rapid whole-body freezing method, by cutting on a freezing microtome and measuring with a microscope and micrometer. Near-term (21st day of pregnancy: term=21.5 days) neonatal rats were incubated at 33 degrees Celsius following caesarean section. The DA constricted quickly after birth, and the DA diameter was 0.80, 0.08 and 0.06 mm at 0, 60 and 90 min after birth. The ductus-dilating effect of a Rho-Kinase inhibitor, fasudil, was studied by intraperitoneal injection at 60 min after birth, and the diameter was studied 30 and 60 min later. The differential effect of fasudil on the near-term were studied by orogastric administration of indomethacin (10 mg/kg) and fasudil into pregnant rats and studying the fetal ductus 4 h later.

Results: Fasudil dilated the neonatal DA dose-dependently. The ductus-dilating effect of fasudil was maximal at 30 min. Fasudil (100 mg/kg) dilated the neonatal constricted DA completely to 0.78 mm. Fasudil (1 mg/kg; clinically equivalent dose) dilated the DA to 0.15 mm. Fasudil inhibited fetal ductus constriction induced by a large dose of indomethacin dose-dependently.

Conclusions: The Rho-kinase inhibitor (fasudil) dilated the constricted neonatal and fetal DA dose-dependently in rats. Rho-kinase inhibitors may be useful in maintaining ductus arteriosus patency, as a bridge to congenital heart surgery.
O-041  Redundant and tissue-specific roles of Hand genes in heart, limbs and cranial development
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Hand genes (Hand1/eHand and Hand2/dHand) encode critical transcription factors required for cardiovascular, pharyngeal arch and limb development. Hand2 is expressed predominantly in developing right ventricle, whereas Hand1 is restricted in left ventricle. Both Hand genes direct overlapping expression in pharyngeal arch mesenchyme, however only Hand2 is expressed in the zone of polarizing activity (ZPA) of developing limb buds. Hand1 cardiac-specific null mice display defects in left ventricle and endocardial cushion. Hand2 null (Hand2−) mice display severe hypoplasia of right ventricle and die at embryonic day (E) 10.5 due to the heart failure resulting in degenerative pharyngeal arch and limb buds. To delineate the genetic redundancy and regional function of Hand genes in murine development we genetically engineered Hand2Hand1/Hand1 mice where a Hand2 gene was replaced by the Hand1 cDNA using homologous recombination so that Hand1 was driven under control of endogenous Hand2 promoter, and Hand2Hand1/− mice from mating of Hand2Hand1/− mice with Hand2− mice. Our observation revealed that Hand2Hand1/Hand1 mice had hypoplastic right ventricle, preserved pharyngeal arch and hypoplastic digits and survived until E13.5. This phenotype was milder than that of Hand2− or Hand2Hand1/− mice, suggesting that Hand1 could partially compensate the function of Hand2 in ventricular and pharyngeal arch formation, but not in limb buds. These results indicate that in mammalian cardiac ventricles and pharyngeal arch, Hand genes may have common function and partial genetic redundancy. The complementally expression of Hand genes may be essential for regionalization of right and left ventricles.

O-042  Electromechanical dyssynchrony in childhood idiopathic dilated cardiomyopathy
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Background: Electromechanical dyssynchrony worsens the prognosis in adults with heart failure and serves as a therapeutic target for cardiac resynchronization therapy (CRT). However, its role in childhood idiopathic dilated cardiomyopathy (IDCM) has not been explored.

Methods: From 1983 to 2007, 89 patients with IDCM were identified. Twenty patients received echocardiography with tissue Doppler imaging. Interventricular (V) dyssynchrony was defined as an interventricular mechanical delay (IVMD) ≥ 40 ms. Intra-left ventricular (LV) dyssynchrony was defined as the standard deviation of Ts (the time from beginning of QRS complex to peak systolic contraction among the 12 LV segments) (Ts-SD) > 32.6 ms.

Results: The 1- and 5-year survival was 70% and 53%. QRS prolongation (≥ 120 ms), found in 16 patients (18%), was associated with worse outcomes. The prevalence of inter-V and intra-LV dyssynchrony was both 86% in patients with QRS prolongation, and 8% and 38%, respectively, in those without. Mechanical dyssynchrony was more advanced in patients with QRS prolongation than those without (61.4 ± 21.0 versus 15.8 ± 11.3 ms, p < 0.001 for IVMD and 45.3 ± 11.0 versus 32.4 ± 8.9 ms, p = 0.011 for Ts-SD). The QRS duration correlated well with inter-V dyssynchrony (r = 0.75, p < 0.001), but not with intra-LV dyssynchrony (r = 0.37, p = 0.11).

Conclusions: Intra-LV dyssynchrony, though more prevalent in patients with QRS prolongation, is not uncommon in patients with normal QRS duration. A subset of childhood IDCM may potentially benefit from CRT following precise assessment of cardiac synchronicity.

O-043  Aerosolized Iloprost for Pulmonary Vasoreactivity Testing in Children with Long-Standing Pulmonary Hypertension Related to Congenital Heart Disease
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Background: In children with congenital heart disease (CHD) and significantly increased pulmonary blood flow and pressure, progressive pulmonary vascular changes can lead to an irreversible stage. Pulmonary hemodynamics are used to determine the stage whether the surgical correction is indicated. In children with pulmonary hypertension (PH) from CHD, the pulmonary vascular resistance (PVR) > 6 Wood U/m2 or a pulmonary-to- systemic resistance ratio (Rp/Rs) > 0.3 has been shown to be associated with a poor operative outcome. Therefore, assessment of the vasodilator capacity is important. Whether aerosolized iloprost could be used for the vasoreactivity testing in children with a long-standing PH from CHD is needed to determine.

Methods: Children with PH from CHD underwent for hemodynamic evaluation and vasoreactivity testing using iloprost 0.5 mcg/kg delivered through jet nebulizer. Hemodynamic calculations, based on the Fick’s principle, were obtained. We consider a decrease in both PVR and Rp/Rs of > 10 % as a responder.

Results: Nineteen children aged 7 months to 13 years, mean age 4.8 years, were tested. Eleven children had a positive response, resulting in a mean±SD decrease in PVR of 6.2±4.3 to 3.5±3.1 Wood U/m2 and in Rp/Rs of 0.33±0.21 to 0.19±0.17 (p<0.01). Nine of the 11 responder children underwent surgical correction of their CHD.

Conclusions: Iloprost induced vasodilator capacity varies among children with PH and elevated PVR. Our study suggested iloprost may be beneficial in preoperative identification of children with long-standing PAH secondary to congenital heart disease for surgery. However, additional vasodilator testing may be required.

O-044  Does “treating” mild rejection prevent significant rejection in pediatric heart transplantation?
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Heart transplantation is an accepted treatment for end stage pediatric heart failure. Life after transplantation include intensive and regular invasive and non-invasive monitoring to preempt acute rejection and the development of transplant coronary artery disease and post transplant lymphoproliferative disease. Compliance is an ongoing challenge in the adolescents. It is generally accepted that mild rejection (ISHHLT grade 1R or 1A, 1B & 2) do not require treatment. However, grade 1B was more likely than 1A or 2 to degenerate to moderate 3A rejection. Over the past decade, 57 children (age 0.5-16.4 years) has been transplanted at Alberta Provincial Pediatric Heart Transplant Program. There were 3 late deaths (compliance n=2, chest infection n=1) and 3 early deaths (high PRAs n=1, multi-organ failure n=2). One teen had a late moderate rejection related to compliance and treated successfully. Excluding the non-compliant patients and early deaths, all remaining patients were monitored with 3-4 biopsies in the first year and annually thereafter if rejection free. All mild rejections (1A & 1B) were “treated” by increasing the immunosuppression, balancing the dose against renal function, and re-biopsied monthly until rejection free (ISHHLT grade 0). Immunosuppression consists of ATGAM for induction, triple therapy (tacrolimus, mycophenolate, prednisone) for 9-12 months. Steroid wean starts at 6 months if rejection free and the patients were usually off steroid by 9-12 months. Rejections ≥ grade 2 has not been observed in the last decade. We conclude that “treating” mild rejections prevent the development of significant rejection in the pediatric heart transplants.
O-045 Noninvasive assessment of pulmonary artery resistance and pressure in patients with congenital heart disease: A new method using M-mode echocardiography

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Aim: Accurate evaluation of pulmonary artery resistance \(<R_p>\) and pulmonary artery mean pressure \(<P_{AMP}>\) were important for management of patients with congenital heart disease \(<CHD>\). It is usually required for an accurate measurement by cardiac catheterization. We assessed the severity of pulmonary artery hypertension in patients with CHD using motions of the interventricular septum \(<IVS>\) by M-mode echocardiography. Method: We performed echocardiography on 46 patients \(<2\) months to 20 years old \(<CHD>\) included in complex CHD. Cardiac catheterization was performed within 1 day of the echocardiography study in all cases. All patients were divided into 2 types by IVS motion evaluated using M-mode echocardiography: type A marked anterior motion in early systole; type B marked posterior motion in early diastole. Result: There were 12 patients with type A and 34 patients with type B. Pulmonary artery resistance in type A patients were significant higher than Rp in type B patients \(<3.70 \pm 2.56 vs. 1.77 \pm 0.86 U; p<0.01 >\). Pulmonary artery mean pressure in type A patients were significant higher than PAMP in type B patients \(<35.3: 18.7 vs. 17.9 \pm 8.93 mmHg; p<0.01 >\). There were also significant difference in right ventricular end-diastolic pressure \(<RV-EDP>\) between type A patients and type B patients \(<6.82 \pm 2.73 vs. 4.53 \pm 1.76 mmHg; p<0.05 >\). Conclusion: The IVS motion evaluated using M-mode echocardiography accurate distinguished between patients with high Rp and high PAMP and patients with low Rp and low PAMP, noninvasively.

O-046 The Impact of Right Ventricular Dilation on Regional Left Ventricular Function in Patients After Tetralogy of Fallot Repair: A Novel Assessment by Speckle Tracking Echocardiography

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Background: Right ventricular (RV) volume overload affects the left ventricular (LV) function in patients after tetralogy of Fallot (TOF) repair. However, the impact of RV dilation on regional LV wall motions was unclear. In this study, we determined the relationships of RV size as derived from cardiovascular magnetic resonance (CMR) with the global and regional LV wall motion.

Methods: Echocardiogram was performed on 25 postoperative TOF patients aged 17.8±4.4 years and data were compared with 23 age-matched controls. The longitudinal, radial and circumferential components of LV wall motion were analysed using speckle tracking method. CMR-derived parameters of all TOF patients were used for correlation analysis.

Results: When compared with controls, TOF patients had reduced global LV longitudinal strain \((p<0.005)\) and SR \((p<0.001)\), and global LV radial strain \((p<0.001)\). Reduced global LV radial strain was contributed by lower strain in inferior, lateral, posterior, and anterior segments \((p<0.05)\). TOF patients had lower circumferential strain of LV inferior-septal \((p<0.001)\) and inferior \((p<0.001)\) segments. In TOF patients, global LV circumferential strain and SR correlated negatively with indexed RV end-diastolic volume \((r=-0.61, p<0.002 and r=-0.45, p=0.03\) respectively) and indexed RV end-systolic volume \((r=-0.61, p<0.002 and r=-0.53, p=0.009\) respectively). LV ejection fraction decreased with indexed RV end-diastolic \((r=-0.67, p<0.002)\) and end-systolic \((r=-0.73, p<0.001)\), and increased with global LV circumferential SR \((r=0.58, p=0.015)\).

Conclusions: The negative impact of RV dilation on LV function relates to its influence on LV circumferential wall motion in patients after TOF repair.

O-047 Novel Two-Dimensional Global Longitudinal Strain and Strain Rate Imaging for Assessment of Systemic Right Ventricular Function

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Background: We sought to determine the usefulness of novel 2-dimensional strain indices, based on speckle tracking imaging, for assessment of systemic right ventricular (RV) function in patients after atrial switch operation for transposition of the great arteries.

Methods: Twenty-six patients, aged 21.0±3.6 years at 19.9±3.2 years after atrial switch operation, and 27 age-matched controls were studied. Two-dimensional imaging at the 4 chamber view was obtained with tracing of the entire RV endocardial border. The RV global longitudinal strain (GLS) and GLS rate were derived using an automated software (EchoPAC, GE Medical), and correlated with tissue Doppler-derived RV isovolumic acceleration (IVA), and, in patient cohort, with cardiac magnetic resonance-derived RV ejection fraction. Results: Intraobserver and interobserver variability for measurement of GLS, as determined from mean ± SD of differences in 2 consecutive results from 20 studies, were 0.06±1.93% and 0.24±1.77%, respectively. Compared with controls, patients had lower RV GLS \((17.1±1.9% vs 26.3±2.9%; p<0.001)\), reduced GLS rate \((0.78±0.11/s vs 1.33±0.23/s; p<0.001)\), lower RV IVA \((1.10±0.36 m/s^2 vs 1.56±0.53 m/s^2; p<0.001)\), and increased RV myocardial performance index \((0.52±0.09 vs 0.38±0.09; p=0.001)\). Both RV GLS and GLS rate correlated positively with RV isovolumic acceleration \((r=0.43, p=0.001\) and \(r=0.46, p=0.001\), respectively), and negatively with RV myocardial performance index \((r=-0.65, p<0.001\) and \(r=-0.57, p<0.001\) respectively). In patients, GLS rate correlated positively with RV ejection fraction \((r=0.62, p=0.001)\).

Conclusions: Two-dimensional RV GLS and GLS rate are novel indices potentially useful for assessment of systemic RV function.

O-048 Role of Computed Tomography (MDCT) in Pulmonary Atresia (PA) with Ventricular Septal Defect (VSD): Focus on the Pulmonary Artery Morphology and Trachea Stenosis

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Background: MDCT had been applied to congenital heart disease for several years. However, large scale application of this new imaging tool to the patients with PA and VSD had never been reported before.

Objective: In a tertiary medical center, 11-year experience of MDCT in PA with VSD will be reviewed with focus on the pulmonary artery morphology and trachea stenosis.

Methods: Between 1995 and 2005, 110 patients with PA and VSD visited our hospital. 211 times of MDCT were conducted in 103 of them. Those who received operation three months before or after their MDCT examinations were enrolled. Four patterns of pulmonary artery morphology were defined: native main pulmonary trunk present (group I); confluent central pulmonary arteries without trunk (group II); nonconfluent central pulmonary arteries (group III); absent intrapericardial pulmonary arteries (group IV). Results of pulmonary artery morphology from MDCT were compared with the operation findings. Existence of trachea stenosis was also evaluated.

Results: Data of 95 times of MDCT (74 patients) with concurrent operations were collected. Based on the surgical findings, distribution of each group is: 53 (group I, 55.8%), 25 (group II, 26.3%), 12 (group III, 12.6%), 5 (group IV , 5.2%). The overall accuracy for MDCT was 91.6% (87/95). The group specific accuracy was between 88.7% and 100%. In addition, trachea stenosis was detected in 8 patients (10.8%).

Conclusion: For PA with VSD, MDCT is a useful tool to define pulmonary artery morphology and possible trachea stenosis, both of which will influence the surgical outcome.
O-049 Neuroanatomical Development of Infants Undergoing Heart Surgery Evaluated by Quantitative Three-Dimensional Magnetic Resonance Imaging

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1Toyama University, Department of Pediatrics, 2Toyama University, Department of Psychology, Toyama University, Department of the first surgery.

Background: Increased survival in infants with congenital heart disease has raised interest in the neurodevelopmental sequelae, but there is no data regarding neuroanatomical development in infants with critical CHD. Volumetric study of the brain using three dimensional magnetic resonance imaging in infants with CHD can help to identify effects on anatomical development of the brain that may be associated with functional impairment.

Methods and Results: Thirty-nine infants with CHD were studied prospectively with brain 3D-MRI several months after heart surgery, and compared to nineteen healthy control infants. Neurodevelopmental assessment was performed using Bayley II infants developmental scales. The global volume of grey matter was significantly reduced in the patients with CHD compared to normal control (P<0.001) while no significant difference of the volume of white matter was observed. Further, decrease of GM volume was more apparent in frontal lobe than that in temporal lobe. Multivariate analysis revealed that preoperative hypoxia is strongly associated with decreased frontal GM volume (P=0.007). Further, hypoxic patients have a trend toward smaller regional brain volumes, most prominently in frontal GM (P=0.017), as well as more delayed psychomotor developmental index PDI score (P=0.005), but not with mental developmental index.

Conclusions: Brain developmental impairments occur in a number of infants with CHD, especially in those with chronic hypoxia. This quantitative volumetric assessment of the brain in infants with critical congenital heart disease can help to identify anatomical brain changes associated with functional impairment.

O-050 Pattern of hospital visits and seasonal variation among Japanese children living in Thailand

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<Objective>
This study was conducted at Bangkok Hospital in Thailand to investigate the disease trends and seasonal variation among children of Japanese expatriates living in Thailand.

<Methods>
Records of Japanese children seen at the out patient clinics at Bangkok Hospital in 2005 were analyzed.

<Result and Discussion>
A total of 4,329 children visited the outpatient clinics at Bangkok Hospital; 2,396 cases had ICD-10 diagnoses.

1. Sharp drops were observed in the number of hospital visits in January, April and August. Many Japanese take vacations during these months. Temporary visits back to Japan could account for these drops in hospital visits.

2. Identical drops in the number of visits were also seen for diseases of the respiratory system, indicating that these diseases are not associated with seasonal changes.

3. The number of hospital visits for infectious gastroenteritis fluctuated during the rainy season, gradually increasing from the middle of the rainy season to the beginning of the dry season. Several years of continual observation is still needed.

4. A large number of patients visited the hospital for viral infection characterized by skin and mucus membrane lesions during the rainy season, indicating the need to emphasize preventive measures this period.

O-051 ASSOCIATION OF DEVELOPMENTAL QUOTIENTS AND FREQUENCY OF ONE-ON-ONE INTERVENTION AMONG CHILDREN DIAGNOSED WITH AUTISM AT DE LA SALLE UNIVERSITY-NEURODEVELOPMENTAL CENTER, DAMARINAS, CAVITE, PHILIPPINES

Marie Karen Nulud Dixon, Rochelle Pacifico, Madeleine Sosa

De La Salle University Medical Center

Objective: To determine which frequency of one-on-one intervention is more helpful and effective in the improvement of the developmental quotients of children with autism enrolled at the De La Salle University-Neurodevelopmental Center. To determine which among the developmental areas improved a lot in the developmental quotients of children with autism enrolled at DLSU-NDC.

Design: Retrospective Cohort Design. Methodology: A review of school records of autistic students enrolled in a Neurodevelopmental Center was done. Data, such as students’ demographics were obtained. Initial developmental quotients and comparing with the developmental quotients at least 6 months after therapy of both groups were gathered. The type of scheduling in which the students were enrolled was done to see if their DQ in the subsequent evaluation were significantly higher than the initial. Improvement is defined by a child’s step up in their level of functionality. Those who obtained the same or lower level were labeled as no improvement. Results: Out of 37 autistic children enrolled in DLSU-NDC, only 30 students were included in the study. Fourteen of them received once-a-week therapy session (Group 1), while the rest receive more than once-a-week therapy (Group 2). Twelve of the students in Group 1 gained a higher DQ, but only 5 of them improved to the next level of functionality. Eleven students in Group 2 had increments in their DQs but only half of them stepped up from their initial functional level. Seventy-seven percent (77%) of subjects improved Personal and Social Area, followed by the Performance area of Development (73%). In Group 1, the average difference between the initial DQ and the subsequent DQ is with marginal significance. While in Group 2, their average difference is statistically significant. Conclusion: The frequency of therapy session is not associated with the development or deterioration of their Developmental Quotients(DQs). Most of the autistic children receiving intervention improved in their performance and personal and social areas, which then helped them to make the most productive use in their advancement in mental skills.

O-052 Prevalence of sleep problems among elementary students in southern Thailand

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Introduction: Sleep problems in children are now recognized to be common and can create adverse effects on physical and mental health. Only a few sleep-problem studies have been reported from Asian populations.

Objective: To determine the prevalence of sleep problems in elementary students.

Methods: A cross-sectional study was conducted using a questionnaire survey with 18 sleep-related items with the parents from 10 randomly selected schools in Hat-Yai, southern Thailand. A sleep problem was defined as one occurring 2 times or more per week.

Results: A total of 1,136 children aged 5.2-14.2 years (9.3±1.8) were enrolled in this study. The average sleep duration ranged from 9.3±0.7 hours among 5-7-year-olds to 8.9±0.8 hours among 11-14-year-olds. The most prevalent specific sleep problems were: requiring morning awakening (59.1%), irregular bed times (38.0%), difficulty getting up (34.5%), and fear of sleeping alone (34.3%). Parasomnia symptoms were less common (bruxism 13.0%, sleep talking 10.1%, and enuresis 5.0%). The frequencies of all sleep problems were similar in boys and girls. Four problems significantly decreased with age: needing a parent in the room to sleep, enuresis, bruxism, and requiring morning awakening. Two problems significantly increased with age: difficulty falling asleep in 20 minutes, and awakening during the night.

Conclusions: Sleep problems are common among Thai children. The most prevalent sleep problem found in this study, the requiring morning awakening, was similar to that reports from China and the USA, while night waking and parasomnia symptoms were less.
O-053  "PCr recovery overshoot" in the developing brain after transient hypoxia-ischaemia: relation to baseline energetics and insult severity

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Background: Phosphocreatine (PCr) overshoot following hypoxia-ischaemia has been observed in cardiac and skeletal muscle; the significance of this supernormal high-energy phosphate reserve is unclear. Following perinatal hypoxia-ischaemia, despite the immediate activation of cytotoxic injury cascade, brain high-energy phosphate levels normalise transiently ("latent-phase") until secondary energy failure (SEF) becomes apparent. Objective: To investigate PCr overshoot in relation to (i) baseline metabolism; (ii) insult severity, (iii) ischaemia, despite the immediate activation of cytotoxic injury cascade, brain high-energy phosphate levels normalise transiently ("latent-phase") until secondary energy failure (SEF) becomes apparent. 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Background: The etiology of febrile seizures (FS) is considered to be multifactorial: fever, genetic predisposition and environmental factors such as infections. A large majority of FS are caused or triggered by viral infections. The innate immunity responses play an important role in viral infections. To identify whether Toll-like receptor (TLR) and related genes (TLR3, TLR7, TLR9, and UNC93B1) contribute to the development of FS, we performed a case-control study using single nucleotide polymorphisms (SNPs). Methods: We genotyped the six SNPs in four genes based from the data of the International HapMap Project in 249 FS patients (186 simple and 63 complex) and 225 control subjects. Genotyping was performed with TaqMan SNP Genotyping Assay. The HapViewer was used to construct haplotypes. Results: The frequency of G allele at rs308328 (UNC93B1; intron?) was significantly higher in FS patients than control subjects (p=0.02). In subgroup analysis, the genotype distributions were significantly different between complex FS, but not simple FS, and controls (corrected p=0.039). No associations were detected between SNPs in TLR3, TLR7, TLR9 and FS susceptibility. Conclusion: The present study suggested that UNC93B1 gene contributed to a genetic susceptibility to development of FS, especially complex FS. UNC93B1 interacts with TLR3, TLR7 and TLR9. The congenital deficiency is linked to the etiology of herpes simplex virus-1 encephalitis in humans (Casrouge, 2006). Inflammatory processes caused by direct viral invasions might be involved in the pathophysiology of complex FS.

Background: Hyponatremia is frequently recognized in preterm infants of less than 30 weeks of gestation. Aldosterone plays a pivotal role in a sodium and potassium homeostasis, but our knowledge on the aldosterone levels in this population is limited. The purpose of this study was to elucidate the patterns of postnatal serum aldosterone levels during the first month of life in premature infants of less than 30 weeks.

Methods: All neonates admitted to Bokutoh Hospital, a tertiary Neonatal Intensive Care Unit with a gestational age of less than 30 weeks were enrolled. After obtaining consent from parents, serum sodium, potassium, creatinine and aldosterone were measured at 7 days, 14 days, 21 days and 28 days. The infants were divided into two groups for further evaluation of the results: group A (gestational age 22-25 weeks), and group B (26-29 weeks).

Results: A total of 47 infants meeting the enrollment criteria were admitted between April 2005 and March 2006. The serum aldosterone levels were elevated at 7 days in both groups, and remained high until 28 days in group B alone. The serum aldosterone levels were significantly lower at 14, 21, and 28 days in group A vs. group B. The calculated FENa was significantly higher in group A vs. group B with comparable serum creatinine levels at 7 days and 28 days.

Conclusions: Insufficient secretion of aldosterone, together with renal tubular prematurity, may contribute to the urinary sodium loss at 28 days in the extremely premature infants of less than 26 weeks gestation.

O-059 THE INFLUENCE OF HEIGHT AND BODY MASS INDEX ON LEFT RenAL VENous FLOW VELOCITY IN CHILDREN WITH HEMATURIA

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Background: To determine the influence of anthropometric parameters on left renal venous flow velocity in children with hematuria.

Methods: During the past 3 years, we performed a renal Doppler ultrasound in 216 children with macro- (n=40) or microhematuria (n=176). Peak velocity (PV) was measured in the transverse plane at two points in the left renal vein (LRV), one at the hilar portion of the LRV, and the other at the aortomesentric portion. Anthropometric measurement of height, weight, body surface area (BSA), and body mass index (BMI) were made at the time of ultrasound.

Results: They were divided into two groups according to the PV ratios of the LRV: nutcracker group (PV ratio > 4.1, n=72) and non-nutcracker group (PV ratio < 4.1, n=144). There were no differences in the mean age, gender, weight and BSA between the two groups. However, height was significantly higher in nutcracker group than non-nutcracker group (p=0.031), and BMI was significantly lower in nutcracker group than in non-nutcracker group (p=0.006). Furthermore, the PV ratios of the LRV in 216 children with hematuria inversely correlated with BMI (PV ratio = 6.936 – 0.17 X BMI, r = -0.188, p=0.006). This inverse correlation was also observed when we selected 113 male patients (r = -0.267, p = 0.004), but not in 103 females (p = 0.478).

Conclusions: These results suggest that patients with nutcracker syndrome were leaner than those without nutcracker syndrome, and height and BMI may influence on left renal venous flow velocity in patients with hematuria.

O-060 Effective and safe treatment with cyclosporine in nephrotic children: a prospective, randomized, multicenter trial

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This prospective, open-label multicenter trial evaluated the efficacy and safety of 2 years of treatment with cyclosporine (CyA) in children with frequently relapsing nephrotic syndrome (FRNS). The patients were randomly divided into two groups. For the first 6 months, both groups received CyA (Sandimmune®) in a dose that maintained the whole-blood trough level between 80 to 100 ng/ml. For the next 18 months, the dose of CyA was adjusted to maintain a trough level between 60 and 80 ng/ml in Group A, while Group B received a fixed dose of 2.5 mg/kg/day of CyA. The primary end point was the rate of sustained remission. At 24 months, the rate of sustained remission was significantly higher in Group A (30%, n=24 patients) than in Group B (15%, n=20, p=0.006). The hazard ratio for relapse was 0.37 (95% CI, 0.18 to 0.79, p=0.01) in Group A as compared with Group B (hazard ratio = 1.0). Mild arteriolar hyalinosis of the kidney was found in 4 (19.0%) of 21 patients in Group A and 1 (5.6%) of 18 in Group B. We conclude that CyA given for 2 years in a dosage producing a trough level between 80 and 100 ng/ml for the first 6 months, followed by a trough level between 60 and 80 ng/ml for the next 18 months is an effective and relatively safe treatment for children with FRNS. With this regimen, about 50% of patients are expected to remain relapse-free during 2 years of treatment, without serious adverse effects.
O-061 Genetic and clinical analysis of 84 cases with Dent disease in Japan
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[Background] Dent disease is a disorder characterized by tubular low molecular proteinuria, hypercalciumia, nephrocalcinosis and progressive renal dysfunction. It has recently been revealed that Dent disease is genetically and clinically heterogeneous. In particular, characteristics of Japanese-Dent disease largely remain unknown.

[Object] To elucidate the genetic backgrounds and clinical features of Japanese-Dent disease in a large scale survey.

[Materials and methods] CLCN5 and OCR1 genes were directly sequenced in 84 cases with Japanese-Dent disease, and the recent clinical data were obtained from the physicians who are taking care of them at present.

[Results] 1. CLCN5 mutations were identified in 42 cases, in which 31 are novel including 12 missense mutations. Three missense mutations, i.e., F703R, F706P, C711W, are localized at the N-terminus of CLC-5.
2. OCR1 mutations, i.e., H127X, R301C, R476W and R318H, were identified in four cases, none of whom manifested any abnormalities in the eyes or neurological development.
3. Hypercalciumia, an essential manifestation of Dent disease in Europe and USA, is only detected in 50 % of patients with Japanese Dent disease.

[Conclusion] The present study reveals that the clinical phenotypes of Japanese-Dent disease are not identical those in Europe and USA, although the genetic backgrounds are similar.

O-062 The Success of Oral Rehydration Therapy for Diarrhea diseases in Thailand
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A simple salt-sugar (SS) mixture has first been produced for ambulatory oral rehydration therapy (ORT) at Ramathibodi Hospital, Bangkok, Thailand since 1971. The rate of hospitalization decreased remarkably. Clinical studies showed the effectiveness and safety of SS solution compare to WHO-ORS. In 1978, the administration of SS solution via nasogastric tube to the dehydrated diarrhea patients was initiated and it could replace intravenous fluid administration by 90.9%. These knowledge has been introduced to health personnel by short course training and workshops yearly for 12 consecutive years. ORT was started early at the home and at all levels of health centers. The people in community as stakeholders performed the surveillance of diarrhea diseases, ORT and reported the outcome. ORT is considered successful in Thailand with the increasing rate of 47.6% in 1990 to 92.8% in 2005. It reduces mortality rate from 0.99 per 100,000 populations in 1986 to 0.09 per 100,000 populations in 2005. The achievement was due to the cooperation of Control Diarrhea Diseases Program of the Ministry of Public Health, researchers at the Universities and people in the community. However there is a challenging question in the Health column in TIME-Asia magazine October 16, 2006 stating that “A Simple Solution. Diarrhea kills more young children around the world than malaria, AIDS and TB combined. Yet a simple and inexpensive treatment can prevent many of those deaths. Why isn’t it more widely used?” This question needs to be answered. If it is widely used, million of lives can be saved.

O-063 Mainstreaming nutrition for improving nutrition in developing countries
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Improved nutrition is critical to improving health of mothers and children in developing countries. Without this improvement in nutrition, the Millennium Development Goals cannot be achieved. Nearly a third of the children in the developing countries are malnourished. About 60% of the deaths in children are associated with malnutrition. There is enough evidence linking nutrition and good maternal and child health (MCH) outcomes; however, nutrition has been poorly integrated with MCH programs in most countries. The Mainstreaming Nutrition Initiative, formed with support from the World Bank, aims to converge the nutrition agenda in selected countries with the MCH agendas towards the achievement of MDGs. This is based on emerging international consensus that convergence of nutrition and MCH is essential. The primary objective of this initiative is to create a partnership between ICDDR,B and global partnerships in health and nutrition to catalyze a convergence of the nutrition and MCH agendas. A conceptual framework for the mainstreaming process as well as tools for assessing the process has been developed. A global review of nutrition has been done with a view to find out evidence for mainstreaming nutrition into MCH programs. The review has contributed substantially to the upcoming Lancet Nutrition Series. Activities related to mainstreaming nutrition have been initiated in several countries including Bangladesh, Viet Nam, Pakistan, Uganda, Ethiopia, Bolivia and Peru. These activities will include assistance in formulating policy on mainstreaming and integration of simple and efficacious nutrition interventions.

For more information on the MNI, please visit http://www.icddrb.org/activity/index.jsp?activityObjectID=2347.

O-064 Is Helicobacter pylori infection a cause of gastric hypoacidity in children in developing countries?
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Background: Little is known about effect of Helicobacter pylori (Hp) infection on gastric acid secretion (GAS) in children. The aim of this study was to determine whether Hp infection in children is associated with perturbation of GAS.

Methods: We conducted this study on 30 asymptomatic Hp-infected (positive urea breath test; UBT) and 30 Hp-non infected children (2-5 years) from a peri-urban community near Dhaka City. The gastric pH and GAS was measured before and 60 days after anti-Hp therapy (omeprazole, clarithromycin and amoxicillin for 2 weeks). Gastric acid outputs (Mmol/h) were quantified and amoxicillin for 2 weeks). Gastric acid outputs (Mmol/h) were quantified during a 1-hr basal period (BAO) and 1-hr stimulated period (SAO) with subcutaneous pentagastrin (6µg/kg). Hp status was reassessed 60 days after anti-Hp therapy. Results: A significantly greater number of infected children had a very high gastric pH (> 5.5) and demonstrated absolutely no acid output (achlorhydria) in basal state compared to the age matched non-infected group. The acid concentration and volume of gastric secretion were also decreased in infected children. Furthermore, the mean BAO and SAO in Hp-infected children were 50% lower than those with non-infected. However, the eradication therapy in infected children resulted in increase in volume of gastric secretion, lowering of gastric pH, reversal of achlorhydria and significant rise of SAO (before vs. after; 2.04 ± 1.4 vs. 3.4 ± 2.5, p=0.001), the values equivalent to the Hp-noninfected children (3.3 ± 2.1). Conclusion: The results suggest a causal link of Hp infection with gastric hypoacidity in this population.

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O-065  Snack and beverage intake among primary school children in southern Thailand

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Background: An increasing frequency of snack and beverage consumption has been observed in recent studies worldwide. Due to their high-energy density and low-nutrient content, snacks and beverages may contribute significantly to the diet of children.

Objective: To examine the snack and beverage consumption pattern of sixth grade primary school children in a school in southern Thailand.

Methods: A cross-sectional study of sixth grade school children from 25 randomly selected primary schools in Hat Yai, Songkhla (southern part of Thailand), was conducted from January to March 2006. Snack and beverage consumption data of children were collected by using 7-day recall semi-quantitative food frequency questionnaires.

Results: Of the 1982 children, 1012 (51.1%) were male. In the week prior to the survey, 92.7% of children consumed high carbohydrate/high fat crispy snacks, 90.6% drank soda and 88.8% drank sweetened milk. Whole milk was taken by 72.2% of the children and 64.6% and 62.0% consumed baked beans and low-fat milk, respectively. No gender differences in the consumption patterns were observed. Urban children obtained 22.8% of their energy intake from milk, while rural children obtained 18.2% (no significant differences between the two groups). Altogether, snacks and beverages (excluded milk) contributed 38.6% of the energy intake in the sampled children.

Conclusions: The results showed that snacks and beverages contributed significantly to the diet of the sixth grade primary school children surveyed. Providing healthy snacks and beverages for children should thus be emphasized to parents and guardians.

O-066  Risk factors for development of sclerema in infants with diarrhoeal disease

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Background: Sclerema is a life threatening condition characterized by diffuse, doughy feeling of the skin and/or rapidly spreading, tallow-like hardening of the subcutaneous tissue. It usually affects newborns with case-fatality ranging from 50-100%. Death usually occurs within hours to days of onset. There is lack of information on the pathogenesis and risk factors for development of sclerema.

Methodology: In this age and sex matched case-control study, we enrolled 30 infants with clinical sepsis and sclerema (cases) and another 60 age and sex matched infants with clinical sepsis but without sclerema (controls) from amongst those attending the Dhaka Hospital of ICDDR,B with diarrhoea during May 2005 through April 2006. Results: The median age of the subjects was 2.1 months. Case-fatality was significantly higher among the cases than controls (30% vs. 2%, p=0.001), and they more frequently presented with severe dehydration (33% vs. 10%, p=0.02), hypoxia (56% vs. 18%, p=0.008), abdominal distension (50% vs. 22%, p=0.01), septic shock (20% vs. 2%, p=0.005), hypoglycaemia (37% vs. 7%, p<0.001) and higher serum CRP (mg/dl) concentration (5.0 ± 4.6 vs. 2.2 ± 2.4; p<0.001). After adjusting for confounders, infants with sclerema were more likely to be hypothermic (OR 11.6, 95% CI 1.1-126.5, p=0.04), and have lower serum total protein (OR 1.12, 95% CI 1.04-1.21, p=0.003) and pre-albumin (OR 1.5, 95% CI 1.1-2.3, p=0.03). Conclusion: Sclerema is associated with high case-fatality, and infants presenting with hypothermia, lower serum protein and pre-albumin along with clinical sepsis are at risk of developing sclerema.

O-067  Endotoxin induces hepatic pro-inflammatory innate immune responses and hepatobiliary injuries in newborn mice

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Endotoxin (LPS) plays a role in neonatal cholestasis syndromes such as biliary atresia. We thus implemented this study to delineate hepatic innate immunity and pathologic outcomes against LPS exposure in newborn mice.

Newborn Balb/c mice were subjected to intra-peritoneal injections of saline (SHAM group), or different doses of LPS (2, 25, or 75 ug/g of body weight) within 24 hours of birth. Hepatic gene expressions of endotoxin receptors (CD14 and TLR4), TNF-a, and IFN-g were measured at different time points. Liver pathology was also evaluated.

We found that Immediate hepatic TLR4 gene activation (3.2 folds compared with SHAM) was observed as early as 30 minutes after LPS. Early hepatic CD14 gene expressions (23.9 folds) was also noted at 1~2 hours. Maximal hepatic TNF-a gene responses were also achieved at 1~2 hours (51.2 folds). Interestingly, maximal hepatic TLR4 and CD14 gene activation was observed at 6 hours (8.1 and 89.9 folds for TLR4 and CD14, respectively), representing secondary responses by recruiting inflammatory cells. However, hepatic IFN-g, rather than TNF-a, gene activation was correlated with the secondary TLR4 and CD14 responses (28.7 folds at 6 hours, and 18.3 folds at 3 days). Furthermore, pathologic features mimicking both biliary atresia and neonatal hepatititis were documented upon different doses of LPS administration.

We thus conclude that neonatal exposure to endotoxin triggers prompt hepatic pro-inflammatory innate immunity and results in hepatobiliary injuries like biliary atresia or neonatal hepatitis. These findings suggest a potential role of LPS in the development of neonatal cholestasis syndromes.

O-068  Mutation of Hepatitis B Virus Surface Gene on T Cell Epitopes in Children with Chronic Infection and Hepatocellular Carcinoma

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[Background] Hepatitis B surface antigen (HBsAg) is an important antigen of hepatitis B virus (HBV). The aim of this study is to investigate the effect of mutation of T cell epitope on HBsAg gene and the clinical course of chronic HBV infection.

[Methods] Totally 441 HBV carrier children followed-up for more than 15 years were recruited. They were grouped based on their initial HBeAg/anti-HBe status. HBeAg (+) group was further divided into HBeAg (+)/HBeAg (-) group (n=152) and HBeAg (-) group (n=299) depending on whether spontaneous HBeAg seroconversion occurred during follow-up. Another 25 children with HBV-related hepatocellular carcinoma (HCC) were also studied. HLA class I-restricted T cell epitope mutation of HBsAg gene was examined by PCR and direct sequencing at the latest follow-up of these carrier children.

[Results] A lowest T cell epitope mutation rate was found in HBeAg (+) group. The overall mutation rate was significantly higher among the HBeAg (+)/HBeAg (-) and HCC groups. Those with mutations had a higher peak ALT level than those who did not (249 vs 145 IU/L, p=0.005). Neither HBV vaccination nor genotype affected the rate of T cell epitope mutation. Totally 10 mutations clustered in the codon 31-51 of HBsAg gene. Codons 40 and 44 were the mutations most frequently found.

[Conclusions] HBsAg seroconversion is the most important factor for the development of T cell epitope mutations in the chronic HBV-infected children. HBV surface gene T cell epitopes are very likely an important target of host immunocytes.
O-069 Biliary Atresia with Oxidative Stress and Mitochondrial Copy Number
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Objectives: Oxidative stress is known to be involved in the pathogenesis of biliary atresia (BA), but the mechanism is yet to be elucidated. We studied 8-hydroxydeoxyguanosine (8-OHdG) and mitochondrial copy number as potential markers for oxidative stress in BA. Methods: Hepatic immunoreactive 8-OHdG expression was investigated during the early stage of BA when the patients received Kasai portoenterostomy (KP), late stage when the patients received liver transplantation (LT), in patients with choledochal cyst (CC) as disease control and in patients with histologically normal liver as normal control. Apoptosis of liver cells was examined by TUNEL stain. The mtDNA copy number was measured by real-time PCR. Results: The number of hepatocytes positive for immunoreactive 8-OHdG was significantly increased in KP (65%) than in LT (30%) (P=0.029) and in CC (25%) (P=0.037). The 8-OHdG labeling index was significantly correlated with the grade of chronic hepatitis activity (r=0.495, P=0.037). The hepatocyte TUNEL labeling index in KP (15%) was significantly higher than that in LT (5%) (P=0.018) and in CC (3%) (P=0.010). Mitochondrial copy number was significantly less in KP than in LT (7.33 vs. 8.91, P=0.045) and in normal control (7.33 vs. 9.20, P=0.021). Conclusions: Early stage of BA is associated with stronger inflammatory reaction, augmented oxidative DNA and mtDNA damage as manifested by higher immunoreactive 8-OHdG and apoptotic activities and by decrease in mitochondrial copy number.

O-070 Mutation of Uridine Diphosphate-Glucuronosyl Transferase Gene is a Contributory Factor to Prolonged Unconjugated Hyperbilirubinemia in Taiwanese Breast-fed Infants
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Background: Prolonged jaundice in nursing infants is very common in Asians. The aim of this study was to investigate whether the genetic mutation in uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) gene of breast-fed infants is a contributory factor to prolonged neonatal jaundice.

Materials and Methods: Twenty breast-fed Taiwanese infants with prolonged jaundice beyond 14 days old were enrolled in this study. Except for the jaundice, these infants did not show any evidence of hemolytic anemia, liver dysfunction, or hypothyroidism. Another 20 breast-fed neonates without prolonged jaundice were selected as controls. Blood was collected for the analysis of the UGT1A1 gene. The PCR-restriction fragment length polymorphism (RFLP) method was applied to detect the known variant sites in the UGT1A1 gene in Taiwanese, which included the promoter area, nucleotides 211, 686, 1091, and 1456.

Results: Seventeen breast-fed infants with prolonged jaundice had at least one mutation of the UGT1A1 gene. We did not detect any homozygous A(TA)7TAA mutation in thesis neonates. The breast-fed neonates who carry the 211 variants in the UGT1A1 gene had higher risk for developing prolonged jaundice (Odds ratio 32.11, 95% CI of 5.66-182.18; p < 0.001). Eighteen infants were followed up in our hospital. After cessation of breast feeding, the serum bilirubin level decreased in all cases. The concentration of serum bilirubin lowered back within normal range and jaundice disappeared visually by 4 months of age. Conclusion: Taiwanese breast-fed neonates who carry the 211 variants in the UGT1A1 were found to have high risk for developing prolonged unconjugated hyperbilirubinemia.

O-071 Effect of docosahexaenoic acid on oxidative stress in placental trophoblast cells
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Aim: Docosahexaenoic acid (DHA) is an indispensable component of cell membranes that is required at high levels during pregnancy. Thus, high concentration of DHA is known to enhance oxidative stress by increasing the likelihood of lipid peroxidation. We investigated the effect of DHA supplementation on oxidative stress in the placenta using a trophoblast cell line.

Methods: BeWo cells were first pre-incubated for 24 hours with 0 to 100 µM of DHA and then challenged with 5 mM H2O2 for 90 min. Survival cell rates, intracellular oxidative stress levels (using a fluorescent probe), lipid peroxidation and oxidative DNA damage were measured.

Results: Oxidative stress was significantly higher and cell survival rates were significantly lower in cells pre-incubated with 100 µM DHA as compared to cells pre-incubated without DHA or with low levels of DHA. Lipid peroxidation was significantly higher in cells pre-incubated with 100 µM DHA as compared to those pre-incubated without DHA or with low concentration of DHA. Conversely, cells pre-incubated with modest levels of DHA (1 or 10 µM) had less DNA damage than those without DHA or with 100 µM DHA. Moreover, cell survival rate was significantly increased after the oxidative challenge in cells pre-incubated with modest levels of DHA than others.

Conclusion: Modest levels of DHA alleviate oxidative DNA damage whereas high levels of DHA accelerate lipid peroxidation. DHA supplementation in pregnant women may have the potential to contribute to both oxidative and anti-oxidative properties through the different mechanisms depending on its dosage.

O-072 A novel LAMP-2 mutation in a family with hypertrophic cardiomyopathy
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Background: Lysosome-associated protein-2 (LAMP-2) mutations, originally reported in Danon disease, have been identified in a significant proportion of cases with pediatric-onset hypertrophic cardiomyopathy (HCM). Methods and Results: We screened LAMP-2 for mutations in a family with HCM, in which the male proband had progressive left ventricular hypertrophy. By the age of 15 years, he had severe dilated cardiomyopathy with heart failure, as well as elevated serum creatine kinase and mild proximal-dominant skeletal muscle weakness. Blood was obtained from the proband and family members and, after DNA extraction, LAMP2 mutation analysis was performed using single-strand DNA conformation polymorphism and DNA sequencing analysis. A novel hemizygous frameshift mutation (573del A) was identified in exon5 of the proband. Two of his sisters were heterozygous for the same mutation and showed mild left ventricular hypertrophy on echocardiography with WPW syndrome. His mother died at 42 years old because of dilated HCM with heart failure. Interestingly, other typical signs of Danon disease, mental retardation or ophthalmic problems, were not evident.

Conclusion: Danon disease is an underrecognized cause of HCM in children. And we believe that LAMP-2 mutations should be considered as a possible cause of HCM, especially in patients with skeletal muscle weakness and/or WPW.
O-073 EFFECT OF MDR1 EXON 26 C3435T POLYMORPHISM ON SERUM DIGOXIN IN THAI CHILDREN WITH CONGENITAL HEART DISEASE

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Background: Digoxin has a narrow therapeutic range. P-glycoprotein (P-gp), a major determination of digoxin, is encoded by human multidrug resistance (MDR1) gene. MDR1polymorphism, C3435T in exon26, was shown to be significantly linked with intestinal P-gp expression and serum digoxin level. Single nucleotide polymorphisms (SNPs) of MDR1gene were elucidated marked differences in genotype and allele frequencies among Asian and others. Several studies reveal conflicting results of functional significance of MDR1exon26 C3435T polymorphism on disposition of digoxin in different ethnic groups. Our objectives are to study relationship between MDR1exon26 C3435T polymorphism and serum digoxin level and to determine genotype and allele frequencies of this polymorphism in Thai children.

Methods: 28 congenital-cardiac-disease children were enrolled. The one-to-ten-years-old subjects had been regularly taking digoxin dose 8 – 12 mcg/kg/day, and blood samples were collected after they had continually taken for at least 8 days and determined serum trough digoxin level, serum creatinine, and MDR1exon26 C3435T polymorphism.

Results: Dosage of digoxin, serum creatinine and estimated GFR were not significantly different. Serum trough digoxin levels were significantly different among three groups (1.08, 0.90 and 0.46 ng/ml in CC, CT and TT genotype, respectively, p =0.003) and between TT and CT or CC genotype (p < 0.001 and p = 0.001, respectively). The frequencies of C and T alleles were 59% and 41%. The genotype frequencies were 39%, 39% and 22% for CC, CT and TT genotype, respectively.

Conclusion: MDR1exon26 3435TT genotype was associated with lower serum digoxin level than others. Genotype and allele frequencies in Thai are compatible with East Asian.

O-074 Genetic analysis of MMP gene polymorphisms in patients with Kawasaki disease

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[Background] Matrix metalloproteinases (MMPs) have been considered to play a pathophysiological role in the development of coronary artery lesions (CAL), therefore, an evaluation of the genetic contributions of the MMP genes to the development of CAL in patients with Kawasaki disease (KD) would be beneficial for the prediction of CAL formation in KD patients.

[Methods] We focused on the known functional SNPs in the MMP genes (MMP-2 -735C>T, MMP-3 -1612 5A/6A, MMP-9 -1562C>T, MMP-12 -82A>G and MMP-13 -77A>G) and performed the association study between these SNPs and the development of CAL in KD. To confirm the genetic association of the MMP-13 gene to CAL formation in KD, we also evaluated the haplotype frequencies of the MMP-13 gene in the promoter region between the groups. The study population consisted of KD patients with CAL (n=44), without CAL (n=92) and controls (n=175). The genotropings of the polymorphisms were performed by PCR-RFLP and TaqMan® real-time PCR methods.

[Results] Allele and genotype frequencies of -77A>G polymorphism in the MMP-13 gene showed significant differences between KD patients with CAL and without CAL (P = 0.00551 for the genotype and 0.00989 for the allele). The estimated frequencies of G-C haplotype in the MMP-13 gene promoter were significantly lower in KD patients with CAL than in those without CAL (P = 0.0155). There was no association between other MMP genes and CAL development.

[Conclusions] Our study has demonstrated that the MMP-13 gene appears to be a susceptibility gene to the development of CAL in KD patients.

O-075 Polymorphisms of HLA Genes in Korean Children with Kawasaki Disease

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Purpose: Kawasaki disease (KD) is a leading cause of acquired heart disease in children. The prevalence rate was reported to be varied in different ethnic groups. Recently, with the remarkable development of the genetic studies, polymorphisms of HLA have been defined by DNA analysis. The aim of this study was to assess the influence of the alleles of HLA to susceptibility and complication of KD in Korean children. Methods: DNA was extracted from children diagnosed with KD (n=74). The polymorphisms of the alleles of HLA-A, -B, -C, -DRB1 of the KD patients were determined by utilizing the PCR-ARMS and PCR-SSP analysis. The polymorphisms discovered were compared to those of normal healthy controls (n=159). Results: There was a significant increase in the frequencies of alleles of HLA-B*35, -B*75, -Cw9/09 in patients with KD when compared to those of the healthy control group. With subgrouping of KD patients into groups with or without a coronary complication, the frequencies of HLA-DRB1*11, were increased in a group with a coronary complication when compared to a healthy control group. In comparison between subgroups with or without a coronary complication, the frequency of HLA-DRB1*09 was only increased in the group with coronary complication.

Conclusions: The results suggest that polymorphisms in some loci of B and C in HLA class I genes are related to the pathogenesis of KD in Korean children.

O-076 Correlation between NT-ProBNP and Tissue Doppler Parameters in Patients with Kawasaki Disease

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Background: NT-ProBNP is a cardiac hormone and its peptide increase in inflammation. Kawasaki disease (KD) is a systemic vasculitis, which affects small and medium-sized arteries. Most important feature of KD is cardiovascular manifestation, especially myocardial inflammation and coronary artery disease. We hypothesized increased plasma level of NT-ProBNP may be correlated tissue doppler parameters in patients with KD. Method: Our study enrolled 31 children (Mean age : 3.7±1.9 year) in patients with acute phase of KD. Plasma NT-ProBNP and laboratory finding (WBC, hemoglobin, platelet, ESR, CRP, CK-MB, troponin I) was obtained in patients of acute phase on the first day of admission. Conventional transmirtal flow parameter (E, A, E/A, DT) and TDI parameters, including peak systolic velocity (Sw) and early (Ea) and late diastolic (Aa) velocity of the mitral annuli were obtained in 31 patients with KD. Results: Mean NT-ProBNP was 693.78±274.20pg/mL. Plasma level of NT-ProBNP correlated with CRP (r=0.42, p=0.17), Ea (r=-0.36, p=0.043), Aa (r=-0.36, p=0.044). No significant relationship was observed between NT-ProBNP levels and other echocardiographic parameters. Conclusions: The increased level of NT-ProBNP in patients in the acute phase of KD might be related decreased early and late diastolic velocity and acute systemic inflammation.
O-077

Impacts of Cord Blood Cotinine Level and Glutathione-S-Transferase (GST) Gene Polymorphisms on Birth Outcomes

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Background: To investigate the association between cord blood cotinine levels and birth outcome, and to determine whether GST genetic polymorphisms coding for enzymes that metabolize exogenous chemicals modulate the effect of environmental tobacco smoke (ETS).

Methods: Cotinine levels from 328 paired maternal and cord blood samples were measured using high performance liquid chromatography. The GSTT1 and GSTM1 subtype polymorphisms were detected by the polymerase chain reaction-restriction fragment length polymorphisms method. The birth outcomes included the reduction of birth weight, length, and head girth, and the risks of having low birth weight (LBW), preterm birth, or small for gestational age (SGA).

Results: Elevation of cord blood cotinine concentration increased the risk of being an infant of LBW (OR=5.00, 95% CI=1.15-21.8) or SGA (OR=6.10, 95% CI=1.26-29.5). There was trend in reduction of birth weight, birth length and head circumference among full term infants, but it reached statistical significance only in head circumference (p=0.03). The neonates who had gene deletion of GSTT1 or GSTM1 were at increased risk of being SGA. A combination of the GSTT1 null and GSTM1 null genotype exacerbated the effect of maternal ETS exposure on SGA more than the presence of either genotype alone (OR=9.90, 95% CI=1.00-97.9).

Conclusions: Cord blood cotinine has adverse impacts on birth outcomes. Presence of GSTT1 and/or GSTM1 genotype in neonates may have protective effects on birth outcomes among mothers with ETS exposure during pregnancy.

O-078

UGT1A1 Gene Mutations in Severe Early Neonatal Jaundice

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Purpose: Mutations in the promoter or coding regions of the bilirubin uridinediphosphoglucuronate glucuronosyltransferase 1A1 (UGT1A1) gene are known to be an etiology of neonatal hyperbilirubinemia. This study examined if a TATA box mutation in UGT-1A1 gene promoter or the amino acid change of glycine of arginine at codon 71 (G71R) is associated with the development of severe early neonatal jaundice in Korean infants.

Methods: Seventy-nine neonatal jaundice patients and 83 controls were analyzed for UGT-1A1 promoter and G71R genotypes by using DNA sequencing and Taqman-based allelic discrimination assays.

Results: The frequency of G71R allele in the patients with severe early neonatal jaundice was higher than that in the controlled group (45.6% vs. 25.3%, P=0.001). The homozygote for (TA)1A1A1 mutation was not found in this study. Comparison of the prevalence of UGT-1A1 promoter (TA)1A1 heterozygotes revealed difference between the jaundice and control groups (8.2% vs. 24.3%, P=0.054). We also found that the frequency of the (TA)1A1A1 mutation, which is the most common cause of Gilbert syndrome in Caucasians, was lower in the patients with G71R mutation group compared with the control group (5.6% vs. 20.2%, P=0.018).

Conclusions: The results suggested that the G71R mutation in Koreans enhance susceptibility to the development of jaundice in early neonatal period. The (TA)1A1A1 promoter mutation alone did not contribute to the severe early neonatal jaundice, and it may have the association with mutations in the coding regions of the UGT-1A1 gene.

O-079

Comparison of High-Frequency Oscillatory Ventilation with Conventional Mechanical Ventilation during Partial Liquid Ventilation in an Acute Lung Injury Model

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Background: To examine the efficacy of high-frequency oscillatory ventilation (HFO) combined with partial liquid ventilation (PLV) in a rabbit model of acute lung injury.

Methods: 17 animals were treated with repetitive saline lavage to achieve a uniform degree of acute lung injury (PaO2 below 100 mmHg on a FIO2 of 1.0), and were randomized to either HFO-PLV or CMV-PLV group. 9 animals in HFO-PLV group received intratracheal administration of 5ml/kg perflubron, and were ventilated with HFO for 3 hrs after the dosing period. 8 animals in CMV-PLV group were provided with 5ml/kg perflubron and ventilated with CMV for 3 hrs. The other 5 animals were not lavaged and served as non-lavaged PLV control. They were ventilated with CMV for 3 hrs after the instillation of 5ml/kg perflubron. After the ventilation, lung lavage fluid of each animal was collected and analyzed.

Results: Animals in HFO-PLV group had significantly higher mean PaO2 and lower PaCO2 values than animals in CMV-PLV group. The proportion of surfactant in large aggregate (LA) forms to total surfactant was significantly higher in animals of HFO-PLV group and non-lavaged PLV control than CMV-PLV group. SA/LA ratio was significantly lower in HFO-PLV group and non-lavaged PLV control respectively compared with CMV-PLV group.

Conclusions: HFO had beneficial effects not only on gas exchange but also on the preservation of active forms of endogenous surfactant during PLV. We conclude that HFO is a superior ventilatory method to CMV in applying PLV for clinical practice from the viewpoint of endogenous surfactant activity.

O-080

In vivo Dilatation of the Postnatal Ductus Arteriosus by Atrial Natriuretic Peptide in the Rat.

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Background: Alpha-human atrial natriuretic peptide (hANP) reportedly increases in premature infants with patent duc tus arteriosus (PDA).

Objectives: To clarify possible hANP effect to reopen the postnatal ductus ar teriosus (DA), we studied in vivo reopening of the postnatal DA by a recombinant hANP (carperitide) in rats.

Methods: Near-term neonatal rats were incubated at 33 degrees Celsius following caesarean section. The DA diameter was measured with a microscope and a micrometer following rapid whole-body freezing. The DA was constricted quickly after birth, and the DA diameter was 0.80 and 0.08mm at 0 and 60 min after birth. The ductus-dilating effect of carperitide was studied by subcutaneous injection at 60 min after birth, and the diameter was studied 7, 15, 30 and 60 min later. We investigated the serum hANP concentrations following subcutaneous injection of carperitide.

Results: Carperitide diluted the postnatal DA dose-dependently. The DA-dilating effect of carperitide was maximal at 7 min, and disappeared at 60 min after injection. Carperitide (10 mg/kg) diluted the postnatal constricted DA completely to 0.79 mm. Carperitide (1 mg/kg) diluted the DA to 0.55 mm. The serum hANP levels at 7 minutes after the injection of Carperitide (1mg/kg) was 790 pg/ml.

Conclusions: hANP reopens the constricted postnatal DA dose dependently in rats. The increased hANP, accompanying symptomatic premature PDA, may delay closure of the DA. Therefore, cyclooxygenase inhibitors should be used before the level of hANP becomes high accompanying symptomatic PDA.
O-081 Neonatal Outcomes among Live Births to Unique Marriage-based Immigrant Mothers in Taiwan

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Objective: Previous epidemiological studies focusing on perinatal outcomes among infants of immigrant mothers revealed controversial results. We aimed to assess the neonatal outcomes among live births to intercultural mothers that immigrate to Taiwan for marriage in adulthood. Methods: We analyzed data from a retrospective cohort study including all neonates born alive from 1998 to 2003, Taiwan, to evaluate neonatal outcomes including the percentage of low birthweight and preterm births; and the rates of early neonatal, late neonatal, and neonatal deaths. We did logistic regression to estimate odds ratios of birth outcomes according to maternal nationality, while Cox proportional hazards models were used to estimate hazard ratios of neonatal deaths. Results: A total of 1,410,518 singleton live births including 93,214 born to foreign-born mothers were included. There existed disparities among the intercultural couples including paternal age, parental educational level, and residential distribution. The rates of low birthweight and preterm births in the neonates born to foreign-born mothers were lower than those of the counterparts. The adjusted odds ratios of these above outcomes were 0.74 and 0.73, respectively. Early neonatal and neonatal mortalities were lower in the former than in the latter. The adjusted hazard ratios of being an early neonatal and neonatal death in babies born to foreign-born mothers were 0.69 and 0.75, respectively. Conclusions: Despite lower levels of parental education, advancing paternal age, and other possible socioeconomic disparity, we demonstrated an epidemiologic paradox of favourable neonatal outcomes among immigrant mothers in Taiwan.

O-082 Efficacy of Azalanstat Towards Inhibiting In Vivo Heme Oxygenase Activity in Newborn Mice

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Background: Heme oxygenase (HO) catalyzes the degradation of heme to produce bilirubin. Because excess bilirubin production can lead to the development of jaundice, use of HO inhibiting drugs, such as metallocorphyrins, may be a promising treatment strategy for the prevention of neonatal hyperbilirubinemia. We and others have reported that imidazole dioxolanes also can inhibit in vitro HO activity with selectivity for the inducible HO-1 isozyme and do not affect nitric oxide synthase (NOS) or soluble guanylyl cyclase (sGC), in contrast to metallocorphyrins. Therefore, our objective was to investigate the efficacy of the imidazole dioxolane, Azalanstat, towards inhibiting in vivo HO enzyme activity in newborn mice.

Methods: Azalanstat (500 µmol/kg) or vehicle was administered to 7-day-old FVB mice via intraperitoneal injections. At various times, mice were sacrificed and liver, spleen, and brain harvested. Liver, spleen, and brain HO activities were then quantified by gas chromatography, calculated as moles of carbon monoxide (CO) produced/hr/mg fresh weight, and then expressed as % inhibition of tissue HO activity from treated versus controls.

Results: HO activity was maximally inhibited in the spleen (54%) and brain (39%) within 0.5h, and in the liver (28%) at 3h after Azalanstat treatment. Liver HO activity returned to control levels within 24h. In contrast, spleen HO activity increased 18%, while brain HO activity was still inhibited (19%).

Conclusions: We conclude that Azalanstat effectively inhibits HO activity, and its action is immediate and tissue-specific. Thus, imidazole dioxolanes may be attractive alternative compounds for use in the treatment of neonatal hyperbilirubinemia.

O-083 Transcutaneous bilirubin (TcB) levels in the first 72 hours in newborn infants of Brunei Darussalam

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Objective: There have been many studies on bilirubin levels in normal newborn infants, the definition of “normal bilirubin level” has not been established. This is because bilirubin levels change rapidly in the first 72 hours and vary considerably depending on gestational age, racial composition of the population, proportion of breastfed infants, and other genetic and epidemiological factors. However, most studies were carried out on infants with white color skin. In Brunei, the majority of newborn infants are Malay. Hospital stays in Brunei are now short, and measurements of predischARGE total serum or TcB (JM-102) are used to determine when additional evaluation is necessary and to predict the risk of subsequent hyperbilirubinemia. In this study, we tried to measure bilirubin levels in normal newborn infants using the new Konica-Minolta transcutaneous jaundice device JM-103. We measured bilirubin levels from 0 to 72 hours after birth in 725 newborn infants (gestational age: >35 weeks) who had been admitted to the well-infant nursery of Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, Brunei Darussalam. Using a daily list of all deliveries, the nurses obtained JM-103 measurements 3 times every day. All infants in the nursery were eligible for the study. This is the first contemporary study, including the velocity of increase in TcB levels, for neonatal bilirubinemia in a predominately breastfed population. In the future, making nomogram of Brunei Darussalam and combining the use of nomogram and JM-103 will be useful for evaluation of neonatal jaundice, especially in newborn infants of Brunei Darussalam.

O-084 A Clinical Pathway to Reduce Readmission due to Hyperbilirubinemia after Discharge from Nursery among Newly Born Infants

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Background: The objective is to develop clinical pathway (CP) to reduce readmission due to hyperbilirubinemia after discharge from nursery.

Method: The first phase of retrospective study included newborns admitted for hyperbilirubinemia (study group, n=152) and those not admitted for hyperbilirubinemia (control group, n=392) during 2001-2004. After evaluating various factors for readmission by univariate analysis, an equation to predict readmission (%) was found using multiple logistic regression analysis. The formula was applied to evaluate predictive values for study (n=46) and control group (n=214) during second phase of study in 2005. Finally, prospective study using CP based on readmission rate was done.

Result: The mean gestational age and birth weight for study and control groups were 38±3 weeks, 3,143gm and 39±1 weeks, 3,228 gm, respectively in phase 1 study. The significant factors for readmission included gestational age, ABO incompatibility, breast feeding, jaundice at discharge, oxytocin, discharge within 72 hrs after birth and meconium stain. The formula to predict the readmission among population of phase 2 had sensitivity and negative predictive values of 87%, 75%, 80%, 74%, and 59%, 76% for 85%, 90% and 95% of readmission, respectively. When readmission rate calculated was <85%, 85-94% and ≥95%, then follow-up in 2 weeks, follow-up in 3 days and held discharge, respectively, were done. Following such CP resulted in decreased readmission from 2.2% to 0.7% (p-value 0.013).

Conclusion: CP based on readmission rate derived by using an equation developed during this study merits further study to verify its accuracy and safety.
O-085  Outcome of very low birth weight infants in Songklanagarind Hospital

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OBJECTIVES: To determine mortality and morbidity rates and selected outcome variables of very low birth weight (VLBW) infants.

RESULTS: A total of 178 VLBW infants (86 males and 92 females) met the enrollment criteria. The mean birth weight and gestational age were 1,123 ± 273 grams and 29 ± 3 weeks, respectively. The three most common neonatal morbidities were respiratory distress syndrome (64%), hyperbilirubinemia (64%) and apnea of prematurity (42%). The mortality rate was 27%. Among the selected outcomes of survivors evaluated at discharge (N=130), the incidence of intraventricular hemorrhage (IVH grade 3) and periventricular leukomalacia were encountered in 3.9% and 7.7%, respectively.

CONCLUSION: The overall mortality and morbidity rates of VLBW infants in this study are similar to other reports from Thailand and some developing countries.

O-087  Neonatal Listeriosis in Taiwan

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Objective: Listeria monocytogenes is an important pathogen for the neonates in Western countries with 20-30% fatality rate. There is limited information of neonatal listeriosis in Eastern countries. The purpose of this study is to investigate the incidence and clinical picture of neonatal listeriosis in Taiwan.

Methods: A questionnaire-based surveillance of 17 medical centers in Taiwan was performed and a literature review of neonatal listeriosis as reported in Taiwan from 1990 to 2007 was made to help display the occurrence of neonatal listeriosis.

Results: A total of 14 cases (M:F=10:4) of neonatal listeriosis were identified including 11 surveyed from 4 medical centers and another 3 collected from literature review. 11 were found after 2000 and 3 prior to 2000. The mean gestational age was 32.2 weeks (range 26-38 weeks) and 12 cases were preterm infants. Most of their mothers had history of fever or flu-like symptoms before delivery. Chorioamnionitis was noted in 4 mothers and one mother had L. monocytogenes bacteremia. The age of onset was less than 3 days in all cases. 11 presented with respiratory distress as the initial symptom. 7 had central nervous system involvement. L. monocytogenes was identified from blood in 13, cerebrospinal fluid in 4 and gastric aspirate in 2. The mortality rate was around 29%.

Conclusions: Our findings have highlighted that listeriosis may emerge as an important health threat among newborn infants in Taiwan.

O-088  Neonatal meningitis in a single center in southern Thailand

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Background: Neonatal meningitis is a disease with high mortality and morbidity. Diagnosing this condition is more difficult in neonates than in children.

Purpose: To determine the prevalence of neonatal meningitis and to look for any factors that might predispose the patient to increased mortality risk.

Materials and methods: The medical records of neonates aged less than 28 days admitted with meningitis in Hat-Yai Hospital, Thailand from January 2002 to December 2006 were reviewed.

Results: The records of 61 neonatal meningitis cases were studied, 29 boys and 32 girls. The prevalence was 1.38 per 1,000 live births. Gestational age was 35.5 weeks, birth-weight 2,412.7 g., and the rate of Apgar scores <3 at 1 minute was 6.5%. The age of disease onset was 9.8 days. White blood cell count in cerebrospinal fluid (CSF) was 741 cells/mm3, with 31.8 % neutrophils. CSF sugar/blood sugar ratio was 0.36. Blood and CSF cultures were positive in 9 cases (14.7%) and 4 cases (6.6%) respectively. E. coli and Enterococci each grew in 2 CSF specimens, and 1 group B streptococcus was detected by latex agglutination. Three cases died (4.9%), all prior to 20 days of age. No independent factors could be associated with an increased risk of mortality.

Conclusions: The incidence of neonatal meningitis at Hat-Yai Hospital was 1.38 per 1,000 live births with a mortality rate of 4.9%. No prognostic factors associated with mortality rate were detected.
**O-089 Systematic Review of the Diagnostic Performance of Procalcitonin for Neonatal Sepsis**

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**Background:** Procalcitonin (PCT) has largely studied as marker for neonatal sepsis. Contradictory results were reported. We aimed to derive a definitive estimate of the diagnosis performance of PCT for neonatal sepsis and identify study-level factors that might predict performance.

**Methods:** We undertook a systematic review of diagnostic studies of PCT that were conducted in neonates. All studies without controlled group were excluded. We searched Medline, EMBASE, Digital dissertation databases, and reference tracking without language restriction. Selected QUANDAS tools were used for validity assessment. Publication bias and its impact were assessed by multiple methods. Random effects meta-analysis was used to derive pooled estimates of positive and negative likelihood ratio, diagnostic odds ratio. Subgroup analysis and meta-regression was used to identify study-level covariates that predicted diagnostic performance.

**Results:** Of 411 studies found (1980-September 2006), 28 were included: 21 (English), 5 (Non-English) and 2 conference proceedings. Kappa was 0.8. There was evidence of publication bias. Trim & fill suggested an over-estimation of test performance by publication bias. Subgroup analysis and meta-regression showed that quality of studies significantly has inverse association with test performance. Although the estimated overall area under curve was 0.89, the pooled positive likelihood ratio (+LR) was 6.1 (95% CI 4.6, 8.6), the negative LR negative (-LR) was 0.3 (95% CI 0.2, 3.5) adjusted for different cut-off value. PCT tended to perform better for late-onset sepsis.

**Conclusion:** PCT is not an ideal test for neonatal sepsis. Publication bias and study design and reporting quality explains an over-optimism of PCT.

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**O-090 Anti-Annexin A2 IgM Antibody in Preterm Infants: Its Association with Chorioamnionitis**

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**[Background]** Intrauterine infection is associated with chorioamnionitis (CAM), which can lead to preterm delivery. We previously reported that the levels of IgM and the incidence of CAM were elevated in preterm infants with Wilson-Mikity syndrome. The molecular target of this IgM remains unclear.

**[Methods]** In order to determine the target proteins, we used Western blot and amino acid sequences. ELISA for annexin A2 was established to titrate the annexin A2 IgM antibody using the recombinant human annexin A2. The plasmin generation inhibition assay was conducted. To examine the correlation between the titer of anti-annexin A2 IgM antibody and CAM, we prospectively titrated anti-annexin A2 IgM antibody in preterm infants who were admitted to the NICU in and after 2005.

**[Results]** We identified annexin A2 as the target of IgM antibody in preterm infants. About 60% of preterm infants with hyper-IgM showed high titer against annexin A2 in their cord blood. The patients’ IgM inhibited plasmin generation. The titer of anti-annexin A2 IgM antibody was significantly higher in patients with high-grade CAM than in patients without CAM and in patients with low-grade CAM.

**[Conclusions]** This is a first report about the autoimmune IgM antibody produced by preterm infants at the local area of the fetomaternal interface. The titer of this anti-annexin A2 IgM antibody and/or annexin A2 protein might be able to function as the marker of CAM, i.e. fetal inflammatory response syndrome (FIRS). Further studies are needed to clarify the participation of this IgM antibody in developing CAM.
P-001  Hemodynamic changes before and after intravenous gamma globulin infusion in patients with Kawasaki syndrome
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BACKGROUND: To determine the difference in cardiac performance before and after intravenous gamma globulin infusion (IVGG) in patients with Kawasaki syndrome (KS).

METHODS: Subjects were 17 patients with KS who were treated with 2 g/kg of IVGG and did not have coronary artery lesion and 9 controls. In Doppler and Tissue Doppler echocardiography, peak aortic velocity (D-AV), peak mitral E and A wave velocity, E/A ratio, aortic ejection time (D-ET), mitral annular peak s', e', and a' velocity, isovolumic contraction time, isovolumic relaxation time (T-IRT), heart rate (HR) were determined. In addition, isovolumic acceleration (IVA) was calculated. Echocardiographic variables were compared between before and after IVGG as well as patients and controls.

RESULT: Mean patients' age was 3.5 years old. Pre- and post-IVGG study were performed at 5.4 and at 11.9 days of illness. In pre-IVGG study, there were significant differences in D-ET (201 vs. 250 ms), D-AV (114 vs. 92 m/s), T-IRT (42 vs. 51 ms), and HR (136 vs. 102 bpm) compared with control. After IVGG, HR (136 to 100 bpm). D-AV (114 to 102 m/s), D-ET (201 to 248 ms), and IRT (42 to 56), have normalized but IVA significantly decreased (pre 2.1 vs. 1.6 m/s2). There were significant differences between IVA (1.6 vs. 2.2 m/s2) and e' (10.6 vs. 13.0 cm/s) between post-IVGG and control.

CONCLUSIONS: In patients with KS, D-A V increases but IRT and ET decrease with tachycardia. With IVGG, these parameters normalize but there may be potential change in intrinsic cardiac performance.

P-002  The Prediction of IVIG Retreatment Group or Occurrence of Coronary Arterial Lesion According(CAL) to the IgG Level at before and after IVIG Treatment in Kawasaki Disease(KD)
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Introduction: About 10-20% of KD patients have persistent or recurrent fever after IVIG treatment. These patients are at increased risk of developing CAL. The half-life of IgG in KD may relate the response of IVIG therapy and the occurrence of CAL. So, the serum level of IgG at before and after IVIG may relate the response of IVIG therapy and occurrence of CAL.

Method: Totally 77 patients with KD treated by a single high dose of IVIG(2g/kg) were analyzed. The patients were classified according to the response of IVIG treatment and occurrence of CAL as CAL group (N=28), non-CAL group(N=49), responder group(N=70), and the non-responder group requiring the additional IVIG(N=7). Before and after the initial administration of IVIG, serum IgG levels were measured. Initially IVIG therapy was given with single 2g/kg for 1 day, and then additional IVIG (1g/kg for 1 day) was treated if the patients had a sustained fever over the 38.0°C after 48hr from starting therapy.

Results: The level of IgG at postIVIG and its difference between before and after IVIG were significantly different between CAL & non-CAL group. The levels of IgG at before and after IVIG were significantly different between responder and non-responder group.

Conclusion: The levels of serum IgG before or after IVIG treatment may have the predictive value of the occurrence of CAL and response of initial IVIG therapy in KD. So, the pharmacodynamic mechanism shifting to shorten the half-life of IgG may be involved in the pathogenesis and outcome of KD.

P-003  Effects of gamma-globulin therapy on cardiac function in Kawasaki disease: evaluation by speckle-tracking and color tissue Doppler echocardiography.
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Background: We previously reported that natriuretic peptides are elevated and decline immediately after gamma-globulin therapy (IVIG). This suggests that silent myocardial damage may exist in Kawasaki disease (KD) and recover with IVIG.

Purpose: To clarify our hypothesis, we evaluated the myocardial function in patients with KD before and after IVIG by using speckle-tracking and color tissue Doppler echocardiography.

Methods: We enrolled 30 children diagnosed as having KD and treated them with high-dose IVIG (2 g/kg/day). Echocardiographic examinations were performed before and at 3-5 days after IVIG therapy. As an index of diastolic function, E/E′ was used. Systolic function was evaluated by peak strain values and A wave velocity, E/A ratio, aortic ejection time (D-ET), mitral annular peak s', e', and a' velocity, isovolumic contraction time, isovolumic relaxation time (T-IRT), heart rate (HR) were determined. In addition, isovolumic acceleration (IVA) was calculated. Echocardiographic variables were compared between before and after IVGG as well as patients and controls.

RESULT: Mean patients' age was 3.5 years old. Pre- and post-IVGG study were performed at 5.4 and at 11.9 days of illness. In pre-IVGG study, there were significant differences in D-ET (201 vs. 250 ms), D-AV (114 vs. 92 m/s), T-IRT (42 vs. 51 ms), and HR (136 vs. 102 bpm) compared with control. After IVGG, HR (136 to 100 bpm). D-AV (114 to 102 m/s), D-ET (201 to 248 ms), and IRT (42 to 56), have normalized but IVA significantly decreased (pre 2.1 vs. 1.6 m/s2). There were significant differences between IVA (1.6 vs. 2.2 m/s2) and e' (10.6 vs. 13.0 cm/s) between post-IVGG and control.

CONCLUSIONS: In patients with KS, D-A V increases but IRT and ET decrease with tachycardia. With IVGG, these parameters normalize but there may be potential change in intrinsic cardiac performance.

P-004  Clinical characteristics and coronary artery outcomes in Kawasaki disease patients with early intravenous immunoglobulin treatment
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Background: Kawasaki disease (KD) is a syndrome of fever and principal clinical characteristics affecting young children. Some patients may be diagnosed before the 5th day of illness. There are conflicting reports on requirement of additional doses of intravenous immunoglobulin (IVIG) and adverse coronary artery outcomes. The aims of this study were to identify clinical characteristics and assess coronary artery outcomes in this group.

Methods: A retrospective case series was performed. All medical records of patients diagnosed with Kawasaki disease at Ramathibodi Hospital during January 1, 1997 to December 31, 2007 were reviewed. The subjects were divided into 2 groups; early IVIG which were diagnosed and treated before day 5, and conventional IVIG which were diagnosed and treated at or after day 5. Demographic data, standard laboratory and echocardiography were analyzed.

RESULTS: A total of 150 KD cases were identified. There were 17 cases with early IVIG treatment. Of these, there were incomplete KD 1.3%, and refractory KD 2.7%. The male: female ratio was 1:2. The initial WBC were 12,900 ± 2700/mm³ in early group compared to 17,600 ± 6200/mm³ in conventional group (p < 0.01). Echocardiography demonstrated coronary artery abnormalities 2.7%, pericardial effusion 5%, and mitral regurgitation 2%. Conclusions: The prevalence of KD patients with early IVIG treatment was 11%. The patients with early treatment were predominantly female and had lower initial WBC count. There were no significant differences in other clinical characteristics, standard laboratory investigations and coronary artery outcomes between patients with early treatment and those with conventional treatment.
Aim and Material: IVIG treatment for Kawasaki disease (KD), but there are 15-20% the case was resistant initial.

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Masahiro Ishii
Shouhei Ogata, Yuki Bando, Sumito Kimura, Hisashi Ando, Yayoi Nakahata,

[BACKGROUND] MEFV gene is responsible for Familial Mediterranean fever (FMF). Several reports revealed that mutations of MEFV gene were associated with vasculitis-related disorders such as Behcet disease, Henoch-Schonlein purpura, and juvenile idiopathic arthritis. As the MEFV gene sequence variant might associate with Kawasaki disease (KD), a systemic vasculitis of unknown etiology, we investigated the association between KD or its coronary artery lesions (CAL) and the MEFV gene variants including E148Q which is the commonest and mildest disease-causing mutation of MEFV gene. [METHODS] A total of 138 Japanese patients with KD that included 45 patients with CAL and 93 patients without CAL, and 170 normal controls were enrolled in this study. Sequence variants for MEFV gene were detected by TaqMan SNP genotyping assay and direct sequence. Genotype and allele frequencies for MEFV gene variants (E148Q, L110P, R202Q, P369S, R408Q) in both groups were compared. [RESULTS] E148Q was observed in 42.4% of healthy controls and E148Q homozygotes were found in 5.3% of them. No significant differences were observed in the allele frequencies of MEFV gene variants between KD patients and healthy controls, between KD patients with and without CAL, or between KD patients with CAL and controls. [CONCLUSIONS] We found that there were no associations between the MEFV gene variants and the development of KD or CAL. The high frequency of E148Q and the low incidence of FMF in Japan strongly suggest that E148Q may be one of the genetic polymorphisms of MEFV gene.

The strategy of immune globulin-resistant Kawasaki disease: a comparative study of additional immune globulin and steroid pulse
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Introduction: Intravenous immuno globulin (IVIG) infusion is a cure effective for Kawasaki disease (KD), but there are 15-20% the case was resistant initial IVIG treatment.

Aim and Material: We compared the effectiveness between 2nd IVIG treatment and steroid pulse therapy for patient who was resistant initial IVIG treatment. From 2004 to 2007, 162 patients with KD were treated by high dose IVIG (2g/kg/day). Twenty-five patients (15%) dose not respond to initial IVIG treatment. Twelve initial IVIG resistant KD patients were treated with steroid pulse therapy intravenous Methylpredonizolone infusion (IVMP) for 3 days (30mg/kg/day). Thirteen patients who were non-responder of initial IVIG treatment were treated with additional IVIG therapy (2g/kg/day).

Results: There was significant difference in period before fever falling from the 2nd treatment (IVMP puls: 1.5 ± 4 days VS IVIG: 3.4 ± 3 days p<0.05). No significant differences were found in incidence of coronary aneurysm between 2nd IVIG treatment and IVMP pulse therapy (IVIG case VS IVMP 0 case).

There was no patient who developed giant aneurysms in both therapies.

Conclusions: Our study data stated that IVMP therapy was equal to additional IVIG therapy to prevent the artery aneurysm.

Functional Implications of the Right Ventricular Myocardial Performance Index in Patients After Surgical Repair of Tetralogy of Fallot
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Background: The myocardial performance index (MPI) has been proposed to be a simple echocardiographic index of right ventricular (RV) function in patients after surgical repair of tetralogy of Fallot (TOF). We tested the hypothesis that RV MPI in postoperative TOF patients relates to parameters of RV function as derived from cardiovascular magnetic resonance (CMR) and exercise testing.

Methods: Thirty TOF patients (11 males), aged 15±3.1 years, were studied. The RV and left ventricular (LV) MPIs were determined using pulsed-wave Doppler echocardiography and related to CMR-derived RV and LV ejection fractions and pulmonary regurgitant fraction and treadmill exercise testing parameters.

Results: Log RV MPI correlated positively with log LV MPI (r=0.38, p=0.037) and negatively with CMR-derived RV ejection fraction (r=−0.4, p=0.028) and pulmonary regurgitant fraction (r=−0.4, p=0.031). No significant correlations were found between LV MPI and any of the CMR parameters. Using ROC analysis, a cut-off value of 0.30 for RV MPI was found to have a sensitivity of 100% and specificity of 74% in predicting a RV ejection fraction < 35%. Right ventricular, but not LV, MPI correlated inversely with exercise duration (r = -0.45, p = 0.013) and peak oxygen consumption (VO2 max) (r = -0.56, p = 0.001). Multivariate analysis identified RV MPI (β=−0.6, p<0.001), male sex (β=0.44, p=0.01), and duration from surgery (β=−0.30, p=0.019) as significant determinants of VO2 max.

Conclusions: Increased MPI is a reflection of reduced RV ejection fraction and exercise capacity in patients after TOF repair.
P-009 Restrictive Right Ventricular Physiology After Biventricular Repair of Pulmonary Atresia with Intact Ventricular Septum

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Objectives: Endocardial and myocardial abnormalities of the right ventricle are well documented in pulmonary atresia with intact ventricular septum (PAIVS). We tested the hypothesis that restrictive right ventricular (RV) physiology is prevalent and has implications on exercise capacity in patients after biventricular repair of PAIVS.

Methods: Thirty-two PAIVS patients (18 males) aged 17.1±5.4 years were studied at 16.0±6.0 years after biventricular repair. The RV function was assessed using echocardiography and related to exercise testing parameters. The results were compared with those of 22 age-matched patients after tetralogy of Fallot (TOF) repair who did not have restrictive RV physiology and 27 age-matched controls.

Results: Compared with controls, PAIVS patients had significantly larger RV end-diastolic dimension, longer RV relaxation time, lower tricuspid annular systolic myocardial systolic and early (e) diastolic velocity, reduced early (E) to late (A) diastolic tricuspid inflow velocity ratio, and elevated tricuspid E/e ratio (all p<0.05). Twenty-seven (84%, 95% CI 71-98%) PAIVS patients demonstrated restrictive RV physiology. Compared with TOF patients, these 27 PAIVS patients had lower tricuspid e velocity (p=0.056), smaller RV end-diastolic and systolic areas (p<0.001), and lower prevalence of severe pulmonary regurgitation (p=0.088). Nineteen PAIVS and 16 TOF patients underwent exercise testing and it showed PAIVS patients had higher peak oxygen consumption (VO2max) (p=0.003). In these 2 cohorts, a significant negatively correlation existed between tricuspid annular e velocity and VO2max (r=-0.55, p=0.001).

Conclusions: Restrictive RV physiology is common in PAIVS patients after biventricular repair, which limits RV dilation and is associated with better exercise capacity.

P-010 Right Ventricular Dyssynchrony in Patients After Atrial Switch Operation for Transposition of the Great Arteries

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Background: Recent data suggest potential benefits of cardiac resynchronization therapy in the management of right ventricular (RV) dysfunction in congenital heart disease. This study aimed to determine the prevalence and functional implications of RV dyssynchrony in patients after Senning or Mustard procedure for transposition of the great arteries.

Methods: Twenty-eight patients, aged 21.1±3.5 years at 19.9±3.2 years after atrial switch operation, and 29 age-matched healthy controls were studied. The times from onset of QRS to peak systolic strain (Tε) at the base of and mid RV lateral wall, interventricular septum (IVS) and left ventricular (LV) free wall were determined using tissue Doppler echocardiography. Intraventricular dyssynchrony was defined as ΔTεRV-LV and left ventricular dyssynchrony as ΔTεRV-LV-LV45ms. In patients, the magnitude of RV intra- and interventricular dyssynchrony was correlated with cardiac magnetic resonance-derived RV volumes and ejection fraction (n=26) and treadmill exercise testing parameters (n=20).

Results: Compared with controls, patients had significantly longer ΔTεRV-LV (48.1±59.9 ms vs 17.0±16.1 ms, p<0.001) and ΔTεRV-LV-LV (63.1±49.5 ms vs 19.0±12.9 ms, p<0.001). Nine patients (32%) exhibited RV dyssynchrony (ΔTεRV-LV-LV≥40ms, control mean=±25SD), while 16 patients (57%) showed interventricular dyssynchrony (ΔTεTRV-LV-LV45ms). In patients, RV intra- and interventricular dyssynchrony correlated negatively with RV ejection fraction (both r=–0.42, p=0.03) and % predicted maximum oxygen consumption (r=–0.50, p=0.03, r=−0.52, p=0.02, respectively), and positively with VE/VCO2 slope (r=−0.49, p=0.03, and r=−0.56, p=0.01, respectively).

Conclusion: Right ventricular dyssynchrony is common in young adults after atrial switch operation and is associated with RV systolic dysfunction and impaired exercise performance.

P-011 The Relationship of Pulmonary Regurgitation and Exercise Performance after Repair of Tetralogy of Fallot

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Purpose: We investigated the relationship between severity of pulmonary regurgitation(PR), exercise capacity, RV volume overload and function in the patients after repair of TOF. Methods: To evaluate exercise capacity, cardiopulmonary exercise test(CPX) was performed in 36 patients and 18 normal controls on a treadmill, and maximal oxygen consumption(VO2max) and anaerobic threshold(AT) were measured. In the patient group, magnetic resonance imaging(MRI) study was performed and PR fraction(%) was calculated. Results: VO2max and AT were significantly decreased in patients(30.9±7.71 vs 38.1±8.53, p=0.02). RVESVI and RVEDVI were increased(18.0±10.3 vs 12.6±7.6, p=0.02). And the decrease of VO2max was more tightly correlated with RVESVI(r=-0.70, p=0.005) than RVEDVI(r=-0.49, p=0.02). Conclusion: The patients after repair of TOF showed impaired exercise capacity than controls. PR has deleterious effects on the exercise capacity and RV volume overload, and the effects may be related with the age and/or duration of PR. RV volume overload may deteriorate RV function, and, especially the RV end-systolic volume was correlated with the impaired exercise capacity.

P-012 Effect of stent implantation for branch pulmonary artery stenosis after surgical repair in children

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BACKGROUND: After surgical repair in congenital heart disease, stent implantation (SI) is the standard treatment for branch pulmonary artery stenosis (PAS). SI for branch PAS in small children is still not common in Japan. OBJECTIVE: This study was designed to evaluate the outcome of SI for branch PAS in Japanese small children. SUBJECTIVE: Between 2004 and 2006, 5 patients with branch PAS that could not be sufficiently dilated by BD underwent SI with weight ranging 7.1 - 17.5 kg (median, 9.3). The primary diagnosis included tetralogy of Fallot (n=4), and corrected transposition of great arteries with subaortic ventricular septal defect and pulmonary atresia (n=1). EARLY RESULTS: 3 patients underwent intra-operative SI. 2 patients underwent transcather SI. Stents were successfully implanted in 5 of 5 patients. Branch PAS were dilated after SI (initial diameter : mean 3.3 (range 2.3 -5.2), post BD : 4.6 (2.5 - 6.0), post SI : 9.3 (8.0 - 10.1) mm, P<0.001). Main PA- branch PA pressure gradient were decreased (initial PG : mean 56 (range 30 - 73), post BD : 4.6 (2.5 - 6.0), post SI : 9.3 (8.0 - 10.1) mm, P<0.001). MIDTERM RESULT: Diameter of PAS was 9.3 (range 7.9 - 10.0) mm. MPA - branch PA were 11 (5 - 22) mmHg. No re-intervention was required after SI (10 - 41 months). CONCLUSION: The outcome of SI for branch PAS in children after surgical repair was satisfactory during early and midterm follow up.
P-013 Risk factors of residual pulmonary hypertension after cardiac surgery for congenital heart defect with Down syndrome

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Introduction: Early development of pulmonary hypertension (PH) is frequently associated with patients with Down syndrome (DS) and congenital heart defect (CHD) that has left-to-right shunt. Although an early surgical intervention is recommended for such patients, it has not yet been clarified that the favorable age for operation to prevent postoperative residual PH. The purpose of this study is to elucidate the proper age of operation for CHD with left-to-right shunt in DS patients.

Patients and methods: 72 consecutive Japanese DS children were included. All of them were operated for CHD with left-to-right shunt and evaluated the pulmonary arterial pressure (PAP) by cardiac catheterization before and after operation. With statistical procedure, several risk factors of residual PH were estimated.

Results: 22 patients had post operative residual PH (mean PAP≥25mmHg). The age of operation showed significance with multivariable analysis (P=0.017). No residual PH was shown among the patients who had operation within 5 months old. With ROC curves, in case age of operation was over first year, sensitivity and specificity of residual PH were more than 50%. The probability of residual PH showed significant difference between patients with operation during the first year and those with operation after the first year (P=0.02).

Conclusion: Our study demonstrates that early operation is effective to prevent postoperative residual PH in DS patients with left-to-right shunt. Operation at earlier than 6 months old resulted in no residual PH and that during the first year significantly reduced a risk for residual PH in such patients.

P-014 Endovascular Stent in Congenital Heart Disease: Siriraj Experience

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Objective: To evaluate efficacy and safety of stent implantation (SI) as compare with conventional balloon angioplasty (BA) and to report intermediate results and complications after SI in congenital heart disease.

Methods: A retrospective study of 31 patients, who underwent SI between January 1998 and December 2006 at our institution. Procedural success is determined by either an increase of the stenotic diameter > 50% (anatomic success) or residual systolic pressure gradient (SPG) < 10 mmHg, decrease of SPG > 50%, decrease of the RV/systemic pressure > 20% (hemodynamic success).

Result: The immediate results have shown that SI had a significant yield of success as compare to BA. In our report, stent success was varied from 50% - 80% while BA providing only 27% - 61%. In addition, when combine anatomic and hemodynamic successes together, SI group had a significant yield of success as compare to BA group, 83% and 24% respectively. The intermediate outcome in stent placement also showed satisfactory results for maintaining their patency over the years after implantation. Only 10% of SI cases developed stent failure. One of them had stent fracture and two had significant neointimal proliferation which only one patient required additional re-intervention. There was no procedure related mortality.

Conclusion: Stent implantation is a feasible, effective and safe procedure in selected patients with either postoperative or congenital vascular stenosis in congenital heart disease.

P-015 Possibility of Congenital Porto-systemic Venous Shunt as Latent Cause in Pulmonary Arterial Hypertension: A Case Study of Clinical Manifestation and Outcome

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BACKGROUND: Pulmonary arterial hypertension has been reported to be a crucial complication in congenital porto-systemic venous shunt and this pathologic state may be latently present in patients with pulmonary arterial hypertension of unknown etiology.

METHODS AND RESULTS: Nine patients with congenital porto-systemic venous shunt were studied from January 1990 through September 2005. Patent ductus venosus was detected in five patients, including three patients with an absence of the portal vein. The presence of either a gastro- or spleno-renal shunt was evident in another four patients. Six patients had a history of hypergalactosemia with normal enzyme activities, as seen during neonatal screening. Six (66.7%) of the nine patients were identified to have clinically significant pulmonary arterial hypertension (mean pulmonary artery pressure: 34-79 mmHg; pulmonary vascular resistances: 5.12-38.07 units). The median age at the onset of pulmonary arterial hypertension was 12 years and 3 months (range; 9 months -12 years and 9 months). Histological studies of lung specimens, which were available in four of the nine patients with CPSVS, showed small arterial micro-thrombotic lesions in three patients (2 with PAH, 1 without PAH). In particular, this characteristic finding was remarkable in the patients with PAH.

CONCLUSIONS: This study demonstrated thromboembolic pulmonary arterial hypertension to be a crucial complication in congenital porto-systemic venous shunt and this pathologic state may be latently present in patients with pulmonary arterial hypertension of unknown etiology.

P-016 Effect of PDA to coronary flow

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[Background] The effect of patent ductus arteriosus(PDA) to coronary flow is unclear. We try to clarify it.

[Methods] Subject: 10 patients(three boys, seven girls) with PDA were entered. They were 1 year and 2 months to 16 year and 1 month of age (median 7 years 0 month). Method: Left anterior descending artery flow velocity (LAD) (maximum (MAX) and mean), left ventricular end-diastolic volume (LVEDV), and left ventricular myocardial mass (MAS) were examined by echocardiography. We used Vivid I (GE Yokogawa medical systems, Tokyo) as the cardiac echo machine. From body weight and height, BSA, expected LVEDV, and expected MAS were calculated.

[Results] Results are below. LAD (max) 36.4±17.0cm/sec, LVEDV98.3±63.9ml/BSA (45.9~302.4, (163.1:±80.2)% of normal), MAS 96.8±61.9g/BSA, (42.6~197.3, (125.0±53.4)% of normal), LAD (max) correct) 0.69±0.77cm/sec/g. In 8 patients, LVEDV was over 120 % of normal. In this group, LAD (max) correct was 0.35±0.25cm/sec/g. They were smaller than in other 2 patients (2.04±0.59cm/sec/g ) (p=0.0002). This suggests that PDA volume overload may make the decreasing of LAD flow corrected by MAS.

[Conclusions] Peak LAD corrected by MAS was decreased depending on the increased LVEDV in patients of PDA.
P-017 Exertional oscillatory ventilation during cardiopulmonary exercise test in patients after total cavopulmonary connection.
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Background: Exertional oscillatory ventilation (EOV) during cardiopulmonary exercise test (CPX) is powerful predictor of poor prognosis and a valuable guide in the management in adults with chronic heart failure. The purpose of this study is to clarify the occurrence and influence of EOV during CPX in single ventricle patients late after total cavopulmonary connection (TCPC).
Patients and methods: We studied 44 patients who underwent symptom-limited CPX at 12.2±4.9 years of age or 5.8±2.0 years after TCPC. Mean age at the time of TCPC was 5.8±3.3. To evaluate hemodynamic function, they also underwent cardiac catheterization subsequently. EOV was defined as cyclic fluctuations in minute ventilation (VE) at rest that persist during effort lasting ≥60% of the exercise duration, with an amplitude ≥15% of the average resting value.
Results: Thirty seven patients were enrolled, excluding 7 patients who had pacemaker implantation (N=2), histories of brain infarctions (N=2) and inoperative behaviors (N=3). EOV was noted in 21 of 37 patients (55%). Patients with EOV had significantly higher peak oxygen uptake (VO2) per body weight (29.6±5.6 vs 35.0±6.8 ml/min·kg, P<0.05). However, other parameters of cardiac index, pulmonary arterial index and increase in heart rate were not significantly different between patients with and without EOV.
Conclusions: EOV was frequently noted during CPX in patients after TCPC. Peak VO2 in patients with EOV was higher than in those without EOV, which suggested that EOV affects exercise tolerance in univentricular patients after TCPC.

P-018 Factor Influencing Survival in Patients After Bidirectional Glenn shunt
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Background: The bidirectional Glenn shunt has used as an intermediate palliative step prior to the modified Fontan operation in patients with a univentricular heart with favorable results. However, the mortality rate is high in the developing country. This study sought to determine which factors influenced the mortality.
Methods: Forty-five consecutive patients with a univentricular heart who underwent the bidirectional Glenn shunt between November 1994 and October 2006 were retrospective cohort studied. Clinical, echocardiographic, and catheterization data were reviewed. Kaplan-Meier and Cox proportional hazard methods were used for survival analyses.
Results: Median age at operation was 20 months (range 9 months to 19 years). Median follow-up time after surgery was 4 years (range 1 day to 11 years). Eleven patients (24%) were death during the follow-up period. The early mortality rate was 4 of 45 patients (8%). The 5- and 10-year actuarial survival rates in patients after bidirectional Glenn shunt were 73±8% and 55±17%. In a multivariate Cox proportional hazard analysis, heterotaxy syndrome (Hazard ratio = 6.7, p < 0.04) and systemic right ventricle (Hazard ratio = 11.8, p = 0.009) were independent predictors of mortality. Age at operation, oxygen saturation, pulsatile Glenn shunt, pulmonary artery pressure, bilateral SVCs, and Nakata index were not predictive of mortality.
Conclusion: Heterotaxy syndrome and systemic right ventricle were the greatest risk for death. The presence of heterotaxy syndrome and systemic right ventricle in patients with a univentricular heart should lead to aggressive investigation and management strategies.

P-019 Efficacy of combination therapy of bosentan, beraprost and HOT in candidates for right heart bypass surgery
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In recent years, effects of the oral endothelin antagonist bosentan has been reported on patients with pulmonary hypertension (PH) related to congenital heart disease (CHD). We report successful combination therapy of bosentan, beraprost and HOT in patients who could not undergo right heart bypass surgery because of PH initially.
In case 1) 1-year-old female with asplenia, SV, DORV, CoA, TAPVR. In case 2) 8-year-old male with SV, DILV, d-MGA, CoA. In case 3) 14-years-old female with Down syndrome, TOF, AVSD. Patients underwent clinical, exercise and haemodynamic evaluation at baseline and after 6 to 18 months of chronic oral administration of bosentan. Although we administered initial doses of bosentan adjusting for their body weight, tachypnea and chest discomfort were recognized in two cases. These symptoms disappeared by reduced dosage of bosentan. Bosentan therapy reduced pulmonary arterial pressure (PAP) and pulmonary vascular resistance (PVR) in all cases. The average changes of PAP and PVR at baseline and after bosentan therapy in three patients are; main PA(mmHg) 52/19(34)→41/6(22), right PA(mmHg) 36/19(28)→19/6(13), left PA(mmHg) 31/16(24)→21/7(14), PVR/unit/m2 5.83→1.83. Clinical symptoms and exercise tolerance improved in all cases, 6-minutes walk distance improved in cases 2 and 3. Bosentan induces mid-term clinical and haemodynamic improvement in patients with PH related with complex CHD. Combined therapy with bosentan, beraprost and HOT may widen the surgical options and improve outcome in Fontan candidates. Larger studies with long-term bosentan are needed to assess the optimal doses and possible therapeutic role of bosentan in this population.

P-020 Conditions Leading to Pediatric Cardiology Consultation at a Tertiary Academic Hospital during the First Quarter of the Academic Year in Thailand
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OBJECTIVE: To determine the basis for cardiac consultations for pediatric patients in an academic hospital setting
METHODS: The activities of the cardiology consultation service were recorded for 3 months, from June to August 2006. Patients were identified from the consultation note records and a division list of echocardiography studies.
RESULTS: A total of 131 consultations were performed during the first quarter of an academic year. The age at the time of consultation was 1 day to 14 years (mean 4.4 years). Clinical concerns included murmurs (25.9%), recent cardiac surgery (25.9%), cardiac function (10.7%), intermittent illnesses among cardiac patients (6.1%), subacute endocarditis (5.3%), cardiomegaly by chest film (5.3%), arhythmias (4.3%), cyanosis (3.1%), syndromes (3.1%), Kawasaki disease (2.3%), cerebrovascular accidents (2.3%), and miscellaneous conditions. Two diagnoses accounted for 58 % of murmur evaluations, were patent ductus arteriosus (PDA) and innocent murmurs. The most common murmur diagnosis in the neonatal intensive care unit and the well-child nursery was PDA. Patients with recent cardiac surgery typically had hemodynamic instability. The most common basis for evaluation of function was oncologic disease and shock assessment. Although endocarditis was a clinical concern, only 20% of screening cases were identified, involving 2 patients with an indwelling intracardiac catheter. Kawasaki disease was the most common acquired condition leading to consultation.
CONCLUSIONS: Although varieties of conditions were consulted, some were encountered more frequently especially the condition that may not required cardiology subspecialty consultation. Future educational curricula developed for hemodynamic assessment and stabilization should appropriately emphasize conditions necessitating consultation.
Objective: It is difficult to predict a risk of sudden death in long QT syndrome (LQTS) before the onset of syncope due to arrhythmia. Subject and Method: Group 1 consists of 15 high risk cases (mean age 13.6 years male/female ratio=8/7) with QT prolongation and with a history of syncope. Group 2 consists of 7 disease controls (mean age 11.1 years, male/female ratio=3/4) with QT prolongation and without syncope. Group 3 consists of 8 controls (mean age 13.1 years, male/female ratio=2/6) without QT prolongation and without syncope. The complex conjugate roots were determined from the characteristic equation of the third order AR model of RR interval from 0 to 5 am. The real part of conjugate root is classified as negative, positive, zero or imaginary root, and is evaluated to discriminate group 1 from the other groups. Results: Absolute negative roots include 13 from group 1 and 2 from group 2. Imaginary roots include 1 from group 1, 1 from group 2, and 5 from group 3. Positive roots include 4 from group 2 and 3 from group 3. Conclusion: As most of the group 1 is characterized a negative root, this position of conjugate root in the complex domain may be useful to predict a risk of syncope and hence a risk of sudden death in LQTS. Sensitivity and specificity of this risk criterion to determine group 1 and 2 were 80% and 40%, respectively. Sensitivity and specificity to determine group 1 and 3 were 82% and 80%, respectively.

P-023 Increased T-wave alternans by modified moving average beat analysis in children with congenital right bundle branch block
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Background: Microvolt T wave alternans (MTWA) has been shown as a marker for increased risk of arrhythmia. Its implication in patients with prolonged QRS duration due to right bundle branch block (RBBB) may however be different, but is still unclear. Methods: Twenty-six, aged 10 to 25 years old, children and adolescents with complete RBBB (RBBB group) and normal cardiac structure identified from school EKG survey received Treadmill by Bruce protocol with modified moving average beat analysis of MTWA. Another 26 age- and sex-matched adolescents served as control. Results: The basic characteristics and EKG parameters other than the QRS duration were not different between the two groups. We used 125 bpsm as threshold heart rate for those older than 15 years old, and 67% predicted maximal heart rate for those younger than 15 years old. The MTWA was larger in RBBB group than in the control (27.8 ± 14.4 µV vs. 14.1 ± 8.1 µV, p<0.001). Using 28µV as cut point, the percentage of positive MTWA was higher in RBBB group (53.8% vs. 3.8%, p<0.001). Using multivariate linear regression model to control confounding factors, RBBB was the only significant factor for increased positive MTWA. None of the children have any life threatening events during 18 months follow-up after Treadmill and 169 person-years since complete RBBB were first detected. Conclusion: In patients with complete RBBB without structural heart disease, the MTWA obtained by modified moving average beat analysis from Treadmill increased and may not be sensitive to predict cardiac risks.
P-025 Lipoprotein (a) levels affect both intima-media thickness of the common carotid artery and Achilles tendon thickness in children with mutation of low density lipoprotein receptor gene

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Background: It has been well known that adult patients with mutation of low density lipoprotein receptor (LDL-R) gene who are accompanied with high levels of lipoprotein (a) (Lp (a)) showed more increasing risks of coronary heart disease (CHD).

Purpose: The aim of this study is to assess the relationship between the severity of carotid atherosclerosis and Achilles tendon thickness (ATT) and Lp (a) in children with mutation of LDL-R gene.

Subjects and Methods: Subjects were 21 familial hypercholesterolemia heterozygous children aged 12.8±5.1 years from our outpatient clinic, who were identified LDL-R mutations by DGGE. Serum lipoproteins were determined by enzymatic method, and LDL-cholesterol (LDL-C) was calculated by use of Friedewald formula. Lp (a) measured immunochemically. Achilles tendon thickness (ATT) was determined by radiographic method. Intima-media thickness (IMT) was measured by B-mode ultrasound.

Results: Lp (a) varied from 4 to 113 mg/dl and was not age-depended in this series. The average/SD, ATT was 8.9±3.5 mm, and the average IMT was 0.60: 0.12 mm. Lp (a) levels were positively related with ATT (r = 0.457, p=0.018), and with IMT (r = 0.392, p=0.023). Lp (a) also significantly associated with LDL-C levels, cumulatively (r = 0.277, p=0.005).

Conclusions: The advanced atherosclerotic findings were notified in children with mutation of LDL-R gene who are accompanied with high Lp (a) levels. These findings may be compatible with the fact that adult patients with high Lp (a) levels frequently affected CHD. Lp (a) measurement may help to manage the children with mutation of LDL-R gene.

P-026 Clinical features of 100 Japanese children with cardiomyopathy —experience in one institution—

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[Background] Clinical features of children with cardiomyopathy remain to be clarified for the better treatments and outcomes of patients.

[Methods] Medical records of 100 Japanese children diagnosed as cardiomyopathy in our institution were retrospectively examined.

[Results] Types: dilated cardiomyopathy (DCM) 63%, hypertrophic cardiomyopathy (HCM) 36%, restrictive cardiomyopathy (RCM) 1%. Sex: male 62%. Age at diagnosis: <1 year old 42%. Causes: DCM: idiopathic 41%, myocarditis 37%, neuromuscular diseases 5%, abnom errors of metabolism (IEM) 2%. HCM: idiopathic 58%, congenital malformation syndrome (CMS) 36%, IEM 6%. RCM: idiopathic 100%. Familial history: 6%. Prognosis: the 1, 2, 5, 10-year freedom rates from death or transplantation: DCM: 89%, 87%, 80%, 77%: HCM: 85%, 85%, 85%, 85%. (idiopathic: 94%, 94%, 94%, 94%, CMS 85%, 85%, 85%, 85%, IEM 0%, 0%, 0%, 0%, Age at diagnosis: <1 year old: 69%, 69%, 69%, 69%, 1 year old: 100%, 100%, 100%, log-rank test P<0.001). RCM 100%, 100%, 100%, 0%.

[Conclusions] In pediatric cardiomyopathy, DCM was the most common type with a male predominance and an incidence peak in infancy. The causes of about half cases were unknown. The most common causes were myocarditis in DCM, CMS (Noonan syndrome) in HCM, and familial cases were rare. The prognosis of IEM and infant cases with HCM was particularly poor.

P-027 Sublingual nitrate-stimulated head-up tilt testing in patients with syncope and a healthy control group

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Background: Head-up tilt testing is a widely used method for eliciting syncope of vagal in origin in children and adolescent with unexplained syncope. Although, it is widely used clinically to confirm the diagnosis of new cardiac pathology. The purposes of this study were to analyze angiotensin converting enzyme (ACE) insertion/deletion polymorphism in hypertensive adolescents and to determine the association between ACE genotype and cardiovascular risk factors. Methods: Forty hypertensive adolescents were included. Fat mass and fat distributions were analyzed by bioelectrical impedance. Serum insulin, vitamin B12, folate, renin, aldosterone, ACE and homocysteine levels were evaluated after a fasting period of 12 hours. The carotid intima-media thickness (IMT) and carotid artery diameter were measured using carotid ultrasound. Pulse wave velocity was measured. Polymerase chain reaction was conducted to amplify DNA with blood samples drawn to analyze ACE insertion/deletion polymorphism. Results: Systolic BP were 148.1±6.5 mmHg vs 115.9±15.9 mmHg. Genotype frequencies were I/I 30.2%, CT 53.5% and TT 16.3%. Plasma ACE levels were 33.5±8.7 U/L in I/I genotype, 48.6±19.8 U/L in D/D genotype and 61.4±22.7 U/L in D/D genotype which showed that ACE levels were significantly higher in D/D and D/D genotype than that of the I/I genotype. IMT was significantly greater in D/D group than that of the I/I group. Conclusion: Subjects with I/D and D/D genotype had higher plasma levels of ACE compared to subjects with the I/I genotype. The highest level of ACE was present in subjects with D/D genotype. Further studies are needed to establish the association between ACE I/D polymorphism and cardiovascular risks in adolescents with essential hypertension.

P-028 Angiotensin Converting Enzyme(ACE) Gene Polymorphism as a Predictor of Cardiovascular Risk in Hypertensive Adolescents

Young Mi Hong

Ewha Womans University

Purpose: Genes encoding components of the renin-angiotensin system have been proposed as candidate genes for hypertension which determine genetic predisposition to hypertension. The purposes of this study were to analyze angiotensin converting enzyme (ACE) insertion/deletion polymorphism in hypertensive adolescents and to determine the association between ACE genotype and cardiovascular risk factors. Methods: Forty hypertensive adolescents were included. Fat mass and fat distributions were analyzed by bioelectrical impedance. Serum insulin, vitamin B12, folate, renin, aldosterone, ACE and homocysteine levels were evaluated after a fasting period of 12 hours. The carotid intima-media thickness (IMT) and carotid artery diameter were measured using carotid ultrasound. Pulse wave velocity was measured. Polymerase chain reaction was conducted to amplify DNA with blood samples drawn to analyze ACE insertion/deletion polymorphism. Results: Systolic BP were 148.1±6.5 mmHg vs 115.9±15.9 mmHg. Genotype frequencies were I/I 30.2%, CT 53.5% and TT 16.3%. Plasma ACE levels were 33.5±8.7 U/L in I/I genotype, 48.6±19.8 U/L in D/D genotype and 61.4±22.7 U/L in D/D genotype which showed that ACE levels were significantly higher in D/D and D/D genotype than that of the I/I genotype. IMT was significantly greater in D/D group than that of the I/I group. Conclusion: Subjects with I/D and D/D genotype had higher plasma levels of ACE compared to subjects with the I/I genotype. The highest level of ACE was present in subjects with D/D genotype. Further studies are needed to establish the association between ACE I/D polymorphism and cardiovascular risks in adolescents with essential hypertension.
P-029 Hypertension among children and adolescents from national mass urine screening program in Taiwan
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Objective: The prevalence of hypertension among children and adolescents was increasing. This study investigated the risk factors associated with childhood hypertension in Taiwan. Design and Methods: Between 1992 and 2000, a national mass urine screening program for glucosuria and proteinuria was conducted annually for approximately 3,000,000 students aged 6-18 years. Among 103,840 students identified urine test positive, further examinations found 5,792 students of hypertension. A nested case-control analysis was performed with randomly selected 5,792 non-hypertensive controls matched with sex and grade. Results: Compared with controls, hypertensive students had higher proportion of high (≥27 Kg/m2) body mass index (BMI) (13.8% vs. 3.1%, p<0.0001), high (≥300 mg/dL) cholesterol (1.7% vs. 0.6%, p<0.0001), high (≥23 mg/dL) blood urine nitrogen (BUN) (1.6% vs. 0.9%, p<0.0002), high (≥1.3 mg/dL) creatinine (17.7% vs. 16.1%, p = 0.028), and high (≥5.0 mg/dL) albumin (6.3% vs. 5.1%, p = 0.0001). The multivariate logistic regression analysis showed the odds ratio (OR) for hypertension in students with high BMI was 7.04 (95% confidence interval [CI] = 5.87-8.46). High cholesterol (OR = 2.54, 95%CI = 1.71-3.79), high BUN (OR = 1.73, 95%CI = 1.20-2.49), and high albumin (OR = 1.24, 95%CI = 1.05-1.47) were also associated with hypertensive risk. Conclusions: Our findings show that the childhood hypertension is strongly associated with BMI and other BMI related factors.

P-030 Redundant roles of Inositol 1,4,5-trisphosphate receptors for region-specific signaling pathways during heart development
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Calcium is a versatile signaling molecule in a number of physiological or pathological events. Inositol 1,4,5-trisphosphate receptor (IP,R) is an intracellular calcium release channel, which converts some extracellular stimuli into intracellular calcium signaling in many organs including heart. Its function during heart development, however, remains to be elucidated. Our previous data that three subtypes of IP,R (IP,R1, 2 and 3) exist in developing heart led us to generation of IP,R1 and 2 double knockout (DKO) mice. During the atrioventricular (AV) cushion development of DKO embryos, the number of mesenchymal cells was reduced and the translocation of a transcription factor NFATc into the nuclei of endocardial cells was inhibited at embryonic day (E) 9.5, suggesting that IP,R1 and 2 activate NFATc in redundant fashion which is essential for AV cushion and valvulopetal development. Microarray analysis conducted with RNA isolated from wild-type or DKO hearts at E9.5 showed upregulation of several genes, including a gene encoding T-box transcription factor, Tbx5, in DKO hearts. The number of mitosis marker-positive cells was significantly decreased in DKO ventricular myocardium around E9.5 compared with wild-type heart. This observation is consistent with previous reports showing that an overexpression of Tbx5 results in decrease in cell proliferation in the developing heart. Our results suggest that IP,R1 and 2 may have redundant roles for region-specific signaling pathways through NFATc and Tbx5 in the development of the AV cushion and the ventricular wall, respectively.

P-031 Cardiogenic Wnt signaling is mediated by a non-cell autonomous mechanism
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Background: Although Wnt signaling is implicated in cardiomyogenesis, how Wnt activation exerts such effects remains largely unknown. In order to characterize the Wnt-responsive cells during ES cell differentiation into cardiomyocytes, we have developed genetically-modified ES cell lines in which the temporospatial profile of both Wnt activation and cardiomyocyte differentiation can be monitored simultaneously.
Method: The 129/Ora-derived hi-fin ES cells were used in this study. We generated stable ES cell lines which express two fluorescence reporters: DsRed driven by a cardiac-specific alpha-myosin heavy chain promoter and cyan fluorescent protein (CFP) driven by a Wnt-responsive promoter containing multimerized beta-catenin/T-cell factor-binding sites. Differentiation of ES cells into cardiomyocytes was induced by aggregation of ES cells in hanging drops for three days. On day 3, the resultant embryoid bodies were transferred to culture plates. Expression of DsRed and CFP was monitored by time-lapse images.
Results: CFP-positive Wnt responsive cells and DeRed-positive differentiated cardiomyocytes were observed from day 5 and day 8, respectively, in distinct areas within an embryoid body. Repression of Wnt signaling by administration of Wnt inhibitors (Dkk1 and/or soluble Frizzled8 protein) from day 0 to day 3 led to a decrease in the number of CFP-positive cells and resulted in loss of DeRed expression/cardiomyocyte differentiation.
Conclusions: Wnt activation is cardiogenic in the early stage of ES cell differentiation into cardiomyocytes, and cardiomyocytes are not derived from Wnt-responsive cells. Thus, the cardiogenic effect of Wnt signaling is mediated by a non-cell autonomous mechanism.

P-032 Hypoxic pulmonary vasoconstriction (HPVC) is prevented by 24 hour pre-treatment with Tadalafil (TAD)
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Untreated PHT has significant morbidity and mortality. The natural history can be modified by pulmonary vasodilators, some with practical limitations such as intravenous administration and rebound phenomenon. Oral phosphodiesterase inhibitors (PDEi) and endothelin (ET) are expensive. We evaluated the efficacy of a single dose oral administration of a long acting PDEi in a conscious untreated PHT animal model of HPVC. The lambs (n=5) were chronically instrumented with a pulmonary artery (PA) flow probe, and catheters in the LA & PV vein. On the study day, additional catheters were placed in the PA, AO, RA and LV (hi-fi catheter). Oral TAD 40 mg was given 24 hours prior to the study. The hemodynamic responses to hypoxia (Hx, Po2 ≤ 49 mmHg) were monitored and compared to normoxic values and control Hx studied separately. In untreated control studies, Hx increased the PA pressure (P) by 122.2 (82.7-213.8)% and PA resistance (PAR) by 360.5 (90.8-799.4)%. The AOP and systemic vascular resistance changed by 6.9% and 4.7% respectively. 24 hour pre-treatment with TAD abolished HPVC. PAP and PAR changed by 1.6% and -2.1% respectively. After TAD treatment, PA flow increased from 2.975 ± 0.343 in Ns to 3.466 ± 0.552 L/m in Hx, and PAP from 13.9 ± 3.2 to 14.0 ± 3.4 mmHg, PA resistance from 19.9 ± 4.3 to 20.3 ± 6.8 U/kg respectively. Oral Tadalafil once daily is effective in preventing HPVC for at least 24 hours. This regimen will reduce cost and likely improve compliance.
**P-033**
Mechanical forces can induce selective differentiation of mouse embryonic stem cells into vascular cells
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**Background** Pluripotent embryonic stem (ES) cells are capable of differentiating into all cell lineages. Mechanical forces, such as shear stress and stretching tension, not only alter the shape and function of various cells but also affect their differentiation. Previously, we have reported that shear-stressed Flk-1-positive (Flk-1+) cells derived from ES cells form tube-like structures in collagen gel and shear stress induces their differentiation into endothelial cells (ECs) via ligand-independent phosphorylation of Flk-1.

**Methods** Using standard immunomagnetic techniques, Flk-1+ cells were obtained from ES cells. Flk-1+ cells were cultured on silicon stretch chambers and cyclic stretch was applied by cyclic-stretch loading system. Then we obtained from ES cells. Flk-1+ cells were cultured on silicon stretch chambers and cyclic stretch was applied by cyclic-stretch loading system. Then we collected mRNA and protein, and examined their expression levels by RT-PCR and Western blotting.

**Results** Subjecting uni-axial cyclic stretching (1Hz, 2~12%) to Flk-1+ cells induced a marked increase in the expression levels of vascular smooth muscle cell markers SM-α-actin, SM-22α-actin and SM-MHC, whereas it had no effect on the expression levels of the ECs, blood cells or epithelial cell markers. Additionally, cyclic stretch phosphorylated platelet-derived growth factor (PDGF) receptor β. But in the presence of AG1296, inhibitor of phosphorylation of PDGFR-β, cyclic stretch-induced increase of smooth muscle cell markers was abolished.

**Conclusion** Cyclic stretch induces the differentiation of Flk-1+ cells derived from ES cells into vascular smooth muscle cells via phosphorylation of PDGFR-β. These results indicate that mechanical forces, such as shear stress and cyclic stretch generated by fluid flow, play an important role in the regulation of early vascular development in embryos.

**P-034**
Endothelin-1 inhibits both L-type Ca2+ current and ATP-sensitive K+ current in neonatal rat ventricular myocytes.
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**Objective:** Endothelin-1 (ET-1), a potent vasoactive peptide, has wide range biological effects in various organs and tissues. In heart, ET-1 is released by endothelial, vascular smooth muscle and myocardial cells especially in various cardiovascular disorders, including congestive heart failure and ischemic heart disease. In these pathophysiological conditions, intracellular ATP contents decrease and catecholamines are released simultaneously with ET-1 and may contribute to the regulation of cardiac function. In this study, we investigated the effect of ET-1 on L-type Ca2+ current (I_{Ca,L}) and ATP-sensitive K+ current (I_{ATP}) in immature ventricular myocytes. **Methods:** Cells were enzymatically isolated from neonatal rat ventricle (aged 3 to 10 days). I_{Ca,L} was measured as the peak inward current at a test potential of +10 mV from a holding potential of -40 mV. I_{ATP} was measured at a test potential of +60 mV from a holding potential of -70 mV. All experiment was done at 37 °C. **Results:** ET-1 (10 ~ 100 nM) decreased not only the basal I_{Ca,L} but also the inosoproterenol-stimulated I_{Ca,L}. On the other hand, ET-1 (10 nM) almost completely inhibited the ATP-sensitive K+ channel opener, pinacidil-induced outward current (i.e. I_{ATP}). Furthermore, ET-1 inhibited the shortening of action potential of cardiomyocyte induced by pinacidil. These effects were reduced in the presence of BQ-123, an ET1 receptor antagonist, suggesting that the action of ET-1 is mediated by the ET1 receptor. **Conclusions:** In neonatal heart, ET-1 will inhibit not only the contractility, but also cardioprotective action by inhibiting inosoproterenol-stimulated I_{Ca,L} and I_{ATP}.

**P-035**
SARS-coronavirus induced different gene expression of chemokine receptors in human monocyte-derived adult and cord blood dendritic cells
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**Background** We have previously shown that SARS-CoV induced low interferons/IL-12 and high chemokine gene expression in dendritic cells (DCs). The chemokine gene expression was significantly higher in cord blood (CB) than adult DCs. We hypothesized that the developmental stages of the host immune system may account for the less severe phenotype of SARS in young children.

To investigate if the chemokines upregulation is implicated in the regulation of DC migration, we further investigated the effect of SARS-CoV on chemokine receptors (CCRs) gene expression in CB and adult DCs.

**Methods** CB and adult CD14+ monocytes were isolated by immunomagnetic separation and differentiated into immature DCs by IL-4+GM-CSF. Mock or SARS-CoV infected DCs were harvested at 3h and 9h post infection. Total RNA was extracted and gene expressions were quantitated by real time PCR based on Taqman fluorescence signals.

**Results** We studied the common receptors that may bind to the chemokines upregulated by SARS-CoV. Basal gene expressions of CCR1, CCR5, CCR7 in CB DCs were 1-2 log higher than that in adult DCs. SARS-CoV induced their expression in adult DCs but not in CB DCs. For CCR3, the basal levels were low in both CB and adult DCs and SARS-CoV induced its expression significantly in some cases.

**Conclusions** The lack of CCRs gene induction in CB by SARS-CoV may reflect the refractoriness of CB DCs to be mobilised in an environment with high chemokines concentration. Further investigation on chemotaxis of CB and adult DCs is needed to substantiate this hypothesis.

**P-036**
Increased nitric oxide production and GFAP expression in the brains of Influenza A/NWS Virus Infected Mice
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1Department of Pediatrics, Tokyo Medical University, 2Department of Pharmacology/Pharmacotherapy, School of Medicinal Pharmaceutical Sciences, Nihon Pharmaceutical University

**Objective**Infected Mice

**Methods**Infected Mice

**Results**Infected Mice

**Conclusions**Infected Mice

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Background: Hyperinflammatory response and differential chemokine expression play important roles in pathogenesis of human H5N1 disease. The 1997 and 2004 strains of H5N1 in human population presented with different severity and mortality, and age-related severity was also reported among these two outbreaks.

Methods: The mRNA expressions of cytokines, chemokines, their receptors and death receptor ligands, TNF-α, CCR1 and CCR5. 483/97 H5N1 also induced much higher expression of death receptors. For 483/97 H5N1, the increase of TNF-α detected chemokines and receptors, including MCP1, MIP1α, RANTES, IP-10, CCR1 and CCR5. 483/97 H5N1 also induced much higher expression of death receptor ligands, TNFα, TRAIL and FasL. However, no significantly different expressions of IFNα and IFNβ were observed between these two viruses-infected macrophages. For 483/97 H5N1, the increase of TNFα and MCP1 expression in virus-infected neonatal macrophages was significantly lower than that in adult macrophages; on the contrary, the increase of IFNα expression was much higher in virus-infected neonatal macrophages. In contrast, for 1203/04 H5N1, no significant difference was shown in the increase of all the detected molecules between neonatal and adult macrophages.

Conclusions: The immune response induced by avian viruses may be strain-specific. 483/97 H5N1 triggers stronger inflammatory response than 1203/04 strain. The different expressions of the mentioned molecules may partly explain the different severity of diseases between children and adults in the 1997 outbreak.

P-038 Evaluation of Immunochromatography Tests for Detection of Rotavirus and Norovirus among Vietnamese Children with Acute Gastroenteritis and the Emergence of a Novel Norovirus GI.4 Variant
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[Background] Rotaviruses and noroviruses are considered as the two most common causes of acute gastroenteritis in infant and young children.

[M methods] A prospective study was conducted to evaluate two immunochromatography (ICG) tests for detection of group A rotavirus and norovirus GI.4, the commercial Dipstick ‘Eiken’ Rota kit (SA Scientific, USA) and the NV IC-1 stick (Immuno-Probe, Japan). Polymerase chain reaction (PCR) with specific primer pairs (Beg9 and VP7-1', for group A rotavirus; COG2F and G2SKR, for norovirus GI.4) was used as the reference method.

[Results] The results of ICG tests were compared with those of reference methods. The sensitivity, specificity and agreement between ICG tests and PCR were 87.8%, 93.3% and 89.4%, respectively, for rotavirus ICG test; and 73.7%, 100% and 95.2%, respectively, for norovirus ICG test. The immunochromatography assay for norovirus used in this study could detect not only common noroviruses but also a novel norovirus GI.4 variant, which emerged in Ho Chi Minh City in 2006.

[Conclusion] Immunochromatography tests are easy, rapid and useful assays for detection of rotavirus and norovirus among pediatric patients with acute gastroenteritis in Vietnam.

P-039 Changing pattern of rotavirus G genotype distribution in Chiang Mai, Thailand from 2002 to 2004: decline of G9 and reemergence of G1 and G2
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Background: Group A rotaviruses are the most common cause of acute viral diarrhea throughout the world. Previous surveillance studies of group A rotaviruses in Thailand indicated that the dominant types were changing from time to time. During 2000 and 2001, the G9 rotavirus emerged as the most prevalent genotype, with a high frequency (91.6%) in Chiang Mai, Thailand.

Study design: Rotavirus was detected in stools using the reverse transcription-polymerase chain reaction (RT-PCR). The G and P genotyping of group A rotaviruses were performed by RT-PCR and multiplex PCR. The representative strains of G1, G2, and G9 were selected and sequenced their VP7 genes.

Results: Of 263 fecal specimens collected, the group A rotavirus was detected in 98 (37.3%). Of these, 40 (40.8%) were G9P[8], 33 (33.7%) were G1P[8], 23 (23.5%) were G2P[4], and 2 (2.0%) were G3P[9]. G9P[8] was found to be the most predominant strain in 2002, but the prevalence rate abruptly decreased during the period 2003 to 2004. In addition, G2P[4] reemerged in the epidemic season of 2003, whereas G1P[8] became the most predominant strain in the following year. Phylogenetic analysis of the VP7 genes revealed that our Chiang Mai G1, G2, and G9 rotavirus strains clustered together with recently circulating strains, isolated from different regional settings in Thailand.

Conclusions: Our study demonstrated a decrease of incidence of G9P[8] and reemergence of G1P[8] and G2P[4] rotaviruses in Chiang Mai, Thailand during the period 2002 to 2004. These data imply that the genotype distribution of group A rotaviruses in Chiang Mai changes over time.
**P-041** Experience of three infants with neonatal bacterial meningitis of Escherichia coli and outcome at 18 month old

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Background: Neonatal bacterial meningitis remained challenge. Since prenatal screening and intrapartum antibiotic, invasive infection of Gram-negative bacilli had regained importance. We presented our experience in diagnosis and follow-up of infants with Escherichia coli meningitis. Patients and methods: Three infants with mean age of 8 days old, mean weight 2760g were presented with fever between August 2005 and March 2006. Cultures of blood, urine and cerebrospinal fluid(CSF) were performed and antibiotics with ampicillin+cefotaxime. Brain images and neurological evaluation were recorded on schedule. We also reviewed Pubmed about neonatal bacterial meningitis in Taiwan and Asia. Results: One of the mothers received prophylactic ampicillin, and none had prematurity ruptures. All CSF showed E. coli with two strains resistant to ampicillin, and the other was all susceptible. Intractable seizures, acute hydrocephalus were complicated in all infants, and two received Omaya shunts. They all survived beyond neonatal period, but complicated with central diabetes insipidus, hydrocephalus, encephalomalacia, shunt infections, optic neuropathy, deafness, endocarditis, open ductus arteriosus. One had urine culture positive to Staphylococcus aureus resistant to ampicillin, and the other was all susceptible. Intractable seizures, acute hydrocephalus were complicated in all infants, and two received Omaya shunts. They all survived beyond neonatal period, but complicated with central diabetes insipidus, hydrocephalus, encephalomalacia, shunt infections, optic neuropathy, deafness, endocarditis, open ductus arteriosus.

Conclusions: Younger age and cytomegalovirus infection are associated with prolonged neutropenia. The detailed mechanism needed to be further elucidated.

**P-042** TLR9 dependent and independent IFN alpha production by human mononuclear cells infected with varicella-zoster virus

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Background: Knowing the defense mechanism of host to organism is important for infection control. In previous study, we had shown that interferon-alpha (IFN-alpha) but not interleukin-12 (IL-12) being produced as human peripheral blood mononuclear cells (PBMCs) infected with varicella-zoster virus (VZV). Here we investigated what signal molecule(s) and what kind of cell(s) involved in the IFN-alpha production.

Methods: PBMCs were isolated and cultured with VZV antigens with or without specific inhibitors as indicated. IFN-alpha were detected with intracellular staining and ELISA. Results: We found that Toll-like receptor 9 (TLR9) was involved in the VZV-induced IFN alpha production since inhibitory CpG ODN could inhibit IFN-alpha production. We also found that UV-inactivated VZV induced IFN-alpha production insensitive to inhibitory CpG ODN treatment indicating another TLR9-independent pathway. Further studies demonstrated dsRNA-dependent protein kinase (PKR) but not DNA-dependent protein kinase (DNA-PK) was involved in the VZV-induced IFNα production. With intracellular staining and ELISA detection, we found that plasmacytoid dendritic cells (pDC) were responsible for IFN-alpha production during VZV infection.

Conclusions: Together, these results suggest that pDC play an important role in the IFN-alpha production in infection through TLR9 dependent and independent pathways.

**P-043** Prolonged acquired neutropenia associated with younger age and cytomegalovirus infection

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Backgrounds: Neutropenia is defined as a decrease in the circulating or absolute Center, Chang Gung University Department of pediatrics, Chang Gung Memorial Hospital-Kaohsiung Medical Kuender D. Yang Jiunn-Ming Sheen, Hong-Ren Yu, Ho-Chang Kuo, Ling Wang, Tzu-Chiang Wu, Kuender D. Yang

Patients and methods: Three infants with mean age of 8 days old, mean weight 2760g were presented with fever between August 2005 and March 2006. Cultures of blood, urine and cerebrospinal fluid(CSF) were performed and antibiotics with ampicillin+cefotaxime. Brain images and neurological evaluation were recorded on schedule. We also reviewed Pubmed about neonatal bacterial meningitis in Taiwan and Asia. Results: One of the mothers received prophylactic ampicillin, and none had prematurity ruptures. All CSF showed E. coli with two strains resistant to ampicillin, and the other was all susceptible. Intractable seizures, acute hydrocephalus were complicated in all infants, and two received Omaya shunts. They all survived beyond neonatal period, but complicated with central diabetes insipidus, hydrocephalus, encephalomalacia, shunt infections, optic neuropathy, deafness, endocarditis, open ductus arteriosus. One had urine culture positive to Staphylococcus aureus resistant to ampicillin, and the other was all susceptible. Intractable seizures, acute hydrocephalus were complicated in all infants, and two received Omaya shunts. They all survived beyond neonatal period, but complicated with central diabetes insipidus, hydrocephalus, encephalomalacia, shunt infections, optic neuropathy, deafness, endocarditis, open ductus arteriosus.

Conclusions: Younger age and cytomegalovirus infection are associated with prolonged neutropenia. The detailed mechanism needed to be further elucidated.

**P-044** Association of surfactant protein D gene polymorphism and severe respiratory syncytial virus infection in Japanese infants

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Background: Surfactant protein D (SP-D), a member of the collectin subfamily of C-type lectins, is involved in innate host defense by binding to microbe carbohydrate antigens. Lahti et al. reported that Sp-D gene polymorphism at the codon for amino acid 11 increases the risk of severe respiratory syncytial virus (RSV) broncholitis in Finnish infants.

Objective: To determine whether SP-D gene polymorphisms altering a single amino acid of mature protein is associated with the severity of RSV infection.

Subjects and Methods: DNA samples from 47 infants admitted into a tertiary hospital for RSV infection were analyzed. A PCR-RFLP reaction or direct sequencing method was performed for genotyping three biallelic polymorphisms at the SP-D codons for the amino acids 11, 160, and 270 in the mature SP-D (Met11Thr: rs721917, Ala160Thr: rs2243639, Ser270Thr: rs3088308). The duration of hospital stay, oxygen supplement, endotracheal intubation and laboratory data on admission were compared among the genotypes.

Results: No significant difference was found among the genotypes and allele frequencies of Met11Thr, Ala160Thr and Ser270Thr. In the subgroup analysis of infants less than 1 year old, the hospital stay of the infants with 11Met/Met was longer than the other genotypes (mean 7.0 vs 9.0 days; p=0.002).

Conclusion: The 11Met/Met genotype may increase the severity of RSV infection in Japanese infants less than 1 year old.
P-045  An effective scoring system of chest CT for assessing the clinical status of neonatal bronchopulmonary dysplasia

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Objective: To develop a new chest CT scoring system for assessing the clinical status of neonatal bronchopulmonary dysplasia (BPD), comparing with a previous Edward’s roentgenographic scoring system. Study design: Forty-two preterm infants diagnosed as having BPD were assessed prospectively. All patients underwent chest CT scanning at the time of discharge. Three radiologists classified their chest CT findings into three categories; (A) Hyperexpansion, (B) Emphysema and (C) Fibrous / interstitial abnormalities, and developed a new scoring system. We assessed an interobserver reproducibility and investigated whether the system reflected the patients’ severity by association studies.

Results: The two scoring systems showed high coincidence and reproducibility whether the system reflected the patients’ severity by association studies. The SP-D score at 36 weeks was associated with the clinical scores (cc; 0.469), the duration of oxygen therapy (cc; 0.367) and the duration of ventilator (cc; 0.402) and the mechanical ventilation (cc; 0.472). Conclusions: The SP-D CT score was correlated with the roentgenographic score at 28 days, but not at 36 weeks, which was associated with the clinical scores (cc; 0.402), the mechanical ventilation (cc; 0.472). Conclusions: The new chest CT scoring system may have higher objectivity and accuracy for pre-discharge assessment of the clinical status and predicting outcomes of BPD patients.

P-046  Association between surfactant protein D gene polymorphism and a predisposition to bronchopulmonary dysplasia

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Background: Surfactant protein D (SP-D) is a member of collagenous host defense lectins. Intrauterine infection and cytokines contribute to the development of bronchopulmonary dysplasia (BPD). Genetic variability of SP-D that nonspecifically participates in the immune and inflammatory regulation within the lung may influence the risk of BPD.

Purpose: To determine whether SP-D gene polymorphisms altering a single amino acid of mature protein is associated with a predisposition to BPD.

Subjects and Methods: DNA samples from 35 premature infants hospitalized in a newborn intensive care unit were analyzed. A PCR-RFLP reaction or direct sequencing method was performed for genotyping three biallelic polymorphisms at the SP-D codons for the amino acids 11, 160, and 270 in the mature SP-D (Met11Thr: rs721917, Ala160Thr: rs2243639, Ser270Thr: rs3088308).

Results: Of the 35 subjects, 15 had respiratory distress syndrome (RDS) and 6 had BPD. Three of the BPD patients were further classified with Wilson-Mikity syndrome (WMS). The frequency of the allele coding for 11 Thr was 0.58 in the BPD group and 0.76 in the non-BPD group. The 11 Thr allele was 0.89, 0.67, and 0.50 in the patients of RDS+/BPD, RDS+/WMS, and RDS+/BPD+/WMS+, respectively. Although the allele for 11 Thr tended to be less frequent among the BPD group, no statistically significant difference was observed. No significant differences were found in the allele frequencies for amino acids 160 or 270.

Conclusion: The SP-D allele coding for threonine 11 may diminish a predisposition to developing BPD.

P-047  High expression of interleukin-10 and platelet-derived growth factor-B genes in tracheal aspirate fluid cells of low birth weight infants with bronchopulmonary dysplasia

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Backgrounds: Bronchopulmonary dysplasia (BPD) is a late critical effect, occasionally occurring in low birth weight infants with and without the history of respiratory distress. Methods: The gene expression of cytokines and associated inflammatory molecules in tracheal aspirate fluid (TAF) cells was quantified by real-time polymerase chain reaction. Results: Interleukin (IL)-10 and interferon (IFN)-γ mRNA levels in TAF cells within the first 24 hours of birth, were higher in the neonates who developed BPD than in those who did not. Platelet-derived growth factor (PDGF)-B was exclusively transcribed at high levels in the neonates who developed BPD but not respiratory distress syndrome (RDS). The morbidity rate of BPD was higher in high expression group of TGF-β, IL-10 and IFN-γ than in the each low expression group. On the other hand, the morbidity rate of RDS in BPD patients was lower in high expression group of PDGF-B than in the low expression group. The immunohistochemistry of lung tissue revealed that PDGF-BB-positive cells were dominantly found in a patient with Wilson-Mikity syndrome. Conclusions: These results suggested that IL-10 expression was involved in the damage of lung tissue irrespective of the presence or absence of RDS, and that PDGF-B in pulmonary inflammatory cells was associated with the development of BPD in the neonates without RDS. IL-10 and PDGF-B levels in TAF cells could be a prognostic marker for the long-term outcome of the newborns with early respiratory distress.

P-048  Different patterns of bronchopulmonary dysplasia in premature infants

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Objective: To determine the incidence and clinical characteristics of BPD in premature infants.

Methods: A retrospective cohort study was conducted on 559 premature infants (GA < 32 weeks) admitted in a university NICU. The definition of BPD and severity proposed by the workshop organized by NICHD in 2000 were used.

Results: Of the 35 subjects, 15 had respiratory distress syndrome (RDS) and 6 had BPD. Three of the BPD patients were further classified with Wilson-Mikity syndrome (WMS). The frequency of the allele coding for 11 Thr was 0.58 in the BPD group and 0.76 in the non-BPD group. The 11 Thr allele was 0.89, 0.67, and 0.50 in the patients of RDS+/BPD, RDS+/WMS, and RDS+/BPD+/WMS+, respectively. Although the allele for 11 Thr tended to be less frequent among the BPD group, no statistically significant difference was observed. No significant differences were found in the allele frequencies for amino acids 160 or 270.

Conclusion: The SP-D allele coding for threonine 11 may diminish a predisposition to developing BPD.

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P-049 Pretreatment with Ibuprofen Attenuates Ventilator-Induced Lung Injury.

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Background: Pretreatment with indomethacin prevents the progression of pulmonary hypertension mediated by TXA2 in surfactant-depleted rabbits, but the effects of prostanooid blockade on ventilator-induced lung injury are unknown. The purpose of this study was to examine the effects of Ibuprofen on the acute lung injury induced by high tidal volume and no PEEP ventilation.

Methods: Anesthetized Sprague-Dawley rats (300-350 g) were randomized to receive Ibuprofen (100 mg/kg) or saline intravenously. PEEP was reduced to zero and VT was increased to PIP 28.6 cmH2O, and ventilation continued for 90 min.

Results: Baseline data were comparable between the 2 groups. Compared to saline animals, pretreatment with Ibuprofen resulted in lower PIP (29.8±3.4 vs. 33.7±2.4 cmH2O, P<0.05), higher static compliance (0.52±0.27 vs. 0.26±0.06 ml/cmH2O, P<0.05), and lower lung Wet/Dry ratio (5.33±0.69 vs. 7.10±0.61, P<0.001). Bronchoalveolar lavage demonstrated lower levels of PGE2 (0.21±0.06 vs. 2.15±0.34 ng/ml) and PGI2 (0.19±0.078 vs. 10.5±1.95 ng/ml) in the Ibuprofen vs. saline groups (P<0.05, in each case). A dose-response relationship whereby higher dose of Ibuprofen reduces lung injury was demonstrated.

Conclusions: Identification and pretreatment of at-risk lungs with cyclooxygenase inhibitors might reduce lung injury associated with mechanical ventilation.

P-050 The Feasibility of Using Venous Catheter in the Treatment of Pneumothorax in Preterm Neonates

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Objective: The aim of the study was to explore the feasibility of using venous catheter in substitution of chest tube in the treatment of pneumothorax in preterm neonates.

Patients and Methods: 16 preterm neonates treated with chest tube insertion (n=9) or venous catheter placement (n=7) for pneumothorax in the neonatal intensive care unit of a tertiary medical center were enrolled retrospectively over a 6-year period. The duration of the procedure, and the chest tube or catheter in place were analyzed. The complication rate of the two groups was also compared. Mann-Whitney U test, and Fisher’s exact test were used for analysis.

Results: High reinsertion rate (42.9%) due to catheter malfunction was noted in the venous catheter group. The duration of the procedure and the duration of the device in place were no longer in the venous catheter group. The complication rate of both groups showed no statistical differences. Obstruction of venous catheters due to blood clots resulted in the only failure of using the venous catheter in the treatment of pneumothorax in a premature infant with underlying coagulopathy.

Conclusions: We concluded that using venous catheter in the treatment of pneumothorax in preterm neonates with underlying coagulopathy is not recommended. Further investigation involving more cases is mandatory for testing the feasibility.

P-051 The Effect of Surfactant Replacement Therapy in the Neonates with Massive Amniotic Fluid Aspiration Pneumonia (AFAP).

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Background: The massive aspiration of amniotic fluid was known as one cause of a fetal postpartal asphyxia and respiratory distress. We conducted this study to evaluate the effect of surfactant replacement therapy (SRT) in neonates who were required ventilatory care due to massive amniotic fluid aspiration pneumonia (AFAP).

Methods: 28 patients received ventilatory care due to massive AFAP who were admitted in NICU of Dongsan Medical Center, Keimyung University from Jan. 2000 to Dec. 2006 were enrolled. It was excluded the patients whose amniotic fluid was contaminated by meconium. All patients were under artificial ventilation care and received SRT, the mean doses of surfactant (modified bovine surfactant) was 120 mg/kg. They were evaluated several clinical data (gestational age, delivery type, duration of ventilator care) and outcome (complications and mortality rate). They were also analyzed the change of oxygenation index (OI) between pre-SRT and post-SRT.

Results: A large number of cases were term infants (82%) and born by caesarean section (85.7%). Radiological improvement was evident in 27 patients 6 hours post-treatment except one who was expired immediately after birth. Compared with pre-SRT, the mean OI was significant improvement at 6 and 12 hours after SRT (p<0.05). Complicated cases (PPHN, pneumothorax, pneumomediatinum, pulmonary hemorrhage) were high (46.4 %) but final outcome were excellently good (survival rate 96.4%).

Conclusion: Our study suggested that SRT seems to be an effective adjuvant therapy in neonates with severe massive AFAP.

P-052 Stat3 is Required for ABCA3 Expression in Alveolar Type II Cells.

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Rational: ABCA3 is a lipid transport protein required for normal synthesis and storage of surfactant lipid. ABCA3 is highly expressed in lamellar body membranes in alveolar type II cells in human and mouse lung. ABCA3 mutations cause surfactant deficiency and respiratory distress during the postnatal period, indicating that ABCA3 plays a critical role in surfactant homeostasis. Our RNA microarray analysis demonstrated that lipid metabolism related genes were decreased in type II cells from Stat3-/- mice (unpublished observation). Because ABCA3 plays an important role in surfactant lipid homeostasis, the present study was undertaken to assess the role of Stat3 in the regulation of ABCA3 in alveolar type II cells.

Method: Stat3-/- mice were generated in which Stat3 was selectively deleted in respiratory epithelial cells. ABCA3 mRNA and protein were assessed in Stat3-/- and control mice.

Results: ABCA3 mRNA and protein were assessed in Stat3-/- and control mice. ABCA3 mRNA and protein were significantly decreased in alveolar type II cells in the lungs of Stat3-/- mice. The deletion of Stat3 was associated with abnormalities in the numbers and sizes of lamellar bodies in alveolar type II cells. Consistent with the role of Stat3, intratracheal instillation of IL-6 enhanced phospho-Stat3 staining and induced ABCA3 expression in type II cells of the adult mouse lung in vivo. IL-6 induced ABCA3 mRNA expression in mouse lung epithelial cells (MLE 15) in vitro. Conclusion: Stat3 signaling pathway regulates ABCA3 expression in alveolar type II cells and plays a role in surfactant homeostasis. Supported by HL61646.
P-053 Effect of health care reform on neonatal transfer patterns in southern Thailand

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Introduction: Following a new policy of tighter financial control in the 2001 Thai-budget, the freely available patient referral system in Thailand changed to a limited registration hospital system, except for emergency cases. The impact of this reform on health care hasn’t yet been evaluated.

Objective: To compare the numbers and characteristics of neonatal transfers to the Neonatal Intensive Care Unit (NICU) of Songkanagarind Hospital before and after the changed referral system.

Methods: We retrospectively reviewed medical records of neonates transferred to our NICU. The period of study was divided into two 2-year periods: before the change (January 1999 - December 2000) and after the change (January 2002 - December 2003).

Results: The total number of cases was 320, with 137 and 183 cases in the periods before and after the change, respectively. There were no differences in the characteristics of patients, clinical conditions before transfer, and mortality rates (16.8% VS 17.5%, p=1) between the two periods. The significant differences were hyperthermia (BT < 36.5°C), which decreased from 62.0% (85/137) to 49.1% (90/183) (p=0.03), and direct transfers, which increased from 76.6% (105/137) to 86.9% (159/183) (p=0.03). The most common surgical condition for transfer was gut obstruction in both periods but the number of congenital heart disease cases, increased from 6.5% (9/137) to 19.6% (36/183) (p=0.002).

Conclusion: Thai health care referral system reform appears to have been unsuccessful during its first two years in our institution, as the number of direct transfers significantly increased. However, the mortality rates were still the same.

P-054 Nationwide birth weight/gestational age-specific neonatal mortality rate in Taiwan

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Background: There is limited nationwide data of neonatal mortality rate in Taiwan. This study aims to provide an updated national reference of birth weight/gestational age-specific neonatal mortality rates and to reflect new socioeconomic impacts in this era.

Methods: We abstracted the birth registration database from the Ministry Interior in Taiwan during 1998-2002 and linked to the death registration database from the Taiwan Department of Health during 1998-2003. A total of infants (n=1,331,785) that gave birth between 20 to 44 weeks of gestational age and weighted within median ± 2 interquartile range in their age group were included in this study. Birth weight/gestational age-specific neonatal mortality rates were calculated by using 250 gm/one-week intervals and as different gender. A Poisson regression model was used in modeling the mortality data.

Results: The total numbers of neonatal deaths were 4,169 through 1998 to 2003. The overall neonatal mortality rates for male and female were 3.39% and 2.80%, respectively. Birth weight/gestational age-specific neonatal mortality rates chart was plotted with curves representing 10th and 90th birth weight percentile. There was a gradual increase in the prevalence of low birth weight and preterm birth together with the percentage of infants born to immigrant mothers during this period.

Conclusion: We provide an easy to use birth weight/gestational age-specific neonatal mortality rates chart as a reference to facilitate decision making for physicians and parents. The normative data is crucial in further investigation of socioeconomic issues and public health policies in Taiwan.

P-055 Two cases of ultra-micropremie of birth weight less than 300 g

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Background: We experienced ultra-premature babies of birth weight less than 300g in 1999 and 2006. We herein report the difference of these two cases. Case reports

Case 1: The baby girl was born by cesarean section at 25 weeks of gestation because of pregnancy induced hypertension. Her birth weight was 289 g. We used an umbilical vein catheter for 24 days. We did not give intravenous amino acids until 17 days of age. Although we supplemented calcium, phosphorus and vitamin D to maintain the serum calcium, phosphorus level of ultra-micropremie of birth weight less than 300 g. We used an umbilical vein catheter for 21 days. We did not give intravenous amino acids immediately after birth. Her weight gain was much better than Case 1.

Conclusion: Thai health care referral system reform appears to have been unsuccessful during its first two years in our institution, as the number of direct transfers significantly increased. However, the mortality rates were still the same.

P-056 Risk factors for rehospitalization within one year after discharge from NICU

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Neonates in NICU are likely to have various medical problems and thus have a risk to be rehospitalized even after discharge from NICU. To identify the risk factor for rehospitalization shortly after discharge from NICU, clinical characteristics of neonates in our NICU were retrospectively studied. The medical records of 579 neonates who had been discharged from the NICU during January 1, 2000 to December 31, 2002 were reviewed for their clinical characteristics in the NICU and histories of hospital admission within one year after discharge from the NICU. Among them, 491 neonates who had been followed by us for more than 1 year were enrolled in this study. Nea...
Stockholm, perfusion. However, in neonatal hearts, magnesium content (853.0 ± 13.8 µg/g) to 607.0 ± 22.8 µg/g; significantly (p<0.01) lower than that after aerobic without hypoxia was 793.9 ± 16.7 µg/g and 819.2 ± 39.1 µg/g, respectively. Heart rate, ventricular contraction in neonatal hearts were maintained higher level by hypoxia and were recovered faster by reoxygenation than those of adult. The recovery level of tension-rate product was not significantly different between neonates and adults after reoxygenation.

spectrophotometry. (Results) Heart rate and ventricular contraction in neonatal myocardium after the perfusion was quantified by atomic absorption spectroscopy.

Myocardial protective effect. (Methods) Rat hearts of adult (10weeks old), n=6) in an experimental model of neonatal encephalopathy. Methods: Hypothermia was instituted 2-26 hours after transient hypoxia-ischaemia with contact, n=6 in an experimental model of neonatal encephalopathy. Methods: Hypothermia was instituted 2-26 hours after transient hypoxia-ischaemia with contact with a radiant warmer (Bodytemp 2000, ArjoHuntleigh) to target Ttoral between 33-34°C. Heart rate, ventricular contraction and systemic arterial pressure were recorded. Results: Heart rate, ventricular contraction in neonatal myocardium after the perfusion was quantified by atomic absorption spectroscopy.

Low-tech low-cost cooling device for global infant population with birth asphyxia

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Background: Therapeutic hypothermia following neonatal encephalopathy ameliorates death/disability in a developed world setting. As the incidence of neonatal encephalopathy is higher in low-resource settings, designing safe, low-tech and low-cost methods may significantly increase the number of infants to have the benefit. Aims: To assess the application of two low-tech cooling methods: (i) commercially available water bottles (WB) filled with tepid water (25°C, n=5); (ii) phase changing material (PCM) (melting point 32°C). PCM works as a heat buffer stabilising the temperature of substance in contact, n=6. (Methods) Twenty neonates were randomised to the two cooling methods: Hypothermia was instituted 2-26 hours after transient hypoxia-ischaemia with the target Ttrectal between 33-34°C. Temperature undershoot was adjusted using cotton blankets; the cooling device was renewed when Ttrectal became above 34°C. Results: Ttrectal in WB and PCM reached 34°C in 4.3 (1.3-13.8) and 1.9 (1.8-2.3) hours (average and range) respectively followed by a brief undershoot below 33°C. The time within the target temperature range was longer for PCM (18.5+/-.2.1, average+/-.SD) compared with WB (11.1+/-.6.0) (p<0.05). The average of absolute deviation for Ttrectal was smaller in the subject cooled with PCM (0.26+/-.08) compared with WB (0.44+/-.014) (p<0.05). Requirements for manipulation to maintain stable Ttrectal was similar. Gradual re-warming at ~0.5°C/hour was achieved by removing the cooling source. Conclusion: Simple cooling modalities can maintain mild-moderate hypothermia in a porcine model of neonatal encephalopathy. PCM may provide with more stable cooling compared with WB. Safe and effective cooling in low-resource settings requires adequate staffing levels and appropriate monitoring.

Body-size determines regional cerebral temperature at normothermia, whole body cooling and selective head cooling

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Background: Phase III trials of hypothermia in neonatal encephalopathy demonstrated neuroprotective effect in some infants; questions remain around the optimal modality and patient selection. For example selective-head cooling was not neuroprotective in low body-weight infants on subgroup analysis in a recent clinical trial (CoolCap Trial, Wyatt et al. 2007). Methods: To investigate the dependence of regional cerebral temperature on body-weight and depth from the cerebral surface, 14 newborn piglets were studied under normothermia (38.5°C), systemic hypothermia (36.5, 34.5, 32.5, and 30.5°C) or SHC (20, 15, and 10°C). Results: At normothermia smaller body-weight led to lower cerebral temperatures at 5, 10 and 15mm from the surface but not at 20mm. During systemic hypothermia, a lower rectal temperature, smaller body-weight and a shorter distance from the cerebral surface all led to a lower regional cerebral temperature (all p<0.01). Systemic hypothermia did not affect the relationships between regional temperatures. During selective head cooling, a lower cap temperature, smaller BW and a smaller sensor depth all resulted in a lower regional cerebral temperature (all p<0.001). Discussion: Brain cooling was more efficient with lower body-weight due to greater head surface-area to volume ratios. In the CoolCap Trial, low hypothbody-weight infants may have been excessively cooled. Therapeutic ermia may require body-weight adjustment to accomplish consistent regional temperatures and optimal neuroprotection.

Why dose immature myocardium have high tolerance against hypoxia.

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(Background) It is widely known that neonatal hearts show a greater resistance against hypoxia than adult hearts, but its mechanism is not clear yet. We examined the effects and kinetics of magnesium ion which is known to have myocardial protective effect. (Methods) Rat hearts of adult (10weeks old) and neonate (1week old) were Langendorff-perfused and subjected to a 45 min hypoxia /30 min reoxygenation. Heart rate, ventricular tension and GOT release were monitored throughout the experiment. The magnesium content of myocardium after the perfusion was quantified by atomic absorption spectroscopy. (Results) Heart rate and ventricular contraction in neonatal hearts were maintained higher level by hypoxia and were recovered faster by reoxygenation than those of adult. The recovery level of tension-rate product was not significantly different between neonates and adults after reoxygenation. Although GOT release increased by reoxygenation in adults, it was not the case in neonates. The magnesium content of adult and neonatal heart after perfusion without hypoxia was 793.9 ± 16.7 µg/g and 819.2 ± 39.1 µg/g, respectively. After hypoxia-reoxygenation, the magnesium content of adult hearts decreased to 607.0 ± 22.8 µg/g; significantly (p<0.01) lower than that after aerobic perfusion. However, in neonatal hearts, magnesium content (853.0 ± 13.8 µg/g) was not significantly different from that without hypoxia. (Conclusion) We suggest that the high tolerance against hypoxia-reoxygenation injury in neonatal hearts may be derived from the ability of maintaining intracellular magnesium.

Endothelial Nitric Oxide Synthase (eNOS) Gene Polymorphism in Neonate with Perinatal Hypoxic Ischemic Encephalopathy

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Purpose; Several studies suggest an association of eNOS gene polymorphisms to cerebrovascular diseases in adults. There are three clinically significant polymorphisms identified in the eNOS gene. We analysed the association of eNOS gene polymorphisms to perinatal hypoxic ischemic encephalopathy(HIE) in neonates.

Method; Thirty seven term newborn infants with moderate to severe perinatal HIE(HIE group) and fifty four normal term infants without any perinatal problems(control group) were genotyped by PCR for two single-nucleotide polymorphisms (SNPs): 786 T in exon 7 → T in exon 7 and 786 C to T in intron 4. Genotype frequencies of the three eNOS polymorphisms between HIE and control groups.

Results; No significant difference was found in the distribution of genotype frequencies of the three eNOS polymorphisms between HIE and control groups. However the increased frequency of the G allele of Glu298Asp polymorphism (853.0 ± 13.8 µg/g) was not significantly different from that without hypoxia. (Conclusion) We suggest that the high tolerance against hypoxia-reoxygenation injury in neonatal hearts may be derived from the ability of maintaining intracellular magnesium.

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P-061 New optical brain imaging in infants by using near-infrared diffuse optical tomography

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An optical 3D imaging method using near-infrared diffuse optical tomography (NIR DOT) to estimate regional light scattering and absorption properties in infants has been developed. The NIR DOT system consists of 16 source-detector fibers, pulsed diode lasers operating at wavelengths of 759 and 835 nm, and time-correlated single photon counting units. The image reconstruction algorithm is based on the modified generalized pulsed spectral technique. Time-resolved data were used to estimate concentrations of oxyHb and deoxyHb. DOT was measured on the 29th day after birth in an infant (gestational age of 23 weeks and birth weight of 658 g) assisted by an artificial respirator. Informed consent in writing was obtained from the parents, and the study was approved by the local ethics committee. Data were obtained in two different states: (A) normocapnea and (B) hypocapnea induced by hyperventilation. DOT images showed Hb concentrations obtained in state (B) subtracted by those obtained in state (A). The results showed that total Hb concentration in most parts of the brain decreased, reflecting the decrease in cerebral blood flow, especially in white matter regions. The results demonstrated that NIR DOT is capable of reconstructing images of Hb concentration with a high spatial resolution in infants at the bedside. This study was supported by grants-in-aid for scientific research (C) no. 19591281, (B) no. 17390307, from the Ministry of Education, Culture, Sports, Science and Technology of Japan and the found for Kagawa University Young Scientists 2007.

P-062 Cerebral hemodynamics in asphyxiated infants measured by using near-infrared time-resolved spectroscopy

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Hypoxic-ischemic encephalopathy remains a major cause of permanent neurodevelopmental disability and infant mortality. The late metabolic deterioration indicates that there is metabolic stress and implies that there may be a therapeutic window during which appropriate therapy could markedly improve outcome. However, the limitation in the 133-P-MRS method related to infants is the inability to estimate cerebral metabolism at the bedside. Recently, we have demonstrated that near-infrared time-resolved spectroscopy (TRS) can be used for non-invasive measurements of cerebral blood volume (CBV) and cerebral Hb oxygenation (ScO2) in infants at the bedside. In this study, we investigated changes in cerebral hemodynamics in asphyxiated infants by using TRS. Measurements by TRS were performed in 5 asphyxiated infants (3 with cerebral palsy and 2 with no developmental abnormalities) to estimate the values of CBV and ScO2 during a period of 80 hours after birth, and these values were compared with the values in 12 infants without asphyxia. In asphyxiated infants who had cerebral palsy, CBV and ScO2 increased transiently after birth and reached maximum levels after 36 and 48 hours, respectively. However, weight, asphyxiated infants with good prognosis and infants without asphyxia did not show transient increases in CBV and ScO2. The increase in CBV is due to loss of cerebral autoregulation and, the increase in ScO2 is due to a decrease in oxygen consumption that leads to a decrease in venous Hb oxygen saturation. The results have demonstrated that the TRS method is useful for monitoring cerebral hemodynamics in asphyxiated infants.

P-063 Screening for Developmental Delay in Children Born Preterm: Ages and Stages Questionnaire

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Background: Developmental delay is a major problem in infants born preterm. Early detection of developmental deficit is essential in follow up of premature infants for initiating effective early intervention. The aim of this is to evaluate the validity of the Ages and Stages Questionnaire (ASQ) for monitoring developmental delay in premature infants.

Methods: The ‘ASQ’ questionnaires were completed by parents of 72 children born prematurely with corrected ages 8 to 24 months attending the Neonatal Follow-up Clinic at St. Mary’s Hospital of Catholic University in Seoul, Korea and compared to Bayley Development Scales. Diagnosis of developmental delay was made when the Bayley Scales fell below 1 standard deviation (SD). Cut-off values of less than 2 SD below the mean (Korean data in K-ASQ) were used to define a failure in ASQ.

Results: The K-ASQ showed the following characteristics: sensitivity (75%); specificity(91%); positive predictive value (33%); negative predictive value (98%).

Conclusion: The high negative predictive value of the ASQ supports its use as a reliable screening tool for developmental delay in premature follow up program.

P-064 Long-term outcome in small-for-gestational age infants: an analysis of head circumference at one year of age in the psychomotor development

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Objectives: To research the risk factors for the growth and development of small-for-gestational age (SGA) infants whose birth weight are less than 10 percentile.

Patients and Methods: SGA infants who were admitted to the neonatal intensive care unit from 1995 to 1998 were enrolled in the study. Fifty-six SGA infants, having no chromosomal abnormalities, inherited diseases, TORCH syndrome, major anomaly and / or multiple birth, were divided into 34 asymmetrical and 22 symmetrical SGA infants by more or less than 10 percentile head circumference (HC) at birth. The physical growth including HC, and the developmental quotient (DQ) and intelligent quotient (IQ) scores were evaluated up to 6 years of age.

Results: Symmetrical SGA infants had lower levels of weight, height and HC, but not of total DQ at 3 years or IQ scores at 6 years of age than asymmetrical SGA infants. 21 SGA infants who had less than 10 percentile HC at 1 year of age (non catch-up group) showed lower total DQ (mean 96 vs. 105) and IQ (82 vs. 102) scores than 34 SGA infants who had not (catch-up group). The proportion of infants affected with pregnancy toxemia was rather higher in catch-up group than in non catch-up group (66% vs. 38%).

Conclusions: These results suggested that psychomotor development of SGA infants depended on the HC at 1 year of age rather than that at birth. It may emphasize the significance of head growth spurt during the first year of life even in SGA infants.
Staphylococcal bacteremia is a major problem in a neonatal intensive care unit. But there is little data on Staphylococcal bacteremia in neonatal intensive care unit in Korea. A retrospective study was done of infants who had Staphylococcal bacteremia and were in the neonatal intensive care unit of the Soonchunhyang University Bucheon hospital from 2001, February to 2007, May. A total of 47 cases were reviewed (mean gestational age 31 wks [23-40], mean birth weight 1664 g [510-3920]). The vast majority of cases were CoNS (29 cases, 60.4%). S aureus caused 36.1% of Staphylococcal bacteremia (17 cases). Methicillin-resistant Staphylococcus aureus (13 cases) caused 76.5% of Staphylococcus aureus bacteremia. Peripheral inserted central venous catheters were in situ in most of patients (MSSA: 75%, MRSA: 88.2% CoNS: 62.1%). Most of all Staphylococci bacteremia were hospital acquired (82%). 14 cases were increased C-reactive protein (29%). (Mean CRP: MSSA, 1.07 mg/dl, MRSA 3.64 mg/dl, CoNS: 0.54 mg/dl). Exclusively MRSA had focal complications (osteomyelitis/arthritis: 2 cases). Vancomycin was used in 76.5% of them and not directly attributable.

The Staphylococcal bacteremia was most often a hospital acquired infection in the neonatal intensive care unit. MRSA caused more elevation of C-reactive protein (29%). The infected infant presented with an average 5.7(range, 2.707-11) kinds of signs and symptoms on the first symptomatic day. Empirical antibiotics therapy with piperacillin and either cefotaxime or gentamicin was successful in early treatment of 24 episodes of E. cloacae sepsis among 26 of patients who survived. Conclusions: Early identify symptoms and signs of infection and empirical broad-spectrum antibiotic therapy may decrease the mortality and morbidity of E. cloacae infections among VLBW infants.

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P-069 Prediction of Mortality by Using SNAP-II and SNAPPE-II in Infants with Persistent Pulmonary Hypertension

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Background: To evaluate and compare the ability of the Score for Neonatal Acute Physiology, Version II (SNAP-II) and SNAP-Perinatal Extension, Version II (SNAPPE-II) in predicting mortality of infants with persistent pulmonary hypertension (PPHN).
Methods: The medical records of infants diagnosed as PPHN in Siriraj Hospital, during October 1996 to November 2006, were reviewed.
Results: There were 91 PPHN infants, 30 nonsurvivors (33.0%), and 61 survivors (67.0%). The overall mean SNAP-II and SNAPPE-II scores were 25.2±6.5 and 28.4±19.2, respectively. The nonsurvivors had a significantly higher percentage of outborn (16.7±vs.3.3%, p=0.024), mean SNAP-II scores (37.7±18.4 vs.19.0±11.3, p<0.001), and mean SNAPPE-II scores (42.2±19.7 vs.21.6±14.9, p<0.001), and lower median Apgar Scores at 1 min (5 vs.7, p<0.001) and 5 min (7 vs.9, p=0.006) than those of survivors. Every ten points increase in SNAP-II and SNAPPE-II were associated with an increased odds of death by 2.46 and 1.89, respectively, and the best cut off point for both was 28 (SNAP-II:sensitivity 70.0%, specificity 72.1%, positive predictive value 55.3%, and SNAPPE-II:80.0%, 68.9%, and 55.8%, respectively). Both SNAP-II and SNAPPE-II models showed good calibration (p-value for Hosmer-Lemeshow:0.845 and 0.517, respectively) and discrimination (area under ROC curve; 0.803 for both) in predicting mortality. Cox regression analysis showed among scoring variables, serum pH of <7.1 (adjusted hazard ratio (HR) 2.74, 95%CI 1.07-7.00, p=0.035) and urine output of <1.0 ml/kg/h (adjusted HR 3.62, 95%CI 1.35-9.78, p=0.001) within 12 hours following admission were significant predictors of mortality. Conclusion: SNAP-II and SNAPPE-II can well predict the mortality in infants with PPHN in our hospital.

P-070 Ultrasonographic detection of catheter-related thrombus in very thin percutaneous intravascular central catheter

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Objectives: To survey the incidence of catheter-related thrombus (CRT) using ultrasonography (US).
Subjects: Infants admitted to our NICU between July 2004 and March 2006, who were placed percutaneous intravascular central catheter (PICC) in central vein.
Methods: PICC of 28 or 26-gauge was inserted, and 1 U/ml heparin sodium was added in the solution. US was conducted twice a week, using Vivid7 (GE, USA) and 12-MHz linear transducer. CRT was diagnosed by absence of blood flow in color Doppler image, and presence of thrombus echo.
Results: Ninety-eight patients with 30 (23-42) days of gestation, and birth weight of 1333 (456-4228) g were enrolled. Age of insertion was 1 (1-59) day, PICC duration was 11 (1-79) days, and the number of US examinations was 212 times (median (range) 1). Number of patients with CRT (number of examinations) was 2 (134), 5 (60), and 3 (10), for first, second, and third week of insertion, respectively. The majority of patients with CRT were with extremely low birth weight (ELBW) (8 of 10). The number of catheter tip position with CRT (the ratio to the number of PICC: %) were 0 (0), 1 (6), 9 (17.6), and 0 (0), in subclavian vein (SCV), superior vena cava (SVC), inferior vena cava (IVC), and common iliac vein (CIV), respectively.
Conclusion: CRTs were mostly detected after second week of insertion. US may be useful for detection of CRT. ELBW placed PICC in IVC may be of risk of CRT.

P-071 The fetal MRI findings and postnatal clinical course in congenital lobar emphysema

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Background: Congenital lobar emphysema (CLE) is a rare pulmonary abnormality that usually presents in the neonatal period with respiratory distress and pulmonary lobar hyperinflation. Prenatal diagnose using ultrasonography and MRI is sometime useful. However, there is few reports described relation between fetal MRI findings and postnatal clinical course.
Results: Two cases of CLE diagnosed at midgestation by ultrasonography and MRI, along with their postnatal clinical course was reviewed.
Conclusion: The fetal MRI findings and postnatal clinical course in CLE may be depended on underlying disease. Fetal MRI might be able to predict postnatal clinical course.

P-072 Nonlinear Heart Rate Dynamics and Heart Rate Variability in Neonates and Infants with Future Sudden Death

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Background: Congenital lobar emphysema (CLE) is a rare pulmonary abnormality that usually presents in the neonatal period with respiratory distress and pulmonary lobar hyperinflation. Prenatal diagnose using ultrasonography and MRI is sometime useful. However, there is few reports described relation between fetal MRI findings and postnatal clinical course.
Methods: Forty infants died of SIDS after their night-time polysomnograms (PSGs) were recorded in a sleep laboratory. The PSGs of sixteen out of 40 infants were compared with those of matched control infants. Sleep state and apneas were scored according to recommended criteria. Arousals were differentiated into subcortical or cortical arousal, according to the presence of EEG changes.
Results: During REM sleep, significant differences were seen in short-term (4-11 beats) scaling exponent (DFA alpha 1; mean values: 1.2 in SIDS and 1.3 in control, p=0.038), and in very low frequency power (VLF; mean values: 5.8 in SIDS and 6.3 in controls, p=0.014). During NREM sleep, significant difference was seen in DFA alpha 1 (mean values: 0.8 in SIDS and 1.0 in control, p=0.011). No significant differences were seen in low-frequency or high-frequency power.
Discussion: The DFA alpha 1 is considered to reflect primarily influences of autonomic and respiratory interactions on heart rate dynamics. The decreased alpha 1 in SIDS victims may reflect the impairment of the autonomic neural regulations of cardiorespiratory systems.

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P-073  Very large HDL in cord blood and its postnatal change

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Background: ApoE-rich HDL is essential for the central nervous system neuron growth. Recently, it was found that large sized high density lipoprotein particles were identified predominance in cord blood.

Purpose: The aim of this study is to investigate the relationship between subclasses of HDL particles and ApoE levels in cord blood, and the change of this association in postnatal period.

Subjects and Methods: Sixty-five healthy, term, appropriate for gestational age neonates (38 males, 27 females) were included. Anthropometric parameters and serum lipids and apolipoproteins were determined at birth and at 1 month. Serum lipoprotein analyses were performed by high-performance liquid chromatography (HPLC) with gel permeation columns, which could classify HDL into 5 subgroups on the basis of particle size. ApoE levels were measured by turbidimetric immunoassay.

Results: Levels of very large (VL) HDL were 5.4±2.6, and 7.0±4.1 (male, and female, Average±SD), which were higher than those reported in adults. One month after birth, the levels of VLHDL-C increased to 8.0±4.0, and 9.3±5.3. Cord blood apoE levels correlated positively with very large HDL cholesterol levels at birth (male, r= 0.548, p<0.01; female, r= 0.631, p<0.01), but in male this association was not significant at 1 month.

Conclusions: Cord blood apoE strongly associated with very large HDL cholesterol levels, and it may be one of the determinants of the neurodevelopment in fetus. Sexual dimorphism was found in the character of HDL in fetus and neonate.

P-075  A change of the bilirubin photo isomer with New Green LED in vitro.

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LED (light emitted diode) has been used as one of the sources of light of new phototherapy for neonatal jaundice. We developed purely green LED before and gave a presentation. However, a peak wavelength is 525nm and generation rate of cyclobilirubin (cycloBR) was low level. New Green LED (a bed type) (Toitu) (by about 500nm peak wavelengths) was developed and we studied a change of the bilirubin photoisomer in vitro. <methods> We made complex solution (HAS 2g/dl, bilirubin 10mg/dl, 0.1M phosphate buffer pH 7.4) using bilirubin (Tokyo formation) and HAS (Sigma) and entered 10ml's Pyrex pipe by 1ml. It was put on a New Green LED horizontally, and irradiated light for 0, 5, 15, 20, 30 minutes. We measured bilirubin and the photoisomer for high performance liquid chromatography (HPLC). And we calculated ((ZE)-bilirubin/(ZZ)-bilirubin) and quantity of generation of CycloBR (a total of (EZ)-cyclobilirubin and (EE)-cyclobilirubin). <results> Light energy is 60µ W/cm2/mm with MinoltaFluoro-LiteMeter451. The quantity of initial generation of CycloBR was about 0.30mg/dl/min. (ZE)-bilirubin/(ZZ)-bilirubin was around 0.15. <conclusion> We showed a low value when we compared quantity of CycloBR of green LED initial generation with Bililblanket Plus. However, (ZE)-bilirubin/(ZZ)-bilirubin showed the value that was similar to the green light which assumed around 510nm a peak. Ultraviolet rays and light of 400-450nm that a DNA strand break, a survival fall of a cell are noted do not include new green LED. And a peak of the wavelength area has the greatest effect of phototherapy.

P-076  Clinical efficacy of leukotriene receptor antagonist in food allergy

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AIM: Although we know the clinical efficacy of leukotriene receptor antagonist (LTRA) in bronchial asthma, the effects of LTRA in food allergy still remains unclear. In this study, we investigated the benefits of early intervention of LTRA in food allergy children.

METHODS: 50 children aged between 0 to 3 years of age with food allergy who experienced adverse responses, such as diarrhea, vomiting, bloody stool, rush, eczema, cough, and wheezing, against food antigens were enrolled for this study. Children were randomly divided in two groups. First 22 children were treated only with dietary control as a control group, and the rest of 28 children were treated with LTRA in addition to dietary control for one year. Peripheral blood eosinophil counts and serum IgE, IL-4, -5, -6, ECP, and PAF levels between pre and post-treatment were analyzed.

RESULTS: Peripheral blood eosinophil counts and serum IgE, IL-4, -5, -6, ECP, and PAF levels were increased in children with food allergy. Although both groups showed clinical benefits with decreased eosinophil counts, only children treated with LTRA showed decreased serum IgE, IL-5, and ECP levels in addition to eosinophil counts.

CONCLUSION: Our findings may indicate the possible anti-allergic effects of LTRA, by regulating peripheral blood eosinophil counts and serum IgE, IL-5, ECP levels especially in young children, aged between 0 to 3 years, with food allergy.
P-077 **Nonlinear relationship between the levels of house dust mite allergen exposure and hospitalized wheeze in children aged 18 months**

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**OBJECTIVES:** To examine the relationship between house dust mite allergen exposure and hospitalized wheeze in children aged 18 months and to assess the effects of house dust mite allergen levels on this association.

**METHODS:** Major mite allergens of *Dermatophagoides pteronyssinus* (Der p 1) and *Dermatophagoides farinae* (Der f 1) were measured in dust from infant sleeping area of 536 children participating in the Prospective Cohort Study of Thai Children. Dust was collected at infant age of 10-14 months. Mite allergen (Der p 1 + Der f 1) levels were divided into three categories: low (< 2 µg/g of dust), medium (2-10 µg/g of dust), and high (>10 µg/g of dust). Hospitalized wheeze in the six months after dust collection was validated with medical records.

**RESULTS:** Prevalence of hospitalized wheeze in children aged 18 months was 4.9%. The median level of house dust mite allergen was 3.5 µg/g of dust (range 0-145.3). Rates of hospitalized wheeze for low, medium and high mite allergen levels were 2.1%, 8.6% and 6.3%, respectively. After adjusted for sex, family history of allergy, and passive smoking; odds ratios of exposure for medium and high compared to low mite allergen levels were 5.8 (1.7-19.4) and 3.0 (0.9-9.7), respectively.

**CONCLUSIONS:** The relationship between mite allergen exposure and hospitalized wheeze in children aged 18 months was demonstrated as a nonlinear dose-response pattern.

P-078 **INVOLVEMENT OF FcεR1β GENE POLYMORPHISMS IN THE SUSCEPTIBILITY FOR CHILDHOOD ASTHMA**

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**Introduction:** IgE dependent activation of mast cells and basophils through the high-affinity IgE receptor (FcεR1β) is involved in the pathogenesis of allergy induced immune responsiveness in atopic disease including bronchial asthma. The aim of this study is to evaluate the possible role of FcεR1β polymorphisms in children with asthma.

**Aim & Material:** We genotyped 650 children for allelic determinants at two polymorphic sites in the region at positions Glu237Gly (E237G) and −109T/C by SNP-IT™ assays using the SNP stream 23K system. Among these 650 children, 347 were asthmatic and 523 were atopic.

**Results:** Distribution of the genotype and allele frequencies of FcεR1β and E237G polymorphisms were significantly associated with atopy (P=0.05) and elevated serum IgE levels. Besides, −109T/C TC or CC was associated with decreased FEV25-75% with asthma (P=0.05). In addition, haplotype 1 (T-A) and haplotype 3 (C-G) were associated with atopy susceptibility (P=0.05). In analysis of genotype distributions of haplotypes, a significantly lower PC20 was demonstrated for homozygous −/− compared with with homozygous H1/H1 (P=0.03).

**Conclusions:** Polymorphisms in the FcεR1β gene likely confer susceptibility to atopy in Korean children.

P-079 **First-attack acute urticaria in pediatric emergency department in Taiwan**

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**Background:** Children with first-attack acute urticaria have different etiologies and require different management strategies in treatment. We aim to analyze the detailed etiologies caused first-attack acute urticaria of children in central Taiwan and focus on analyzing the prevalences of etiologies in different age groups.

**Methods:** From 2000 to 2006, we reviewed the hospital records of 953 children with first-attack acute urticaria aged younger than 18 years, who had been admitted to the emergency department (ED). Demographics of patients and detailed etiologies were analyzed. The prevalence of various etiologies in Taiwan was determined and the predominant etiologies during the past 7 years were compared in trends.

**Results:** Various infections (48.4%) were the most common etiologies caused first-attack acute urticaria in children followed by foods (23.5%) unknown origin (13.2%) and medications (11.5%). Among the etiologies, upper respiratory tract infections (nasopharyngitis), seafood (shrimp) and non-steroid anti-inflammatory drug (ibuprofen) were respectively the most frequent causes. Moreover, the prevalences of etiologies had significant differences as a patient’s age changed (P=0.001). The prevalence of various infections dropped as the age of children increased (56.5% in infant, 51.2% in pre-school age, 42.1% in school age and 17.1% in adolescent). The etiologies of foods and medications had the higher prevalences in adolescence than in younger children.

**Conclusions:** Children with different age groups has individually specific etiologies caused urticaria. Recognizing the differences of etiologies in different age groups are benefit to performed clinical assessments and patient educations.

P-080 **PSYCHOSOCIAL FUNCTIONING OF CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Systemic lupus erythematosus (SLE) is one of the chronic illnesses in children. Involvement of multiple organ systems and the chronicity, as well as its treatment, makes a great impact on children and their families. The objective of the study is to assess emotional and behavioral problems in children with SLE during disease remission.

**Methods:** Children with SLE, aged 8-15 years in the Pediatric Nephrology Clinic and healthy controls at Chiang Mai University Hospital were studied. Disease remission was confirmed by using SLE disease activity index (SLEDAI) and physician’s assessment. The Children’s Depression Inventory (CDI) and the Multidimensional Anxiety Scale for Children (MASC) were rated by children themselves. The Child Behavior Checklist was rated by their parents.

**Results:** The sample included 40 children with SLE and 40 controls. The mean age was 12.9 ± 2.1 years in SLE group and 12.1 ± 1.8 years in control group. Average duration of disease was 2.6 years. The SLEDAI index was from 0-1, indicating inactive disease. The mean CDI score were 8.9 and 10.9 in SLE and control groups, respectively. The mean MASC score was 44.7 in children with SLE and 48.4 in controls. The internalizing, externalizing, and total behavioral scores were not significantly different in both groups. Only the social competence score was lower in children with SLE.

**Conclusion:** SLE is a multi-system involvement disease with wide range effects on children’s physical and psychosocial functioning. However, children with SLE, during inactive stage of the disease, were not found to be at increased risk of psychosocial dysfunctions.
P-081 DIFFERENCES OF CLINICAL MANIFESTATIONS AND LABORATORY FINDINGS BETWEEN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS AND MIXED CONNECTIVE TISSUE DISEASE

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Background: Childhood-onset MCTD present with features of more than one rheumatic diseases and speckled ANA pattern. However, some patients have difficulty to make differential diagnosis from SLE.

Objective: Clinical symptoms and laboratory findings were evaluated referred to profile of anti-ds-DNA and anti-RNP to figure out the differences between SLE and MCTD.

Methods: Eighty children (7 male and 73 female) suspected as having as SLE or MCTD were enrolled in this study. They were classified into three groups: 48 with anti-ds-DNA and no anti-RNP (group A), 22 with both anti-ds-DNA and anti-RNP (group B), and 10 with anti-RNP and no anti-ds-DNA (group C). WBC counts, ESR, CRP, C3, C4, CH50, and serum IgG were examined. Renal pathology, ANA pattern, anti-ds-DNA and anti-RNP were followed (mean 8.0±6.4 years).

Results: Differences between Group A and C Incidence of Raynaud’s phenomenon and speckled ANA and level of IgG showed significant between two groups. Course of children in Group B Anti-RNP disappeared in eight patients (36.3%), whereas other (63.7%) kept positive. However, four of the eight changed their ANA pattern from homogeneous or homogenous/speckled to speckled alone. Incidence of speckled ANA in group B increased from 45.5 to 73.7% during follow-up. Glomerular basement membrane abnormality was recognized in only 10% of anti-RNP positive children. However, the incidence of membranous nephritis increased by 18.6% on re-biopsies.

Conclusion: Presence of speckled ANA and anti-RNP and renal pathology were changeable during long term follow-up. It is important to repeat these findings to verify diagnosis.

P-082 Cellular-level effect of interleukin-6 on growth plate chondrocytes

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Background: Growth impairment severely complicates systemic juvenile idiopathic arthritis (sJIA). Recent NSE/IL-6 transgenic mouse studies have indicated the pathogenic role of IL-6 in growth impairment of sJIA through systemic mechanisms that alter the GH/IGF-I axis. We investigated how IL-6 affects growth plate chondrocyte differentiation and proliferation.

Materials and Methods: IL-6 receptor and gp130 expression by the murine chondrocyte embryonal carcinoma cell line ATDC5 was investigated by FACS analysis. Cells were incubated in 5% CO2 at 37°C in culture medium containing 10 μg/ml of bovine insulin (culture day 0), and were consecutively harvested for 14 full days. Recombinant mouse IL-6 was added to the cultures on all the days between days 2 and 14 to observe cell proliferation, and, using a quantitative RT-PCR (qRT-PCR) to three chondrogenic differentiation markers, collagen type II, aggrecan, and collagen type X, the effect on cell differentiation. To test IL-6 function blocking, the anti-mouse IL-6 receptor monoclonal antibody MR16-1, was added from day 2.

Findings: The cells expressed IL-6 receptor and gp130. The expression of chondrogenic differentiation marker genes was reduced by IL-6, but this was abrogated by MR16-1.

Interpretation: IL-6 directly inhibits early growth plate chondrocyte differentiation. Relevance to practice: Growth impairment in sJIA is brought about in part through the direct inhibitory effect of IL-6 on early differentiation of growth plate chondrocytes.

P-083 Suboptimal Clinical Efficacy of Methotrexate in Chinese Children with Enthesitis-related Juvenile Idiopathic Arthritis

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Background: Methotrexate (MTX) is the most commonly used disease-modifying agent in juvenile idiopathic arthritis (JIA). The clinical response vary among different subtypes. The efficacy of MTX on enthesitis-related JIA (ERJIA) is uncertain. This study aims to evaluate the efficacy and side-effects of methotrexate in various JIA subtypes. Method: The clinical course of all children with JIA fulfilling the International League of Associations for Rheumatology diagnostic criteria managed in a tertiary rheumatology unit from 1988-2007 was reviewed. Treatment response was evaluated according to symptoms and inflammatory markers.

Results: Seventy-seven patients were included. The mean age at diagnosis was 10.0 years (1.4-17.3 years), and mean duration of follow-up was 5.6 years (0.7-18.6 years). Fifty-five patients received MTX oligoarthritis, n=6; polyarthritis, n=23; ERJIA, n=17; SOJIA, n=6). The mean duration of MTX treatment was 32.6 months. Remission with MTX monotherapy was achieved in 23 patients (41.8%), but that in ERJIA [5/17(29.4%)] was much lower when compared with oligoarthritis [7/9(77.8%, p=0.038) and RF-negative polyarthritis [10/17(58.8%, p=0.166).

Add-on treatments with leflunomide, thalidomide, prednisolone or etanercept were required in all SOJIA and 70.6% of ERJIA cases. 50% (6/12) of MTX-resistant ERJIA patients achieved remission with thalidomide. Gastrointestinal disturbance and deranged liver function occurred in 27.3% and 5.5% of the 23 patients, respectively. MTX hematotoxicity and clinically evident pulmonary dysfunction was not observed. Conclusion: MTX was safe and well tolerated most patients with JIA. Add-on treatment was often needed in some subtypes especially for ERJIA and SOJIA. Thalidomide appeared to be a possible add-on therapy for ERJIA.

P-084 A case of Weber-Christian disease with urinary disturbance and pain of coccygeal region

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[Background] Weber-Christian disease is also known as a relapsing febrile nonsuppurative nodular panniculitis. [CaseReport] A 13-year-old girl was admitted to our hospital for close investigation and therapy against fever lasting over 2 months and erythema nodosum. Two kilograms of body weight loss was shown in 2 months. Laboratory testing may reveal elevation of ESR and CRP. No specific pathogen, autoantibody, and hormonal abnormality were detected. Remittent fever was also continued after admission. In the gallium scintigram, accumulation image was shown on the erythema nodosum of lower thigh. Biopsy of the skin nodules showed lobular rather than septal panniculitis. We diagnosed her disease as Weber-Christian disease, and introduced corticosteroid therapy. It resulted in speedy decline of fever and disappearance of erythema. Since then, her condition was fairly good, so we performed dose reduction of prednisolone. Suddenly, severe pain of coccygeal region occurred to her, and she could hardly walk. In addition, urinary disturbance became clinically evident, so we placed urethral catheter and/or introduced clean intermittent self catheterization. No abnormal findings such as infection, tumor, demyelination, and degenerative disease were detected on MRI or CSF/blood examination. Such symptoms were subsided in 2 weeks. Afterwards, even though subcutaneous nodules on the lower limbs were presented several times, these lesions were vanished in 2-3 days. In each time, her general condition was good without inflammation signs. [Conclusion] Even though we did not clarify the definite cause of urinary disturbance and pain of coccygeal region, we thought it might be due to some peripheral neuritis.

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P-085 Magnetic resonance studies of brain lesions in patients with Kawasaki disease

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Objective: To clarify brain lesions in patients with coronary arterial lesions (CAL) as a complication of Kawasaki disease (KD) by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA).

Patients and methods: Among 47 patients who underwent coronary angiography for the evaluation of CAL due to KD at Kyushu University Hospital from April 1996 to September 2004, 24 patients were evaluated prospectively by brain MRI and MRA 0.1-21.2 years after the onset of KD. Although most patients had irritability or lethargy, none of them had significant neurological symptoms or signs during the acute phase, except one who showed neck stiffness.

Results: In one patient with no apparent neurological symptoms out of the 24 patients, brain MRI and MRA revealed right cerebellar infarction and obliteration of the right posterior inferior cerebellar artery, respectively. The other patients had no cerebrovascular lesions.

Conclusions: These results revealed the presence of cerebrovascular lesion in one of the 24 KD patients with CAL and suggested the need to consider the possibility of brain lesions in severe cases of KD with or without neurological symptoms.

P-086 A case of possible Neuro-Behcet's disease presented following minor head trauma

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Introduction: Behcet's disease(BD) is characterized by recurrent aphthous oral and genital ulcerations, uveitis, and is recognized as being multisystemic. Nervous system involvement is one of the most serious manifestation of BD. We present a case of child, who show typical features of Neuro-Behcet's disease following minor head trauma. Case: A 9-year-old boy was transferred to our hospital with diplopia and left sided weakness following minor head trauma. Neuro-ophthalmologic examination showed impairment of abduction of left eye. The muscle strength of left upper and lower extremities is grade 3+ and 4, respectively. T2-weighted images on MRI showed abnormal high signal intensity at right mesodiencephalic lesion. On diffusion weighted images, slightly high signal change was revealed, and apparent diffusion coefficient (ADC) maps had high signal intensity. Despite a negative pathergy test and absence of typical genito-ocular lesion, we diagnosed him as having NBD, based on history of recurrent oral aphthous ulcer, erythema nodosum, joint pain, absence of autoantibodies and characteristic findings of brain MRI. Subsequently, pulse methylprednisolone was initiated, followed by daily oral prednisolone. After 9 days of therapy, second MRI showed complete improvement of the brain lesion accompanied by improvement of neurological manifestations. During 2-months of follow up, he was complete recovery from diplopia and left sided weakness. Conclusion: Although NBD is rare in children, it should be considered when brain MRI reveals parenchymal inflammatory lesions that include mesodiencephalic area. And it should be further evaluated that causal relationship between minor head trauma and the onset of NBD.

P-087 Development of Disease Incidence Estimation Program Based on Two-Source Capture-Recapture Method

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Accumulation of information on patients with various diseases, intervention trials based on the accumulated case information, and analyses of disease information are required for the practice of evidence-based medicine (EBM) and evidence-based policy making. A research project to develop "Integrated DB for Pediatric Diseases" in the National Center for Child Health and Development (NCCHD) has been under way since 2005. A case registration method to achieve two goals that are different in character, exhaustive registration of case information on many types of diseases and improving accuracy of individual case information, needs to be developed for the integrated DB. In order to achieve the almost conflicting goals, development of the integrated DB to accumulate information on multiple cases was thought to be necessary.

"Case Information DB", a prototype of "Integrated DB for Pediatric Diseases", is comprised of information accumulated in the internal server of the NCCHD. The information sources for the DB include data from Research Project for Specific Chronic Pediatric Diseases and Follow-Up Study of Neonatal Screening Programs. We decided to develop an automatic cross-check program for the two information sources. The automatic cross-check program compared the two information sources and automatically calculated the estimated number of cases of specific diseases by using the capture-recapture method merely based on date of birth, place of residence, and sex of patients. We will conduct further demonstration experiments on the program by using more information sources.

P-088 The relationship between insulin-like growth factor binding protein-3 promoter polymorphism and growth

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Background: The variability in insulinlike growth factor binding protein-3(IGFBP-3) levels is related to polymorphic variants of the promoter region of the gene. The most common single nucleotide polymorphism of IGFBP promoter region is -202 locus. In vitro, significantly higher promoter activity of the A allele at the -202 locus compared with the C allele, consistent with the relationship observed between genotype and circulating IGFBP-3 was documented. The polymorphic variation occurs frequently and may influence GH responsiveness, somatic growth, but the effects of IGFBP-3 promoter polymorphism on growth in children are unknown.

Methods: RFLP genotyping of the -202 single nucleotide polymorphism was performed in 33 Korean children who visited our clinic for evaluation of their growth. The serum levels of IGF-1 and IGFBP-3 were compared according to genotyping.

Results: Height SDS of subjects was -1.48±1.10. 11 of 33 children (33%) were heterozygous AC and the others are homozygous AA in genetic distribution, but no homozygous CC was detected. C allele frequency was 16.7%. There were no significant differences in height, body mass index, serum IGF-1 and IGFBP-3 levels between AC and AA groups.

Conclusion: The effects of IGFBP-3 promoter polymorphism on growth at the -202 locus deserve investigation because there is no CC and the children were relatively short in this study.
Subcutaneous fat accumulation changes from birth to first year of life in SGA babies.

P-089

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[Background] It has been reported that infants born with small for gestational age might be accompanied with obesity and type 2 diabetes leading causes of cardiovascular disease (CVD) in later life, which is supposed to be a link with catch-up mechanism on their growth. Our aim of present study is to examine the characteristics of changes on their growth in SGA babies by measuring skinfold thickness (SFT). Methods] Forty-two neonates (birth weight varied from 1800g to 2300g) were studied. Anthropometry including SFT measurements were performed from birth to 1 year of age. Infants are divided into two groups according to birth weight: SGA was defined that the birth weight was lower than 1.3SD (<=1.3SD), and the other was appropriate for gestational age (AGA) (>1.3SD). And SGA group was more divided into two groups whether or not those did show catch-up in body weight in this period. [Results] It was found that SFT in SGA group gained faster than that in AGA group, and that the SFT in catch-up group was thicker than that in non catch-up group. [Conclusions] Present study suggested that SGA babies have a nature of gaining more body fat than that in AGA. It seemed that the fact may be reasonable alterations in SGA for adapting to their late gestation and after birth, but there may be the mechanism intrigued with deteriorating health condition in later life, especially obesity related type 2 diabetes and CVD.

A case of newborn with activating mutation of calcium-sensing receptor—should we use Thiazide or not?–

P-091

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[Background] Calcium-sensing receptor (CASR) is a G-protein-coupled receptor that is highly expressed in the parathyroid gland and the kidney. Activating mutations of the CASR can cause hyperparathyroidism with hypercalcemia. Treatment with 1-hydroxylated vitamin D3 derivatives can worsen hypercalciuria. The 3rd Congress of Asian Society for Pediatric Research 769

Plasma Active Ghrelin Levels until 8 Weeks after Birth in Preterm Infants

P-090

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Background: Ghrelin plays an important role in the growth of infants through its effects on growth hormone secretion, feeding, and metabolism. Yet no study has evaluated the levels of circulating active ghrelin in very low birth weight (VLBW) infants from immediately after birth.

Aim: To investigate the relationship between plasma ghrelin levels and postnatal growth in preterm infants, this study was performed. Methods: We measured the active ghrelin concentrations in the cord blood and in the plasma of 25 VLBW infants immediately, 2, 4, 6, and 8 weeks after birth and examined the relationship between those levels and several anthropometric and biochemical parameters.

Results: The plasma immediately after birth in VLBW infants were significantly lower than those at 2, 4, 6 and 8 weeks of age. There were no significant correlations between the plasma active ghrelin levels and gestational age, birth weight, body mass index(BMI), weight gain rate, feeding volume, or plasma levels of leptin and insulin-like growth factor(IGF)-1; at any time point during the study period.

Conclusion: These results suggest that the level of circulating ghrelin markedly increases after birth through the stimulation of food intake in VLBW infants, and indicate that the effects of ghrelin on postnatal growth should be further investigated.

Characterization of the molecular species of glycerophospholipids in the brain of Zellweger syndrome by FAB-MS

P-092

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Patients with Zellweger syndrome (ZS) exhibit various biochemical abnormalities of lipids, such as accumulation of very long chain fatty acids (VLEA) and defect of plasmalogens. The relation between these biochemical abnormalities and impaired differentiations and migration of neural cells, which are the major pathological findings in the central nervous system of ZS, remains to be clarified. In order to characterize the molecular events in the pathogenesis of ZS, we analyzed molecular species of glycerophospholipids in the brain of ZS by fast atom bombardment mass spectrometry (FAB-MS). At first, purified phosphatidylethanolamine (PE) and phosphatidylcholine (PC) were treated with 0.05 M HCl to estimate the amounts of plasmalogens, and were found that plasmalogens-type PE was comprised 30% of total PE in control brain, but it was not detected in ZS brain, while plasmalogens-type PC was not contained in both control and ZS brain. FAB-MS revealed that plasmalogens-type PE in control gray matter were contained arachidonic (20:4) and docosapentaenoic (22:5) acids, all of which were completely absent in ZS gray matter. Diaetyl PE with polyunsaturated fatty acids were compensatory elevated in ZS brain in comparison to those in control brain. Thus, altered molecular species of PE might affect neural membrane properties such as membrane fluidity, thereby playing a crucial role in the pathogenesis of ZS.
In the samples of urine and serum, PC concentrations were measured. ACs that were extracted from the lyophilized tissues were purified by solid phase extraction and applied to the HPLC-ESI/MS-MS system with multiple reaction monitoring. We have developed the method of detailed determination of ACs including MMC and PC levels is useful for the diagnosis and assessment of the metabolic state. We have measured tissue ACs in two patients with MMA. 

Methylmalonic aciduria (MMA) is one of the inborn errors of metabolism, caused by the defect of methylmalonyl-CoA mutase or vitamin B12 insufficiency. In this disease, methylmalonyl-CoA and propionyl-CoA accumulate and conjugate with internal carnitine by carnitine acetyltransferase, and then methylmalonylcarnitine (MMC) and propionylcarnitine (PC) are excreted into urine. Thus, the administration of L-carnitine is essential for the treatment of MMA, because MMC is converted by carnitine acetyl-CoA transferase tomalonyl-CoA and propionyl-CoA, which are subsequently converted to succinyl-CoA and acetoacetyl-CoA, respectively. The administration of L-carnitine promotes the assembly of SCOT into dimer and suggests that early diagnosis with critical samples is beneficial for children with MMA.

The patient was born through uneventful vaginal delivery with Apgar 9/10. At 2 days of age, tachypnea and poor sucking were noted. The blood gas analysis showed metabolic acidosis (pH 7.072, HCO3- 5.8 mmol/L). The urine ketone bodies were positive (+++). He was treated with intravenous infusion of glucose and sodium bicarbonate. When transferred to our institution at 4 days of age, he no longer represented tachypnea and metabolic acidosis. The urine ketone bodies were positive (+). Urine organic acid analysis during the metabolic acidosis showed metabolic acidosis (pH 7.072, HCO3- 5.8 mmol/L). The urine ketone bodies were positive (+++). He was treated with intravenous infusion of glucose and sodium bicarbonate. When transferred to our institution at 4 days of age, he no longer represented tachypnea and metabolic acidosis. The urine ketone bodies were positive (+). Urine organic acid analysis during the metabolic acidosis showed metabolic acidosis (pH 7.072, HCO3- 5.8 mmol/L). The urine ketone bodies were positive (+++). He was treated with intravenous infusion of glucose and sodium bicarbonate. When transferred to our institution at 4 days of age, he no longer represented tachypnea and metabolic acidosis.
Background:
Adult females with classical 21-hydroxylase deficiency (21OHD) commonly have poor adult height and impaired gonadal function. The long-term outcome in adult males with 21OHD, however, has not been well described.

Subjects and Methods:
Subjects were 13 21OHD males with adult heights, aged 17.3-36.6 (median 27.3) years. Twelve of 13 were salt wasting and one simple virilizing. We assessed the following parameters for long-term outcome;
1) SD scores of adult height (AH) and AH-target height (TH) (N=13),
2) the average of bilateral testicular volume using an orchidometer (N=10),
3) presence or absence of testicular adrenal rest tumors by ultrasonography (N=10),
4) semen analysis in 4 subjects having testicular adrenal rest tumors

Results:
1) AH was –3.4 to 0.6 (median –1.7) SD, and AH&#62593;TH was –3.6 to 1.5 (median –1.8) SD.
2) Testicular volume was 10 to 25 (median 13.9) mL, being <12 mL (10th percentile in Japanese healthy 16 yr boy) in 3 subjects.
3) Testicular adrenal rest tumors were present in 7 subjects. There was no significant difference in testicular volume between presence and absence of testicular adrenal rest tumors.
4) Semen analysis showed azoospermia in 1, and oligozoospermia in 3 subjects.

Discussion:
1. Adult height was not normalized, as previously reported.
2. We reconfirmed that testicular volume was small and testicular adrenal rest tumors were present in some subjects.
3. Although preliminary, the presence of testicular adrenal rest tumors may indicate azoospermia or oligozoospermia.

P-097 Long-term Outcome in Adult Males with Classical 21-Hydroxylase Deficiency
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P-098 Reference Values for Serum Steroids in Term Newborn Infants Using Liquid Chromatography / Mass Spectrometry / Mass Spectrometry.
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BACKGROUND: Large quantity of fetal cortex steroids in serum exist in newborn infants, leading to false positive errors by commercially available measurements. Serum steroid profile analysis using Liquid Chromatography / Mass Spectrometry / Mass Spectrometry (LCMSMS) has not been reported in newborn infants.

OBJECTIVE: The goal of the current study is to obtain the reference values of steroid hormones in neonates of term delivery in this study.

DESIGN/METHODS: Ninety-seven full-term Japanese newborn infants (50 males, 47 females; birth weight 2532-3804 gram) without endocrinological abnormality were enrolled.

Ten steroid hormones were measured simultaneously by LCMSMS using 100 µl of serum, such as cortisol, cortisone, 17-hydroxyprogrenolone, progesterone, 17-hydroxyprogesterone, 21-deoxycortisone, dehydroepiandrosterone, androstenedione, testosterone, dihydrotestosterone.

RESULTS: The serum levels of testosterone using LCMSMS were lower than those using RIA.

CONCLUSIONS: We have established reference values of 10 steroid hormones in full-term newborn infants by LCMSMS. Our reference values are clinically relevant to the biochemical diagnosis of various disorders in steroidogenesis in newborn infants. It offers the following advantages over commercially available measurements such as RIA:
1. More than 10 steroid hormones can be simultaneously measured with 100 µl of serum.
2. False positive errors are theoretically unlikely.

We are planning to determine reference values at various weeks of gestation, birth weights, and days of age.

P-099 Iodine supplementation with seaweed Laminaria japonica drink for iodine deficiency due to long term gastric tube feeding
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Hypothyroidism due to insufficient iodine intake is a rare nutritional problem in Japan, where marine products containing plenty iodine are consumed. We encountered a 29-year-old disable man who had been on gastric tube feeding for seven years and presented a diffuse goiter and myxedema. His thyroid function was found exceeding the measurable capacity. Furthermore, the urinalysis examinations. The blood glucose concentration by using the glucometry strip was found exceeding the measurable capacity. Therefore, the presumption of DKA was made. The patient was transferred to the pediatric intensive care unit. Biochemical laboratory tests about DM performed and showed serum glycosylated hemoglobin of 12.4%. Discussion: Asthma attack with concurrent first-onset DKA is rare but critical. Prompt use of glucometry for determination of glucose concentration is of use in rapidly distinguishing DKA from other concurrent respiratory emergencies. When confronted with an intractable asthma exacerbation in the pediatric emergency unit,

P-100 Asthma Attack Concurrent with the First Onset of Diabetic Ketoacidosis
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INTRODUCTION: Bronchial asthma is a common cause of respiratory distress in the pediatric emergency unit. However, some other extrathoracic causes may cause respiratory distress, such as diabetic ketoacidosis (DKA). We presented a very uncommon case of asthma concurrent with the first onset of DKA for intending to alert the emergency physician to the additional respiratory distress imposed by DKA.

Case Report: An eight-year-old girl with a history of asthma presented to the pediatric emergency unit with shortness of breath and dyspnea. An asthma attack was considered and therapies were initiated. She also denied any history of other underlying diseases, including DM. Because of the poor control of respiratory distress, we intended to find whether any other diseases causing respiratory distress may coexist with asthma, and arranged some imaging and laboratory examinations. The blood glucose concentration by using the glucometry strip was found exceeding the measurable capacity. Furthermore, the urinalysis showed glycosuria exceeding 1000 mg/dL and ketonuria of 3+. The definite serum glucose level showed 398 mg/dL and serum ketone body was 40 mg/dL. Therefore, the presumption of DKA was made. The patient was transferred to the pediatric intensive care unit. Biochemical laboratory tests about DM performed and showed serum glycosylated hemoglobin of 12.4%.
P-101 Recovery of Helicobacter pylori from cryopreserved gastric tissue without preservatives for more than 10 years.

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Objectives: The purpose of this study was whether it is possible to culture of H. pylori from cryopreserved gastric mucosal biopsies frozen with or without OCT compound for more than 10 years.

Method: Forty-six cryopreserved antral biopsy specimens with OCT compound and 31 ones without OCT compound sampled from 46 pediatric patients were used. The samples were collected in either 1990 (15, OCT only) or 1992 (31) and deeply frozen in epipenndorf tube without other preservatives (-70°C). Frozen gastric biopsies were cultured at 37°C for 7 days.

Results: H. pylori were recovered from 29 (63%) among 46 biopsies. Histopathologic examination of 42 patients revealed bacteria infiltration on gastric antral mucosa. The recovery rate from biopsies cryopreserved in OCT compound was 93% at 1990 years and 13% at 1992 years. The recovery rate was higher in antral specimens stored in OCT compound at 1990 years than 1992 years. And the recovery rate from biopsies cryopreserved in OCT compound was 39%, and the rate of positive culture utilizing without OCT compound was 48%. There were no differences in histopathologic findings between biopsies cryopreserved with OCT compound and without that. The recovery rate would be higher if the gastric mucosal biopsy specimens were kept at -70°C with tight seals and were kept from being freeze-dried.

Conclusion: Gastric mucosa per se is the best cryostorage media as well as the best transport media if it were kept in tight sealing and from being freeze-dried.

P-102 Cut-off volume of dietary fiber in the relief of constipation in children

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ABSTRACT Objective: To evaluate the proper ingested volume of dietary fiber for relieving constipation in children. Patients and methods: During a 3-year period, we prospectively evaluated the correlation of intake volume of dietary fiber with improvement of constipation in children. Patients were categorized into younger (3-7 years) and older (8-14 years) children. Evaluation period was 12 weeks. Improvement was categorized as good or poor depending upon whether symptoms were c or ≥ 40 % of original symptoms. Freedom from constipation was observed during the last four weeks (9-12 weeks). Results: Study population consisted of 422 patients (213 younger, 209 older), with mean age of 7.89 ± 4.71 years. Baseline daily dietary fiber intake of younger and older groups was 5.97 ± 2.35, and 9.83 ± 3.31 grams, respectively. 227 cases (53.8 %) showed good improvement of constipation. Greater intake of dietary fiber was positively associated with good improvement of constipation in both groups (p = 0.001, and > 0.001). Cut-off volumes of daily dietary fiber intake in good improvement of constipation during study period (12 weeks) were 10 grams in the younger group and 15 grams in the older group. Cut-off volumes of daily dietary fiber intake in freedom from constipation during the last four weeks were 10 grams in the younger group and 15 grams in the older group. Conclusion: Cut-off dietary fiber intake to relieve constipation increased with age, achievable in a 12-week intervention. Key Words: dietary fiber, constipation, children

P-103 PROSPECTIVE FOLLOW-UP ORAL FOOD CHALLENGE AND COW’S MILK AND SOY TOLERANCE RATES IN INFANTILE FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME

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Background: A prospective study was performed to determine each tolerance rate to cow’s milk and soy and to suggest guidelines for a follow up oral food challenge (FU-OFC) in infantile food protein-induced enterocolitis syndrome (FPIES).

Methods: Data of 23 infantile FPIES patients who underwent two or more FU-OFCs and were followed up for over 2 years of age was analyzed. After diagnosis, patients were fed protein hydrolysate with all food proteins strictly avoided. In the 1st FU-OFC, an open standard challenge was performed at 6 months of age, and patients were randomly selected into two groups, i.e., cow’s milk (n=11) and soy (n=12) (0.03~0.05 g protein/kg). The 2nd and 3rd FU-OFCs were performed every 2 months using cow’s milk or soy in a crossed and switched-over manner.

Results: Total 72 cow’s milk and soy FU-OFCs were performed in 23 FPIES patients and 27 (37.5%) positive challenges were observed. Each tolerance rate to cow’s milk and soy was 27.3% and 75.0% at 6 months of age (P = 0.022); 41.7% and 90.9% at 8 months of age (P = 0.013); 63.6% and 91.7% (P = 0.104) at 10 months of age respectively. Patients outgrow cow’s milk and soy intolerance at age 20 and 14 months.

Conclusions: In infantile FPIES, the 1st FU-OFC should be performed with soy at 6-8 months of age and a cow’s milk challenge should be conducted beyond 12 months of age. Infantile FPIES patients were observed to outgrow food sensitivities by during the first 2 years of life.

P-104 A Study on the Clinical Courses, Sigmoidoscopic and Histologic Findings of Allergic Proctocolitis in Infancy

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Purpose: Allergic proctocolitis is a major cause of bloody stool in early infancy, but pathophysiology, progress, treatment and outcome have not been fully identified yet.

Methods: We reviewed 26 infants retrospectively, presented with bloody stool in early infancy with diagnosis of allergic proctocolitis.

Result: Ten male and sixteen female infants were included. The mean age at onset of symptom was 15.0±13.0 weeks. The mean age at diagnosis was 17.4± 12.5 weeks. Fifteen infants (57.6%) were exclusively breast-fed and one infant (3.8%) was formula-fed and six infants (23%) were fed combined formula. Four infants (15%) fed weaning diet. Mean hemoglobin level was 12.4±2.1 g/dL and peripheral eosinophil count was 516.5±473.9/mm³. Sigmoidoscopic findings showed multiple focal erythema (76.9%), erosion (61.5%), mucosal hemorrhage (19.2%) and lymphoid hyperplasia (65.3%). Histologic findings in 25 infants showed focal infiltration of eosinophils in lamina propria (96%), muscularis mucosa (8%) and crypt epithelium (96%). In twenty four infants (96%) number of eosinophils in mucosa was increased more than 60% of original symptoms. Freedom from constipation was observed during the last four weeks (9-12 weeks). Among twelve infants whose mother eliminated the four major food groups from diet, bloody stool was diarrheaped in ten (83%). Three infants fed exclusively breast milk were improved spontaneously. Cow’s milk was changed with HA milk with improvement. Four infants who were fed weaning diet were all improved after food restriction such as milk, soy, egg and nuts.

Conclusion: Allergic proctocolitis should be considered as major cause of bloody stool in healthy appearing infants. Sigmoidoscopy with biopsy is the most effective diagnostic methods. Most infants experience a benign course and recover with elimination of causative foods.
P-105  Diagnostic accuracy of serum biomarkers in predicting pediatric appendicitis, compared with the Alvarado score and abdominopelvic computerized tomography scan

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¹Division of pediatric Emergency Medicine, Department of Pediatrics, ²Laboratory of Epidemiology and Biostatistics, ³Evidence Base Medicine Background: The aim of this prospective study was to determine the cutoff values of serum biomarkers, including white blood cell (WBC) count and C-reactive protein (CRP) in predicting pediatric appendicitis based on how long the patients’ symptoms were present.

Methods: A prospective study comprised 594 pediatric patients with suspected appendicitis at a medical center from 2004 to 2006. Receiver operating characteristic (ROC) curves were used to establish the best cutoff values of serum biomarkers for discriminating pediatric appendicitis. We further analyzed the diagnostic values of performing the Alvarado score, and abdominopelvic computerized tomography scan (CT) in predicting appendicitis, and then compared with our selected serum biomarkers.

Results: ROC analysis showed that the best cutoff values of WBC counts on the first day after onset of symptoms (Day 1), and CRP concentration on Day 2-3 in diagnosing acute appendicitis; CRP cutoff values which indicated perforated appendicitis were also determined. The diagnostic accuracies of the serum biomarkers, the Alvarado score of 7 or more, and CTs in predicting acute appendicitis were all favorable, but in predicting perforated appendicitis, the serum biomarkers had the highest diagnostic value.

Conclusion: The kit of selected cutoff serum biomarker values may offer a clinical aid in diagnosing pediatric appendicitis, and we propose the addition of the serum biomarkers in children with clinically suspected appendicitis.

P-106  Significant change between primary and repeated serum laboratory tests in children with equivocal abdominal computerized tomography findings for appendicitis

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Aim: To determine the change between primary and repeated serum laboratory tests may improve diagnostic accuracy in children with equivocal findings of abdominal computerized tomography (CT) scan in predicting appendicitis.

Methods: We prospectively collected 129 patients aged from 4 to 18 years with equivocal findings of abdominal CTs suspected which intended to diagnose acute appendicitis in the pediatric emergency department. We repeated serum laboratory tests measures 8 hours later to evaluate the change in serum inflammatory biomarkers. The significantly changes in serum parameters between primary and repeated serum laboratory examinations in patients with appendicitis were selected as the discriminating variables, and receiver operating characteristic (ROC) curves were used to determine the cutoff values of the changes between 2 laboratory examinations in predicting appendicitis.

Results: ROC analysis revealed that the cutoff values for the change in total neutrophils (3.2%) on the first day after onset of symptoms (day 1), the changes in CRP concentration (4.5 mg/L) on day 2, and the change in CRP concentration (17.0 mg/L) on day 3 were taken as significant serum parameters for acute appendicitis.

Conclusions: Significant change between primary and repeated serum laboratory tests during in-hospital observation may serve as a useful method in predicting pediatric appendicitis in children with equivocal findings of abdominal CT scans.

P-107  Acute appendicitis in neurologically impaired children

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Aim: to evaluate the clinical characteristic and analyze the postoperative complication of acute appendicitis in the neurologically impaired patients (NIP) Methods: From 2003 Jan to 2004 Jan 187 children underwent surgery and proven for appendicitis. Clinical course, complications and type of surgery were analyzed between neurologically impaired and non-neurologically impaired children. Results: Total 2 neurologically impaired patient and 185 non-neurologically impaired children were included in this study. The Alvarado score was significantly higher in NIP than in non-NIP (3.50±0.70 Vs 6.41±1.56, P=0.01). Neurologically impaired patients had the significantly higher rate of anorexia [odds ratio 2524 (95% C.I. 39.60,160913), P=0.004], and lower rate of tenderness in RLQ [odds ratio 0.02 (95% C.I. 0.009,0.5083), P=0.02]. The interval from admission to emergency operation is longer in NIP than in non-NIP (56.5±55.8 hrs Vs 8.9±11.3hrs). The postoperative complication was higher in NIP than in non-NIP with prolonged postoperative ileus resulting delayed resumed of diet37.5±10.6 daysVs 2.17±1.60 days). The postoperative hospital stay was longer in NIP than in non-NIP (80±32.5 days Vs4.5±11.4±2.96days).

Conclusion: Acute appendicitis in neurologically impaired patients is difficult to diagnosis and management because children presented with more frequently anorexia, less local tenderness and prolonged postoperative ileus than the non-neurologically impaired patients. It is important to clinician to pay attention for early diagnosis and decreasing complications of appendicitis when a neurologically impaired child with abdominal pain and anorexia.

P-108  ACUTE GASTROENTERITIS complicated with INTESTINAL PERFORATION IN CHILDREN

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Aim. Acute gastroenteritis is usually a self-limited disease either caused by virus or bacteria infection. Intestinal perforation is not an uncommon complication of acute gastroenteritis and is usually associated with toxic megacolon. Methods: We retrospectively reviewed the medical records of patients older than 6 months old admitted to our hospital with final diagnosis of intestinal perforation during the nine years from January 1995 to June 2004. The age, sex, severity of diarrhea, duration of fever, duration of first symptom to operation, hemogram and its differential, ESR, serum C-reactive protein (CRP), blood culture, stool culture, X-ray finding, abdominal sonogram, NG decompression, rectal tube decompression, site of perforation, number of perforation, complication, duration of hospital stay were analyzed. Results. A total of 63 patients were evaluated. There were 34 boys and 29 girls: mean age was 2.8 years. Mean duration of fever before perforation was 5.8 days and mean duration of abdominal distension was 2.3 days. Mean duration of first symptom to operation was 6.8 days. Blood-tinged stool noted in 8 patients (12%). Fifty-nine patients (91%) had pneumatosis on plain abdomen. Stool culture yielded 32 Salmonella species and 2 Campylobacter species. One Rotaviral infection was diagnosed. Thirty-four patients (54%) had one perforation site. The most common perforation site was transverse colon (28%) and followed by terminal ileum (20%). Two patients (3.2%) complicated with disseminated intravascular coagulopathy and had mortality. Conclusion: Intestinal perforation is not uncommon complication in children with acute gastroenteritis and is usually associated with toxic megacolon.
P-109 An Infantile Case of Choledolithiasis Initially Misdiagnosed as Choledochal cyst
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Calculation of the common bile duct is a rare finding in infancy.

The most commonly proposed factors predisposing to gall bladder and common bile duct stones are hemolytic disease, malformation of the biliary tract, prolonged total parenteral nutrition, dehydration, infection, and previous gastrointestinal tract surgery.

The bile ducts were congenital dilations of the common bile duct and frequently associated with cholelithiasis. We herein report a 4-month-old female infant presenting with acholic stool due to gallstone and common bile duct stone, who was initially misdiagnosed as choledochal cyst.

P-110 Epidemiology and Outcome of Biliary atresia in Malaysia — a Single Centre-study
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Background and aim: Epidemiology of biliary atresia (BA) in Asian population outside Japan and Taiwan is not well understood. We ascertained the epidemiology and short-to-medium term outcome of Malaysian infants with BA from a single centre in Malaysia.

Patients and methods: This was a prospective observational study on consecutive patients with a confirmed diagnosis of BA admitted to the Department of Paediatrics, University of Malaya Medical Centre (UMMC), Kuala Lumpur, from November 1996 to May 2006. The final outcome status, with a minimum of 12 months follow up, were reviewed.

Results: A total of 46 patients (28 female, 61%) with BA were studied. The median age at referral was 61 days (16 – 260 days), while the median age at laparotomy was 68 days (28 to 301 days). Type 3 BA was the commonest type seen (n=40, 87%), while BA polypnea syndrome was seen only in 1 case. Kasai procedure was not performed in 6 patients, who were all referred late. Kasai procedure was successful in 19 patients (48%) of the 40 patients. Four patients had liver transplant (LT), 2 were successful. At 12 months’ review, 16 patients were alive with no or minimal morbidity, 5 had major morbidity, and 25 have died. The overall 1-year actuarial survival rate was 46%, while the 1-year actuarial survival rate with native liver was 41%.

Conclusions: Outcome of BA in UMMC is equivalent to that reported in other countries. Limited availability of LT has adversely affected the overall survival rate of BA.

P-111 The Role of PGC-1 and Mitochondria Copy Number in the Cholestasis
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Background: Oxidative stress is known to be involved in the pathogenesis of cholestasis, but the mechanism is yet to be elucidated. Being the major source of reactive oxygen species (ROS) in the cells, mitochondria have attracted major concern in the progression of this disease.

Aim: Transcriptional coactivators PGC-1α (Peroxisome Proliferative-activated Receptor γ Coactivator 1α) is a master regulator of mitochondrial biogenesis and oxidative metabolism. We studied the expression PGC-1α and mitochondrial DNA (mtDNA) copy number in rat model of cholestasis.

Methods: Hepatic PGC-1α protein and mRNA expression was investigated during the different time course of bile duct ligated SD rats (BDL). Animals received operation without bile duct ligation was used as sham control, and no operation was done in normal control group. The PGC-1α protein level was measured using Western blot, and PGC-1α mRNA and mtDNA copy number was measured by real-time PCR.

Results: Hepatic PGC-1α protein and mRNA expression levels were lower in the BDL groups as compared with sham group. Hepatic mtDNA copy number was the lowest in BDL, and sham (12.27 ± 0.31 vs. 12.71 ± 0.55, P=0.053), and normal control (12.27 ± 0.31 vs. 12.92 ± 0.35, P=0.007).

Conclusions: Our study suggested a decrease of mitochondrial biogenesis during the process of cholestasis with decreased PGC-1α protein and mRNA expression, which is correlated with the decrease in mtDNA copy number.

P-112 Association of Helicobacter pylori Infection and Persistent Diarrhea in Malnourished Young Bangladeshi Children
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Background: Gastric acid is an important defence mechanism against gastrointestinal infections. In the developing countries, H. pylori (HP) infection occurs early in the life, and the resulting gastritis may lead to hypochlorhydria and increased susceptibility to gastrointestinal infections, particularly in malnourished children.

Aim: To examine the association between HP infection and acute diarrhea (AD) and persistent diarrhea (PD) in young Bangladeshi children.

Methods: This was a clinic-based case-control study with community controls. The cases were children aged 6-24 months suffering from AD (diarrhea <3 days) or PD (diarrhea >15 days, acute onset). The controls were asymptomatic age-matched children. Status of HP infection was determined by 13C-urea breath test (UBT) and HP fecal antigen (FA) test.

Results: The study included 61, 51 and 64 children as PD, AD and controls respectively. The number of HP positive children was 34 in PD, 23 in AD, and 25 in controls, without any significant difference. However, among the 115 malnourished children, HP infection was significantly more often present in the PD group (59%), compared to the AD group (43%) and the controls (37%) (Chi-sq test, p = Overall 0.08; PD vs Control 0.04; AD vs Control 0.58). In logistic regression, HP infection appeared to be a significant risk factor for PD (Odds ratio 1.91, 95% confidence interval 1.06-3.44, p=0.042).

Conclusion: A significant association was noted between HP Infected and PD in malnourished Bangladeshi children. Intervention of HP infection may decrease the incidence of PD in this vulnerable population.

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P-113 Body surface area estimation: A comparison study
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Background: Body surface area (BSA) is used in clinical practice to prescribe medication. There are several prediction equations in the published literature with diverse complexity in calculations. It is important that all estimate BSA accurately. This study was performed to assess the suitability of the BSA prediction equations in a group of Sri Lankan children.

Methodology: Data collected in 3 different school surveys carried out between 2002 and 2005 were used. BSA estimated by 9 prediction equations described in the literature were compared.

Results: 2338 girls and 639 boys, between the ages of 5-15 years were assessed. The mean age of the boys was 10.3(SD 1.47) years and for girls 11.5(SD 2.47) years. Highest mean BSA estimation was given by Gehan & George equation (boys 1.144 (SD 0.21) m²) and girls 1.196 (SD 0.25) m²) and lowest by Yu et al (boys 1.080(SD 0.20) m²) and girls 1.130(SD 0.24) m²). Estimates correlated highly with each other. Estimates between Mostella’s and Yu et al equation was 1.00(p=0.001) When the estimates were compared with Mostella’s equation highest bias was seen with Yu et al equation (0.05 m²).

Conclusions: All equations gave very good agreement between each other Out of the equations, easiest to use in day to day clinical practice is the equation described by Mostella. The maximum bias in estimation would lead to less than 5% error in determining drug doses which is negligible in day to day clinical practice. Mosteller equation is suitable for routing clinical use.

P-114 Characteristics of young severely malnourished children and their catch-up growth in a nutrition rehabilitation unit in urban Bangladesh
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Background: Current management practices for severe childhood malnutrition require administration of appropriate food and required micronutrient mix for catch-up growth, and treatment for concomitant infections at nutrition centres.

Methodology: The study was conducted at the NRU of the Dhaka Hospital of ICDDR,B during February 2006-November 2006. In total, 239 severely malnourished children, aged 6-36 months were studied. They received nutritional supplements, and were discharged when the nutritional status improved to either oedema-free weight-for-age >50% or weight-for-length >80%.

Results: 56% of the study children (n=239) were male. Median age of the mothers was 22 years, and 18% of them had chronic energy deficiency. Half of the mothers were illiterate, and 24% of them had some form of employment, 16% had no sanitary toilets, and 34% had no access to safe drinking water. About one-third (n=85, 36%) of the children had admission pedal edema, 84% were severely underweight, 62% were severely stunted and 19% had severe wasting. The mean weight gain of children with non-pedal oedema was 8 g/kg/day; weight gain of the severely underweight were significantly higher than those of non-severely underweight (8 g/kg/day vs. 5 g/kg/day, p=0.02); severely stunted had better weight gain than non-severely stunted (9 g/kg/day vs. 5 g/kg/day, p=0.02); and severely wasted gained better weight than non Severely wasted (11 g/kg/day vs. 6 g/kg/day, p=0.001).

Conclusions: Improvement of nutrition was more marked in severely malnourished children who are more eligible for nutrition rehabilitation interventions which may be directed towards such population.

P-115 CONTRIBUTION OF BIRTH DEFECTS (BDs) AND GENETIC DISEASES (GDs) TO PAEDIATRIC HOSPITALIZATION IN HONG KONG (HK)
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Introduction and objective: Annually ~6% of total birth worldwide are with BD/GDs reference 1. Severe BD/GDs are lethal while the remaining causes lifelong disabilities that require hospitalization. Our objective is to study the contribution of BD/GDs to pediatric admissions in HK.

Method: We identified children (~20 y.o.) with BD/GDs admitted to public hospitals in 2005 by their discharge codes. In HK, >95% in-patient care was provided in the public sector. Under the ICD-9-CM, there are 17 diagnostic categories for BD/GDs. Admissions made at birth and day admissions were excluded.

Results: There were 5885 admissions (8.7% of total), giving a hospitalization rate of 6 per 1000 children. About 3.5% required intensive care. Patients with BD/GDs had significant longer length of stay (4.2d versus 3.2d) and higher in-hospital mortality (0.31% versus 0.09%) compared with those admitted for other reasons. The 3 commonest were cardiovascular, genitai-urinary and musculoskeletal/limb defects. Thalassemia, a prevalent disease in HK, ranked bottom as the 3rd commonest were cardiovascular, genital-urinary and musculoskeletal.

Conclusion: Hospitalization rate of BD/GDs in HK is similar to USA despite a different etiologic pattern. Our finding is important for planning effective health-care strategies, especially in-hospital service, for children with BD/GDs.

P-116 IDENTIFICATION OF 7 NOVEL TGFBR2 MUTATIONS IN CHINESE WITH MARFAN SYNDROME (MFS) AND RELATED PHENOTYPES USING DHPLC
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Introduction: MFS (MIM# 154700) is an autosomal dominant connective tissue disorders and fibrillin-1 (FBN1; MIM#134797) mutations are causative in ~90%. Recent studies show TGFBR2 (MIM#190182) mutations could be identified in 10% non-FBN1 probands reference 1. We examine the mutation spectrum of TGFBR2 in non-FBN1 Chinese with MFS and related phenotypes.

Methods: All Chinese probands referred for evaluation of MFS and negative for FBNI mutations were included. Mutational screening was performed by DHPLC reference 2. Amplicons with abnormal elution pattern were selected for direct sequencing.

Results: Seven novel mutations were identified in 7 of 41 probands. All had prominent cardio-skeletal phenotypes without ocular or dural involvement, confirming previous findings reference 3. Six were missense (R190H, D2247V, T325P, G357R, I510N, T530I) and 1 was frameshift (P501fsX17). Except R190H, all were found in the functionally-important kinase domain. Bioinformatic analyses showed that all mutations occurred in conserved positions by cross-species comparison between 6 orthologs, and (ii) R190H, T325P, T530I and G357R were also found in conserved positions among 3 paralogs (TGFBR1 and activin receptors AVR2A, AVR2B) in the TGFBR superfamily. All 7 were not found in 50 normal individuals. With the TGFBR2 mutations, 4 additional probands would fulfill the diagnostic criteria of MFS.

Conclusion: TGFBR2 mutation is identified in 17% of our non-FBN1 probands. It should be considered in the evaluation of MFS after FBNI screening, especially if there are compatible clinical features.
P-117 Effects of CYP2D6 genotypes on risperidone metabolism in Japanese patients with schizophrenia
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[Background] Risperidone is an antipsychotic in wide use for psychiatric disorders such as ADHD and autism in paediatric patients. It is converted by P450 enzymes into 9- hydroxyrisperidone, which has a pharmacological activity comparable to its parent compound. Substantial inter-individual variability has been observed in the dose-normalized concentrations of risperidone and the 9-hydroxy metabolite. This variability has been partly accounted for by polymorphisms in CYP2D6, which has more than 10 mutant alleles.

[Methods] In the present study, 90 adult Japanese patients with schizophrenia receiving risperidone were evaluated to see whether their CYP2D6 genotypes were associated with the altered metabolism of risperidone and its metabolite. A P450 microarray system was used, by which most major mutant alleles of CYP2D6 can be scored.

[Results] The dose-normalized concentrations of risperidone exhibited significant differences among the three CYP2D6 genotypes (*1/*1, *1/*10 and *10/*10; p=0.025). The concentrations were 2.8 times higher in the homozygous *10 (n=7) than in the wild type (n=16). Among the patients who were given concomitant phenothiazines (n=44), the total active moiety (i.e. risperidone and 9-hydroxyrisperidone) was higher in those with the *10 allele than in those with the wild type (p=0.014).

[Conclusions] The CYP2D6 genotypes and the concomitant phenothiazine administrations were identified as the major determinants of the steady-state concentrations of the total active moiety of risperidone. The present finding is particularly relevant for Asian populations, among whom the *10 allele is quite prevalent.

P-118 Molecular diagnosis for atypical cases with Wilson disease
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[Introduction] Wilson disease is an inborn error of copper metabolism. This disease is caused by mutations in the ATP7B gene. Biochemical features are low serum ceruloplasmin levels and high urinary copper excretion. However, some patients do not show typical biochemical findings. In this study, the authors report the molecular diagnosis of Wilson disease patients with atypical biochemical findings. [Patients] Case 1 is a 5-year-old girl. She presented with chronic liver dysfunction. Her serum ceruloplasmin level was within normal range. Urinary copper excretion was not so elevated. Case 2 is a 43-year-old woman. She presented finger tremor and dysarthria. Her serum ceruloplasmin was low, but urinary copper excretion was not elevated enough for diagnosis. Case 3 and 4 are sibling cases, 5-year-old girl and 1-year-old girl. Their serum ceruloplasmin levels were low. However, urinary copper excretions were not elevated. [ATP7B gene analysis] Genomic DNA was isolated from peripheral blood leukocytes of patients. All exons of the ATP7B gene were amplified by genomic polymerase chain reaction (PCR), and then analyzed by direct sequencing as described. Gene analysis was performed under written informed consent. [Results and conclusion] All patients had ATP7B gene mutations in both alleles. And the authors diagnosed them as Wilson disease. High urinary copper excretion was very specific for diagnosis of Wilson disease. However, urinary copper excretions of all patients were not elevated. Thus, definitive diagnosis for these patients was very difficult by biochemical analysis. Molecular diagnosis is very effective for definitive diagnosis for atypical cases with Wilson disease.

P-119 Child fleck (Mongolian spots): Distinguishing from evidence of child abuse
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The child fleck is a very common stain in infants of the Asian population (Mongolian population) including Japanese, which typically disappears spontaneously. It is often called as a Mongolian spot. It is found in other populations as well, but is rare in the Caucasian population, and it is poorly understood in America and Europe. Because of this, child flecks are often mistaken as subcutaneous bleeding caused by child abuse. To educate non-Japanese health care professionals about the child fleck, we produced an English pamphlet describing the child fleck (Mongolian spot). The prevalence of child flecks varies among different ethnic groups according to the overall depth of pigmentation. Child flecks are common among Asian, East Indian, and African populations, but rare among Caucasian and other populations. Reported incidences in representative ethnic infants are as follows: Asian: 95-100%, East African: 90-95%, Native American: 85-90%, Hispanic: 50-70%, and Caucasian: 1-10%. However, investigation of the prevalence rate is not done recently. An international collaboration study of child fleck (incidences, forms, colours, distributions, and variant forms) will be required.

P-120 Critical region for trigonocephaly in a patient with monosity 9p syndrome analyzed by CGH-array
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[Background] Monosity 9p syndrome is mostly caused by chromosomal deletions spanning 9p22-p24. Most patients have characteristic findings including mental retardation; dysmorphic facial expression with midface hypoplasia, upward-running palpebral fissures, and long philtrum; and characteristic trigonocephaly. The critical candidate region has been reported to be in a 4.7-Mb interval at 9p22.2-p23 (Kawara et al., 2006). [Patient and Methods] We here describe a 2-year-old Japanese boy with clinical features of monosity 9p syndrome, including trigonocephaly. G-banded chromosomal analysis revealed a deletion of 9p. We performed array-based comparative genomic hybridization (CGH-array) to detect the precise deletion region. To confirm array data, fluorescence in situ hybridization (FISH) analyses were performed using BAC clones. [Results] CGH-array analysis identified the deletion of 9pter-p23.3 in this patient. FISH analyses refined breakpoint of the deletion region. [Conclusion] CGH-array was effective to detect the region of deletion for this patient. FISH analyses agreed the result of CGH-array. The deletion region in this patient was not common with the previously reported region responsible for trigonocephaly, but the physical distance is not so far away. Thus, we still believe that the critical region for trigonocephaly is in this narrow region.
P-121  Natural history of trisomy 18 fetus diagnosed in the third trimester
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Trisomy 18 is the second most common autosomal trisomy in liveborn infants, and occurs at a frequency of 1 per 3,000-5,000 live births. Combined with the ultrasonographic examination, multiple marker screening test involving the maternal serum AFP, uE3, and hCG in second trimester was reported to identify about 60% of trisomy 18 with a 0.4% false positive rate. The life expectancy of trisomy 18 after live born reveals the high infant mortality rate. About 90% children with trisomy 18 die before their first birthday. Recently the natural history of trisomy 18 of live born was investigated and reviewed extensively. To delineate the natural history of 18 trisomy fetus prenally diagnosed in the third trimester, we reviewed the 50 cases diagnosed after 27 weeks of gestation in our institute between 1994 and 2003. 57% of the cases were live births, and 43% were stillbirths. Prenatally diagnosed cases reached to live-born showed no difference in the prognosis and life expectancy to the control group. The sex ratio was about 1 at that time of prenatally diagnosed, but rapidly declined at term. This information was valuable for counseling to families with the prenatally diagnosed cases and will provide insight into the sex ratio of the disorder.

P-122  Gene therapy of neonatal Fabry mice to prevent disease progression
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[Background] Fabry disease is an X-linked disorder caused by the deficiency of lysosomal enzyme, α-galactosidase A (α-gal A). Accumulation of glycosphingolipids in systemic organs results in pain, hypohidrosis and angiokeratoma during adolescence and renal and cardiac failure at the later stage. Enzyme-replacement therapy is now available, but its efficacy is often inadequate for adult patients with advanced clinical symptoms. AAV vector mediated continuous and systemic supply of α-gal A is an important option for treatment of Fabry disease.

[Methods & Results] We compared therapeutic efficacies of AAV vector delivery to neonatal and adult Fabry mice. When adult male Fabry mice (12 weeks old) were treated by intravenous injection of AAV1 vector carrying the n-gal A cDNA, sustained high levels of α-gal A activity were detected in plasma, liver, and heart. AAV1 mediated in vivo transduction was significantly suppressed in female adult mice. Injection of AAV1 vector into neonatal mice (3 days old) resulted in long-term cardiac specific expression of α-gal A irrespective of sex of mice. Accumulation of globotriaosylceramide was efficiently inhibited in the liver and heart by a single injection at the neonatal period.

[Conclusions] AAV1 mediated gene therapy at the non-symptomatic early stage of the disease should be beneficial for prevention of major organ failure in adulthood.

P-123  Selective in vivo reversion of an inherited WASP duplication mutation to normal in T-cell lineages
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Background: Wiskott-Aldrich Syndrome (WAS, MIM# 301000) is a rare X-linked recessive immunodeficiency disorder. The causative WAS protein (WASP) gene is expressed selectively in haematopoietic stem cell-derived lineages and is involved in cytoskeleton rearrangement and cellular signaling. Mutations in WASP are highly heterogeneous and are related to wide range of clinical phenotypes. We present a Chinese boy who was diagnosed with WAS at 7 months with a classical presentation of recurrent infections, thrombocytopenia, diffuse eczema, generalized lymphadenopathy and hepatosplenomegaly. He underwent a successful haemopoietic stem cell transplant at 10 months and attained full recovery.

Methods: Genomic DNA and total RNA were extracted from buffuc cells, peripheral blood, isolated CD3+ T-lymphocytes, CD3- mononuclear cells and B-lymphocytes. Molecular analysis of WASP was performed by genomic PCR and RT-PCR direct sequencing.

Results: A novel 14 bases duplication insertion (TTGGACGAAAATGC) 3 bases 5’ to the exon1/intron1 splice junction, coupled with frameshift and predicted protein truncation (T455X66) was identified. The mother was diagnosed as a carrier. Somatic mosaicism, with normal and mutant gene, was detected in the peripheral blood of the patient but not in his buffuc cells. Molecular analysis of the purified immune cells indicated that the revertants were selectively CD3+ T-lymphocytes.

Conclusions: Reversion of T-cell lineages was not enough for full reconstitution of immunity in our patient. However, our results suggested that the revertants originated from postzygotic somatic mutation of the primitive haematopoietic progenitor. It also supported the hypothesis that revertant T-lymphocytes show selective advantages in clonal expansion over the mutant T-lymphocytes.

P-124  Comprehensive molecular investigation for moyamoya disease
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INTRODUCTION
Moyamoya disease is a rare cerebrovascular disorder mainly involving the middle cerebral arteries, is a steno-occlusive disorder which cause ischemic events in the childhood period. Etiological aspects of moyamoya disease are somewhat similar to that of idiopathic pulmonary hypertension. Because, both diseases are caused by narrowing of arteries and their incidence is higher in female than in male. Some responsible genes have been identified in idiopathic pulmonary hypertension, i.e. endoglucanase (ENG) and activin A receptor type II-like (ACVRL1). In this study, we analyzed these genes in patients with moyamoya disease.

MATERIALS AND METHOD
Materials were DNA purified from blood of six typical moyamoya patients. All coding regions of ENG and ACVRL1 were analyzed

RESULTS
There was no mutation in the candidate genes.

DISCUSSION
Because moyamoya disease is popular only in east Asian people, we believe that there should be a common mutation in patients with moyamoya disease, and that the number of mutations with six samples would be enough. However, we identified no mutation in ENG and ACVRL1, and failed to confirm positive relationships between them. Since pathways of signal transduction in vascular system are suspected to be involved in moyamoya disease, other molecules should be studied in the future.
P-125 Association between Genetic polymorphism of -cell differentiation genes and Insulin resistance (-cell dysfunction) in Survivors of Childhood Acute Lymphoblastic Leukemia

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Background: The purposes of the study were to determine β-cell function and insulin sensitivity and the association of variants in β-cell differentiation genes with insulin resistance (β-cell dysfunction) in childhood ALL survivors.

Methods: Childhood ALL patients who had been diagnosed during 1987-2004 and completion of treatment for at least 6 months. The oral glucose tolerance test and lipid screening were performed. Impaired glucose tolerance and diabetes were defined according to WHO criteria. Common polymorphisms of TCL7L2 were genotyped and assessed their effect on β-cell function and insulin sensitivity. Results: 110 children were included in this study (45 females and 65 males; age 4-20 yr). 101 children (91.8%) had normal glucose tolerance (NGT). The others (8.2%) had impaired glucose tolerance (IGT) which associated to older age at test (13.7 and 10.3 yrs, p = 0.006), longer period of completion of treatment (47 and 26 months, p = 0.003), and lower value of insulin sensitivity indices (WBISI) (9.56, p = 0.001) than children in NGT group. The typical signs of metabolic syndromes (hyperglycemia, low HDL-C, obesity) were found up to 20%. The genotypes of TCL7L2 were not difference between NGT and IGT group (p=1). Conclusion: Impaired glucose tolerance (IGT) related to longer period of completion of treatment and older age group. Long-term survivors of childhood ALL had potential risk of impaired β-cell function and impaired glucose tolerance (IGT), even in non-obese children. Our findings did not support association of TCL7L2 variants with insulin resistance (β-cell dysfunction) in childhood ALL survivors.

P-126 Association of regulatory polymorphisms of multidrug resistance 1 (MDR1) gene with the development of childhood acute lymphoblastic leukemia

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Background: The polymorphisms of genes encoding enzymes and transporters eliminating xenobiotics may have a potential role in the development of childhood acute lymphoblastic leukemia (ALL). We determine whether the polymorphisms of the MDR1 gene are associated with the development of childhood ALL. Methods: The MDR1 gene polymorphisms, -2352G>A, -934A>G, -692T>C (5' regulatory region) and 3435C>T (exon 26), were examined in 157 ALL patients and 96 healthy children. The amounts of MDR1 mRNA were quantified in 54 healthy individuals using normal peripheral blood mononuclear cells to evaluate the effect of each polymorphism on the gene expression. Results: The frequency of the G/G genotype of the -2352 G>A was significantly higher in ALL than in controls (74/109 vs. 52/96, p=0.04). The frequency of the T/T genotype of the 3435C>T was also significantly higher in ALL (29/118 vs. 10/96, p=0.006). In a haplotype analysis using the 5' regulatory sites, the frequency of a certain haplotype was higher in ALL than in controls (59/90 vs. 42/88, p=0.048). When the -2352G>A was examined in different age groups, patients aged six or older were found to have the G/G genotype more frequently than the controls (42/51 vs. 52/96, p=0.0014), while no difference was observed in the younger age group. The amounts of MDR1 mRNA were significantly higher in either G/G or G/A genotype of the -2352 G>A than in A/A genotype (p=0.04). Conclusions: The genetic background of MDR1 may be associated with the development of childhood ALL.

P-127 NQO1 polymorphisms and the susceptibility to MLL rearrangement in infant leukemia

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[Background] Several groups have suggested that two types of single nucleotide polymorphisms (SNPs), NQO1 C690T and C465T, are significantly associated with increased risk of infantile leukemia with MLL translocation. NQO1 contributes to p53 protein stability through regulating 20S proteasome pathway. Poor induction of p53 in NQO1 null mice has been reported. These observations lead us to investigate whether NQO1 status is correlated to p53 expression level, playing some roles in the induction of MLL gene rearrangement by etoposide.

[Methods] We genotyped germ line NQO1 allele in Epstein-Barr virus transformed lymphoblastoid cell line (EB-LCL) derived from 7 infants who developed acute leukemia. p53 induction after 50Gy irradiation (IR) and MLL gene cleavage by etoposide was also analyzed using EB-LCL with various NQO1 SNPs status.

[Results] We identified one heterozygote and one homozygote of C690T, and one heterozygote of C465T in EB-LCLs derived from 7 patients. C690T homozygote showed normal p53 induction in response to IR. On the other hand, C465T heterozygote showed significantly lower p53 induction. There was no association of NQO1 SNPs with the susceptibility to MLL gene cleavage by etoposide.

[Conclusion] NQO1 deficiency identified in C465T, but not that in C690T, was associated with defective p53 induction. Thus NQO1 deficiency by itself may not play direct role for leukemogenesis, but C465T may underlie leukemia susceptibility through defective p53 response by unknown mechanisms. Further studies are needed to identify the possible role of NQO1 polymorphisms for the susceptibility to MLL rearrangement in infant leukemia.

P-128 Minimal residual disease monitoring in childhood acute lymphoblastic leukemia by flow cytometry, WT-1 and fusion transcript (TEL-AML1): do they correlate?

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The detection of minimal residual disease (MRD) is of great significance when pediatric hematologists follow leukemia patients for early detection of relapse. MRD was monitored in TEL-AML1 positive childhood ALL patients with three methods, PCR amplification of fusion transcripts, expression levels of t(12;21)(p13;q22) translocated gene (WT-1), and flow cytometric (FCM) detection of aberrant immunophenotypes. TEL-AML1 is a fusion transcript as a result of a fusion chimeric gene (12,21)(p13;q22), which is known to be an indicator for favorable prognosis. We examined to know which method is the most sensitive and if the results correlate each other. [Patient 1] 5 year old girl. The leukemic blasts still persisted by light microscope after 8 days of prednisolone. A more intensive chemotherapy was needed to achieve marrow remission 32 days after. It took 64 days of chemotherapy for WT-1, while it took 78 days for TEL-AML1, and 79 days for MRD monitored by FCM to be undetectable in the bone marrow, respectively. [Patient 2] 3 year old girl. The leukemic blasts were undetectable by light microscope after 8 days of prednisolone. TEL-AML1 and WT-1 were undetectable in the bone marrow after 43 days of chemotherapy, but WT-1 elevated again 55 days after, while TEL-AML1 remained negative. MRD monitored by FCM disappeared after 30 days of chemotherapy, but elevated again 69 days after without any evidence of clinical relapse. More data about clinical courses and MRDs of other patients will be shown in the presentation.
P-129  Expression of matrix metalloproteinase (MMP) and tissue inhibitor of MMP (TIMP) genes in blasts of infant ALL with organ involvement

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Background: Matrix metalloproteinases (MMPs) and their natural endogenous inhibitors (tissue inhibitors of MMP, TIMPs) play an important role in tumor invasion and metastasis of various solid tumors. These enzymes may also be potentially important for dissemination and tissue invasion of malignant lymphocytes. We examine, in this study, the correlation of MMP and TIMP gene expression in leukemia cells with the clinical characteristics of infants with acute lymphoblastic leukemia (ALL), especially with the extramedullary organ involvement. Methods: The mRNA contents of MMP-2, MMP-9, TIMP-1 and TIMP-2 in leukemia cells from 33 infants with infant ALL were quantified at initial presentation by the real time quantitative RT-PCR (TaqMan methods). The association between their expression and patient clinical characteristics was examined, including patients’ age and white blood cell count at diagnosis, MLL gene rearrangement in leukemia cells, and presence of hepatosplenomegaly or central nervous system (CNS) involvement. Results: The mRNA contents of MMP-2 and MMP-9 were not associated with any patient characteristics. The MMP-2/TIMP-1 and MMP-2/TIMP-2 ratios were significantly higher in patients with hepatosplenomegaly than those without it (p=0.005 and 0.009). The MMP-2/TIMP-2 ratio was also higher in patients with CNS involvement (p=0.012). The MMP-9/TIMP-1 and MMP-9/TIMP-2 ratios did not associate with the organ involvement. Conclusions: The MMP/TIMP balance, but not the mRNA amounts of a single gene, may play an important role in dissemination and organ invasion of leukemia cells in infant ALL.

P-130  Age-associated difference in gene expression of myelo-monocytic AML

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Acute myelogenous leukemia (AML) is a heterogeneous disease with a variety of genetic alterations including the MLL gene rearrangement. Microarray-based gene expression profiling has been applied to diagnose AML patients and to explore their underlying molecular pathology. In this study, we analyzed gene expression of 54 (14 adult and 40 pediatric) myelo-monocytic AML patients with FAB M4 and M5 subtypes (excluding inv(16) and t(8;21) cases), and found striking differences among the patients in an age-associated manner. Especially most of the infant patients (less than 1yr) displayed very distinct gene expression. With the use of this distinctiveness, we were able to divide the pediatric patients into three age-associated subgroups with different outcomes. In addition, we found that gene expression signature of MLL rearrangement was different among these pediatric subgroups as well. These results suggest that age is an important factor contributing to the biology of myelo-monocytic AML.

P-131  Folate Pathway Genetic Polymorphisms and Susceptibility of Central Nervous System Tumors in Thai Children

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Folate is an important micronutrient participating in the DNA synthesis, methylation and repair mechanisms. Genetic polymorphisms in folate pathway related enzymes including methyleneetetrahydrofolate reductase (MTHFR) C677T and A1298C, methionine synthase (MTR) A2756G, thymidylate synthase (TYMS) G2691A, 5,10-methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C conferred an increased risk to develop embryonal CNS tumors (OR 3.9; 95% CI 1.3-11.4, p = 0.02). Our findings suggest that in Thai children folate metabolism may play a role in the pathogenesis of specific subtypes of pediatric brain tumors, especially embryonal CNS tumors.

P-132  Outcome of Children With Diffuse Pontine Glioma (DPG) Treated With Concomitant Radiation (RT) Plus Temozolomide (TMZ) Followed by Adjuvant Temozolomide and cis-Retinoic Acid (cRA)

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The prognosis for children with DPG is very poor. Multiple trials involving various regimens with RT did not show any improvement of outcome in DPG children. While TMZ and cRA were demonstrated the activity in malignant gliomas, they have never been reported in DPG. Twelve patients, 3 males and 9 females, median age 4.2(2.8-9.1) yr, diagnosed with DPG by typical imaging findings were enrolled. TMZ of 75 mg/m²/day was given concomitantly with RT (57.6-59.4 Gy). Two weeks after RT, a 4-week cycle of 5 days of TMZ (200 mg/m²/day) and 21 days of cRA (100 mg/m²/day) were initiated. Imaging studies were performed after RT and at every 3-month period. The median follow-up time was 14.5(6.9-42) mo. At the end of RT, 7 patients had partial response (PR), 4 stable disease, and 1 progressed. All magnetic resonance spectroscopy in 5 available patients showed decreased Choline/Creatine ratio. One-year progression free survival (PFS) was 41.7% with median progression time of 10.2±3.0 mo (95% CI 4.2-16.1). One-year overall survival (OS) was 58.3% with median survival time (ST) of 13.5±6.6 mo (95% CI 6.4-20.5). Patients with PR after RT had longer PFS than others (p=0.036). Patients whose age <5 yr had longer ST than ≥5 yr (p=0.036). Conclusion: Our approach demonstrated a better outcome than previous regimens. Patients whose age <5 yr is the prognostic indicator for better ST including 1 patient who survives >3 yrs. In the future, protracted low dose TMZ with other biological agent should be investigated to determine an even better outcome.
P-133 Hemophagocytic lymphohistiocytosis in Langerhans cell histiocytosis: A report of 2 cases

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Langerhans cell histiocytosis (LCH) is a disease of antigen presenting dendritic histiocytes, compared to hemophagocytic lymphohistiocytosis (HLH) which is a disorder of macrophages. These two diseases should be differentially diagnosed each other for planning of adequate treatment.

Case 1: Twelve-month-old girl. Watery diarrhea and fever began 1 week prior to admission. On admission there were abdominal spotted eczema, cephalic seborheic dermatitis, cervical and abdominal lymphadenopathy, hepatosplenomegaly, cytopenia, hypofibrinogenemia, hypoalbuminemia, hyperferritinemia, and skull punched out lesion. Skin and liver biopsies showed Langerhans histiocytes, while the bone marrow examination revealed massive hemophagocytosis. This child died at age 21 months, in spite of intensive chemotherapy.

Case 2: Fourteen-month-old girl. Spotted eczema began 1 month prior to admission. One week before, she expressed unusual fatigue. On admission there were cephalic seborheic dermatitis, petechiae and protrude dark red eczema in head and body, cervical lymphadenopathy, hepatosplenomegaly, anemia (Hb 2.1 g/dl), metabolic acidosis, and consciousness disorder. Skin biopsy revealed Langerhans histiocytes infiltration, whereas bone marrow contained hemophagocytic non-Langerhans histiocytes. This child responded to chemotherapy. Two months after diagnosis, she had no evidence of LCH and HLH except a punched out resion of ilium.

P-134 Malignant hepatic tumor occurring 10 years after a histocompatible sibling donor bone marrow transplantation for severe aplastic anemia

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Bone marrow transplantation (BMT) has increased the number of cures of malignant or non-malignant diseases. Meanwhile, second/new malignancy has become a problem arising in the long-term survivors. BMT from a histocompatible sibling donor is the first line treatment of severe aplastic anemia (SAA) children. Non-irradiated conditioning has been preferably employed concerning the late effects on the growth and fertility, and the risk of malignancy. Reduced intensity conditioning raises the risk of graft failure and/or mixed donor chimerism that involves incomplete hematological recovery and clonal diseases. We have no information of solid malignancy in SAA survivors in Japan who underwent allogeneic BMT at <15 years of age.

Case Reports and Results: We present a 13-year-old boy who developed malignant liver tumor. At 3 years of age, this patient underwent a histocompatible sibling donor BMT (infused cell number 4.6x10^6/kg) for idiopathic SAA, after a conditioning with antithymocyte globulin (10 mg/kg) and cyclophosphamide (200 mg/kg). He became a hepatitis B virus carrier after BMT. Stable mixed chimerism (donor: 65–70%), mild thrombocytopenia and no active hepatitis allowed his active school life. At age 13, abdominal pain was a sign of massive tumor. Extremely high levels of α-fetoprotein (1,650,000 ng/ml) indicated the clinical diagnosis of hepatoblastoma. This might be the first report as post-BMT malignancy. The necropsy specimens revealed that the tumor was recipient cell-origin and showed the histopathological features of both hepatoblastoma and hepatocellular carcinoma.

Conclusions: Prolonged mixed chimerism and hepatitis virus infection might induce a rare oncogenesis after non-irradiated conditioning.
P-137 New treatment strategy against malignant tumors-A vaccine with human umbilical vein endothelial cells and very low dose IL-2

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[Background] Most of immunotherapy against a patient with malignant tumor have been developed as a target of tumor specific antigen; however, their effect was not more than expected. We have developed a vaccine therapy with human umbilical vein endothelial cells (HUVEC) to target tumor angiogenesis in combination with very low dose IL-2. We havet tried this treatment for two patients and demonstrated their favorable course. [Methods] Case 1 was a 28-year-old female with cervical small cell carcinoma, stage 4, and Case 2 was a 14-year-old boy of pancreatoblastoma with multiple lung metastasis. Before treatment, their immune function, including NK cell activity and CD4(Th1/Th2) were tested. HUVEC were isolated from an umbilical cord at cesarean section, and were cultured and expanded in vitro. After fixation with glutaraldehyde, they were stored in a refrigerator until vaccination. A vaccine mixed with HUVEC and PPD was injected intradermally to our patients every 2 weeks interval, and 1500 JRU/kg of IL-2 was administered intravenously by drip infusion for 4-5 consecutive days. [Results] In case 1, NSE was within normal range after 3 months of treatment. She has been still tumor free for more than 2 years. Case 2 became a stable condition without elevating tumor marker after 3 months of treatment. Major side effects were not seen. After immunotherapy, activated T and NK cells were remarkably increased in both cases. Skin test for HUVEC was positive in both cases. [Conclusions] Anti-angiogenic therapy, using HUVEC and IL-2 is safe and presumably effective in our cases. Additional trials on many patients are required, and at the same time the mechanism should be analyzed in detail.

P-138 The Correlation of Transferrin Saturation and Ferritin in Non-Splenectomy Thalassemic Children

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Thalassemia is a public health problem in Thailand. Progressive iron overload is the life-limiting complication commonly found in thalassemic patients. The assessment of body iron stores is essential for determining the need and efficacy of iron chelation. The parameters of serum iron, total iron binding capacity (TIBC), and serum ferritin were studied in 79 children with thalassemia diseases. The ages ranged from 1 to 17 years with a mean of 7 years and 10 months. Neither of them had clinical symptoms of hypophosphatemia. The correlation between transferrin saturation (TS = serum iron/TIBC x 100) and serum ferritin was shown in the equation of TS = 10.253 ln (ferritin) (r = 0.956, p = 0.000). For example, TS = 70.83% indicates serum ferritin of 1,000 ng/ml. Thus, where serum ferritin is not feasible but serum iron and TIBC are available, TS can be used to estimate the level of serum ferritin. Therefore, the assessment of iron stores and monitoring of iron chelation in thalassemic patients can be effectively achieved.

P-139 Pathophysiology for Osteoporosis in Severe Thalassemia Patients Suggested by an in Vivo Gene Expression Study of Isolated Marrow Mesenchymal Stem Cells (CD105+)

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Background: Osteoporosis represents an important cause of morbidity in patients with severe thalassemia. The pathogenesis of osteoporosis in severe thalassemia is multifactorial, and includes bone marrow expansion, endocrine dysfunction, and iron overload. However, the mechanism through which these factors lead to bone loss have not been complete clarified. Osteoblasts are the bone-forming cells and arise from mesenchymal stem cell (MSCs). We therefore would like to study the MSC function in severe thalassemia patients to elucidate the bone formation dysfunction mechanism in these patients.

Patients and Methods: Twenty ml of heparinized bone marrow was recovered from 10 severe thalassemia patients and 12 healthy volunteer donors. CD105+ cells were purified from each marrow sample by immunomagnetic isolation. Osteoblast differentiation genes expressions by Quantitative Real-Time RT-PCR were studied from these CD105+ cells. The osteoblast differentiation genes were consisted with cbfa1, osteonexin, osteocalcin, alkaline phosphatase, bone morphogenic protein-2, MesoX-2, and type I collagen.

Results: The medians of fold difference of the most of osteoblast differentiation genes expressions from thalassemia patients were lower than healthy controls (genes expression = 1). The fold difference of genes expression from healthy controls was demonstrated: cbfa1 = 0.228 (p < 0.05), MesoX-2 = 1.502, Osterix = 0.356 (p < 0.05), BMP2 = 0.668, Collagen type 1 = 0.919, Alkaline phosphatase = 0.722, and Osteocalcin = 0.246 (p < 0.05).

Conclusion: The osteoblast differentiation of mesenchymal stem cells from thalassemia is impaired. This may be from the environmental factors in the bone marrow which inhibit this process.

P-140 Change in the Absolute Neutrophil Count after IVIG Administration in Children with Idiopathic Thrombocytopenic Purpura

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Purpose: IVIG is effective for the treatment of ITP in children. Recently, several reports have been published that show its impact on the absolute neutrophil count (ANC). This study was performed to confirm these findings.

Methods: Data on 26 patients was analyzed. The patients with febrile illness or increased C-reactive protein levels at presentation or steroid use, which would influence the neutrophil counts, were excluded to determine the sole impact of IVIG.

Results: Sixteen boys and ten girls were analyzed. Dosage and duration of IVIG varied from 0.4 g/kg for 1 to 5 days to 1 g/kg for 2 days according to the individual clinical situation. In 22 out of 26 cases (84.6%), the absolute neutrophil count (ANC) significantly decreased (p = 0.037) after IVIG administration. However, when analyzing the cases that received an IVIG dose of 0.4 g/kg (n = 17), the ANC was not significantly decreased (p = 0.44). However, with the IVIG dose of 1 g/kg (n = 9), the ANC was significantly decreased (p = 0.017). Among six cases with profoundly decreased ANC, over 1,000/mm3, four patients (67%) received IVIG at a dose of 1 g/kg.

Conclusion: IVIG treatment for ITP patients appears to influence the ANC count. The changes observed were more pronounced at a higher dose of IVIG. However, the number of samples was not sufficiently large to reach an accurate conclusion.
P-141  **Ligneous conjunctivitis in a child with plasminogen deficiency**

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**Background:** Ligneous conjunctivitis is a rare form of membranous conjunctivitis characterized by fibrin-rich, wood-like membranes mainly on tarsal conjunctiva. The disease usually affects children, girls more than boys, but may occur at any age. It appears to be the ocular manifestation of a systemic disease, which might be accompanied by formation of pseudomembrane or membrane in multiple organs such as the mouth, the tracheobronchial tree, and the female genital tracts. Most treatment attempts have so far been unsatisfactory. This report describes a case of ligneous conjunctivitis presented at early infancy whose investigation revealed a plasminogen deficiency.

**Method:** Case report

**Result:** A 4 year-old girl presented with bilateral recurrent membranous conjunctivitis since 1 month of age. Plasma plasminogen functional activity from the patient and mother was 15.2% and 78% respectively (normal 80-120%). Multimodality treatment was given including membrane excision, topical corticosteroid, topical cyclosporin, topical heparin, topical serum and 80-120%). Multimodality treatment was given including membrane excision, topical corticosteroid, topical cyclosporin, topical heparin, topical serum and fresh frozen plasma, with improvement. Histology of the excised membranes revealed thick amorphous material composed predominantly of mononuclear inflammatory cells, scattered polymorphonuclear cells and areas of fibrin, consistent with ligneous conjunctivitis. A patient was improved with nearly resolved of the membrane in her right eye and thin layer of membrane in her left eye.

**Conclusion:** Ligneous conjunctivitis associated with plasminogen deficiency should be considered in differential diagnosis of cases with recurrent membranous conjunctivits.

P-142  **Hematopoiesis in regenerated bone marrow on the hydroxyapatite scaffold**

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**Background:** Bone marrow (BM) stromal cells are capable of supporting hematopoietic stem cells (HSCs). Recent studies suggest that osteoblastic cells lining the bone surface are a key component of the hematopoietic niche to promote and regulate HSCs. Anatomical architecture of BM could be generated by culturing mesenchymal stem cells on the hydroxyapatite (HA) scaffold. In the present study, we examined whether the regenerated BM has the ability to support HSCs. **Methods:** 1) BM stromal cells from C57/BL6 mice were cultured on the HA scaffold with numerous small pores for 3 days and the scaffold with attached cells was implanted subcutaneously onto the back of C57/BL6 recipient mice. 2) Lineage negative (Lin-) BM cells transduced with a lentiviral vector containing the luciferase (Luc) gene were intravenously administered into the recipient mice after lethal irradiation. 3) After 8 weeks, the scaffolds were removed and re-transplanted into the lethally irradiated second recipient mice along with normal BM cells. **Results:** In the secondary transplanted mice, Luc+ hematopoietic cells were detected on the scaffolds by in vivo bioluminescence imaging for at least 3 months after transplantation. Bioluminescence signals were also detected on the whole body including the head, extremities, chest, and abdomen after G-CSF injection. **Conclusions:** The regenerated BM on the HA scaffold is capable of maintain hematopoiesis in vivo suggesting that the functional niche is reconstituted. Expansion of hematopoietic cells in the regenerated BM may be useful for treatment of various hematopoietic diseases.

P-143  **Immune response to influenza vaccination in children receiving chemotherapeutic/immunosuppressive agents**

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**Background:** The aim of this study was to assess the safety and the humoral response to inactivated trivalent split influenza vaccine in children with cancer and aplastic anemia.

**Methods:** In autumn, 2005 and/or 2006, 23 children with various types of malignancies and aplastic anemia were received one or two dose of influenza vaccine 2-4 weeks apart. Hemagglutinin-inhibition (HI) antibody titer were determined in paired sera obtained just before and after influenza vaccination. Effective immune responses were measured as four-fold or more rises in HAI titers.

**Results:** Influenza vaccine was administered to all children without any serious adverse effects. Children on chemotherapy showed lower immune response to both influenza A and B than those having completed chemotherapy. No children with aplastic anemia receiving immunosuppressive agent had four-fold rises HAI titers.

**Conclusions:** Influenza vaccine was safe for children with cancer or aplastic anemia. Vaccination after completing chemotherapy was followed by sufficient elevation of antibody titers, whereas patients got an insufficient immune responses under administration of therapeutic agents.

P-144  **Insulin-like growth factor-II: a novel autocrine growth factor promoting the apoptosis, proliferation, and maturation of umbilical cord blood erythroid progenitors**

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**Backgrounds & Objectives:** Human umbilical cord blood (CB) contains abundant erythroid progenitor cells (EPCs), which could help compensate for intrauterine hypoxia. We searched a novel function of EPCs circulating as the major nucleated cell population in umbilical CB cells. **Methods:** Human CB-derived CD34+ EPCs were subjected to DNA microarray. The gene expression and biological property of CB-EPC and adult PB-EPC were compared by using real-time PCR and serum-free culture system with erythropoietin (EPO). **[Results]** The microarray revealed 124-fold higher levels of insulin-like growth factor-II (IGF-II) gene expression in CB-EPCs than in stimulated-lymphocytes of adult PB. Real-time PCR verified that IGF-II mRNA levels were highest in CB-EPCs compared to either CB- or adult PB-fractionated cells. When CB-EPCs were cultured with EPO in serum-free medium, anti-IGF-II-antibody (Ab) reduced the number of erythroid colonies. When CB- and adult PB-derived erythroid colony-forming cells (EFCFs) were cultured with interleukin-3, stem cell factor and EPO, mRNA levels of IGF-II, type 1 and type 2 receptors increased with both EFCFs maturation. The maturation rate by IGF-II was higher in CB-EFCFs than in adult PB-EFCFs. The majority of CB-EFCFs expressed IGF-II protein. Anti-IGF-II-Ab, but not anti-IGF-I-Ab, reduced the number of CB-EFCFs in liquid culture with EPO. Anti-IGF-II-Ab inhibited proliferation, and accelerated apoptosis of EFCFs, assessed by MTT and BrdU assays. EFCFs failed to attain full maturity in the presence of anti-IGF-II-Ab. **[Conclusions]** These results suggest that IGF-II is produced by EPCs themselves, and has a crucial role in fetal erythropoiesis by modulating apoptosis, proliferation and maturation in an autocrine fashion.
Clinical course and immunological study of an infant with Wiskott-Aldrich syndrome (WAS)

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Wiskott-Aldrich syndrome (WAS), a primary human immunodeficiency, results from defective expression of the hematopoietic-specific cytoskeletal regulator protein (WASP). Children with WAS are compromised immunologically and also exhibit a high prevalence of autoimmune disease. We experienced severe phenotypes of WAS infant who presented life-threatening inflammatory bowel disease very early in life with recurrent ulcer which resemble to Bechet’s disease. <Case history> A 13-day-old Japanese boy, presented with fever, bloody stool with raised serum CRP. At 1 month, he developed recurrent oral aphtha, genital ulcer. Intermittent fever continued with persistent leukocytosis and thrombocytopenia. Examination of bone marrow was compatible with the myelodysplastic syndrome (MDS). Colonicoscopy at 2 months showed numerous small ulcers in the sigmoid and descending colon. A tentative diagnosis of BD was made because the manifestations were sufficient to meet the Criteria for BD despite the early age of presentation. The efficacy of treatment with systemic steroids, mesalazine, additional colchicine was unsatisfactory. At 8 months, a massive colonic resection was done. Because of persistent thrombocytopenia, eczema with high IgE, we analyzed WASp gene. Exon4, G431A, (E→K) No expression WASp by western blot. <Discussion> Patient with WAS exhibit in both immunodeficiency and marked susceptibility to systemic autoimmunity. The impairment of regulatory T cell functions might explain these paradoxical findings. Our current goal is to perform more profound immunogenetic studies in an attempt to discover the pathogenesis of BD-like auto inflammatory disorders in WAS.

Phosphorylation of Neph1 during podocyte injury in vivo

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[Background] Recent investigation revealed that slit diaphragm protein complex not only serves as a filtration barrier, it also conducts phosphorylation-mediated signals to integrate podocyte intercellular junction and cytoskeletal dynamics. Our previous biochemical studies revealed that slit diaphragm component Neph1 is tyrosine phosphorylated by Src-family tyrosine kinase Fyn. To extend our knowledge of the mechanism regulated by phosphorylation of slit diaphragm, we investigated phosphorylation of Neph1 in vivo. [Method] To characterize the phosphorylation of tyrosine residues, we produced several antibodies which specifically recognize the phosphorylation of tyrosine residues of Neph1 along with an antibody against C-terminus of Neph1. Using these antibodies, tyrosine phosphorylation was evaluated by western blot analysis using glomerular lysates or by immunohistological analysis using cryosection from protamine-sulfate (PS) perfused rats (podocyte injury model). <Results> Western blot analysis using Neph1 precipitates from glomerular lysate with anti-phosphotyrosine (PS) perfused rats (podocyte injury model) revealed that Neph1 was significantly increased in PS-treated glomeruli. Affinity-purified rabbit polyclonal antibodies against Neph1 phosphopeptides specifically recognized phosphorylated tyrosine residues of Neph1 in vitro. Western blot analysis with phospho-Neph1 antibody revealed that Y637 was phosphorylated in vivo in PS model, but not in control. Biochemical analysis revealed that phosphorylation of Y637 was responsible for binding of Neph1 with Grb2, and also had a negative effect on ERK activation. [Discussion] Neph1 is transiently phosphorylated by Fyn in response to podocyte injury which may serve as a link between junctional structure with intracellular signaling.

Functional Role of Na+-Independent System L Amino Acid Transporter 3 (LAT3) in Podocyte

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We previously reported that human Na+-Independent System L Amino Acid Transporter 3 (LAT3) is already expressed at S-shaped stage of the fetal kidney co-expressed with podocyte marker, synaptopodin. The aim of the present study is to determine the functional role of LAT3 in podocyte biogenesis. Immuno-fluorescence and confocal microscopy showed the specific distribution of LAT3 as a linear pattern on the plasma membrane of mice podocyte foot processes (FP) as well as human. When mice were starved for 24 h and 48 h, this linear distribution pattern of LAT3 on the plasma membrane was gradually but apparently diminished compared to the fed-mice. Moreover both transmission electron microscopy and scanning electron microscopy showed that the nutrient starvation induced apparent morphological change of podocytes as 1) foot processes became thin and elongated, 2) podocyte cell body became flat and wide. Finally, to determine the functional conservation of lat3 in the development of podocytes, we targeted the zebrafish lat3 ortholog using antisense morpholino oligonucleotide. Interestingly embryos injected with lat3 exon1 donor morpholino showed apparent cell number loss of glomerulus and extended bowman’s space in addition to severe cardiac edema at day 5 development. Recently identified study suggests that amino acids could activate new signaling pathway, rapamycin-insensitive pathway (mTOR2), regulating the cytoskeleton. We speculate that LAT3 likely transports branched chain amino acids into the podocyte, activating mTOR2 pathway and regulating actin-cytoskeleton system, which may play an essential role in the podocyte development and differentiation and maintenance of FP structure in the mature podocyte.
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Implication of Na+-Independent System L Amino Acid Transporter 2 (LAT2) in the pathomechanism of the glomerular crescent formation

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Glomerular crescent formed mainly by proliferated Bowman’s cells (BC) leads to rapidly progressive glomerular injury and requires early stage therapy. We reported that LAT2, specifically expressed in the basolateral membrane of proximal tubules. The aim of the present study is to determine the efficacy of some serotonin uptake inhibitors (SSRI) in combination with corticosteroid therapy in the treatment of diffuse proliferative GN. We reported that LAT2, specifically expressed in the basolateral membrane of proximal tubules. The aim of the present study is to determine whether LAT2 is directly involved in the cell proliferation machinery, we established S2 cell line expressing full-length human LAT2 (S2hLAT2). Starvation experiment revealed significant increase of phosphorylation with eIF4E binding protein and ribosomal protein S6 (p70) kinases in S2hLAT2 cells compared to wild S2 cells. Taken together, we conclude that LAT2 may participate in the crescent formation through activating mTOR1 pathway via the transport of branched-chain amino acid into BC in various glomerular diseases.

Rapamycin may be a candidate of new therapeutic tools for rapid progressive GN.

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Childhood recurrent urinary tract infection

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Introduction: Recurrent urinary tract infection (UTI) is one of the major problems in children because of its high rate of occurrence.

Objective: To evaluate the prevalence and risk factors of recurrent UTI in Thai children.

Patients and Methods: The medical records of children aged less than 15 years diagnosed with UTI at the Department of Pediatrics, Songklanagarind Hospital from 1995-2004 were reviewed.

Results: A total of 307 children (144 boys, 163 girls) were followed up for at least one year. 56 children, 31 (19.0%) boys and 25 (17.4%) girls, developed at least one recurrence, with a total of 153 recurrent UTI episodes. The recurrence rate was not statistically different between the sexes (p = 0.8). On multivariate analysis, GU anomalies, particularly urethral reflux (VUR), were the most significant risk factors. Children aged greater than 5 years had a slightly higher rate of recurrence, irrespective of gender.

Conclusion: One-fifth of UTI children had a recurrence, with a similar rate for males and females. Independent risk factors for recurrent UTI were found to be age > 5 years, and underlying disease of either GU anomalies or VUR.

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Association of 5HTR2A polymorphism with non-monosymptomatic primary nocturnal enuresis

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Background. Tricyclic antidepressants(TCA) was used for treatment of NE for decades of years. Recently, some case studies demonstrated the efficacy of some serotonin reuptake inhibitors (SSRI) in the treatment of enuresis. Both TCA and SSRI have the similar influence on serotonin neurotransmission. Serotonin participates in many physiologic processes such as sleep, thermoregulation, pain perception and hormone secretion. Animal studies also exhibits TCA exerts an inhibitory action on the micturition reflex by a central cholinergic mechanism. This study aimed to investigate 5-hydroxytryptamine (serotonin) receptor 2A (5-HTR2A) gene polymorphisms in children with primary nocturnal enuresis (PNE). Methods. The 5-HTR2A gene polymorphism was investigated in 151 Taiwanese children (99 PNE cases and 62 healthy, non-enuretic controls). The 5-HTR2A genes polymorphism (rs6313) of the 5-HTR2A genes were genotyped using PCR. Results. There were no significant differences when comparing the allelic frequencies and genotypes of 5HTR2A polymorphisms between NE with and controls. We subsequently compared in turns: arousal score, diurnal voiding symptoms (DVS), and constipation according to 5HTR2A genotypes and allelic frequencies. A significantly differences in genotype distribution in NE patients with DVS or constipation compared with mono-symptomatic NE patients were observed (p=0.037 and 0.010 ) and allele T was also increased in non-monosymptomatic NE patients. Conclusions. This study is the first to search the 5-HTR2A gene polymorphisms in children with PNE. It was determined that 5-HTR2A gene polymorphism, a predominantly TT genotype, may be associated with non-mono-symptomatic PNE in Taiwanese children.

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Pulse cyclophosphamide induction treatment in Thai children with diffuse proliferative lupus nephritis

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Background: Intravenous cyclophosphamide has been the standard treatment for diffuse proliferative lupus nephritis for more than 20 years. Recently, this recommendation is questioned regarding its effectiveness and side effects. We reported the effectiveness of pulse cyclophosphamide induction therapy and identified predictors for unresponsiveness to treatment in Thai children.

Methods: Children under 15 years of age with biopsy-proven diffuse proliferative lupus nephritis who were admitted to Chiang Mai University hospital between 2001and 2006 were retrospectively studied. Responsiveness to treatment, defined as urinary protein to creatinine ratio of less than 0.3, was assessed at the end of induction period. The clinical characteristics and laboratory data including gender, age at diagnosis of SLE, duration of disease before treatment, hypertension, clinical nephrotic syndrome, amount of proteinuria, serum creatinine, creatinine clearance, serum C3 level and presence of crescentic formation were compared between responsive and nonresponsive groups.

Results: A total of 29 patients (90% female) with the mean age of 10.3 ± 2.6 years were studied. Hypertension, microscopic hematuria and nephrotic-range proteinuria were seen in 66%, 86% and 60% of the patient respectively. Forty one percent of biopsy showed cellular or fibrocellular crescents. Twenty patients (69%) achieved remission at the end of induction therapy. There were no significant differences in all parameters studied between responsive and nonresponsive groups.

Conclusions: Pulse cyclophosphamide is an effective regimen for induction therapy in children with diffuse proliferative glomerulonephritis. No definite predictor for unresponsiveness was detected in this study.
P-153 Detection of Mutations in Adenine Phosphoribosyltransferase Deficiency in two families with 2,8-Dihydroxyadenine Urolithiasis by the LightCycler system

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[Background] Recently, a number of methods have been devised for detection of mutations in the field of molecular genetics. The newly available LightCycler® system has been used for rapid PCR, while simultaneously quantifying and analyzing the amplification results. We tried to apply the LightCycler® system to the diagnosis of Japanese-type (type 2) adenine phosphoribosyltransferase (APRT) deficiency in two families with 2,8-dihydroxyadenine urolithiasis.

[Cases] The first patient was a 3-year-old girl who presented with left flank pain. The second patient was a 2-year-old girl who presented with complaints of sudden dysuria. The spectrophotometric analysis of the stone fragments revealed an absorption spectrum for 2,8-DHA.

Results of Gene Analysis: We used the LightCycler® system to detect APRT*J and the PCR-SSCP method to detect APRT*Q0. The first patient was homozygous for APRT*J/APRT*J and the second patient was compound heterozygous for APRT*J/APRT*Q0.

[Discussion] The analysis of the APRT gene is the most reliable diagnostic method in infants. Major problems with the present PCR-SSCP method, however, are that it requires multiple manual steps, and it takes a very long time prior to the detection can be confirmed. Meanwhile, the analysis of the APRT gene using the LightCycler® system can provide mutation results within approximately 30 minutes after DNA isolation, and the results are easily and clearly visualized. The genetic diagnosis of APRT deficiency using this system may be useful not only as a diagnostic test for infants with known 2,8-DHA, but also as a screening of infants with a suspicion of urolithiasis.

P-154 Immunohistochemical analysis of cardiomyopathy in autopsy cases of sevev motor and intellectual disabilities

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OBJECTIVES: We reported the preliminary results of clinical analysis on cardiomyopathy in autopsy cases of severe motor and intellectual disabilities (SMID) (2006, 2nd ASPR). To further explore pathomechanisms, we immunohistochemically examined accumulation of oxidative products and expressions of antioxidant enzymes.

METHODS: The subjects consisted of 5 SMID autopsy cases of cardiomyopathy aged 3-59 years, and 4 controls aged 3-66 years. The cause of cardiomyopathy was speculated to be chronic carditis of unknown origin, cor pulmonale, suspicious selenium deficiency, subacute carditis related to hepatitis C virus (HCV) infection and acute selenium deficiency, respectively. Serial sections of cardiac tissue were treated with monoclonal antibodies against mitochondria and oxidative stress markers to DNA, lipid, and protein, in addition to polyclonal antibodies against cytochrome c oxidase (COX) and superoxide dismutases (Cu/ZnSOD and MnSOD).

RESULTS: Remnant cardiac tissues were immunoreactive for oxidative product to protein in cases but not controls, whereas neither cases nor controls showed accumulation of oxidative products to DNA or lipid. The remaining cardiac tissues demonstrated patchy or reduced expressions of mitochondria, COX and SODs in three cases of cardiomyopathy, being related to selenium deficiency and HCV infection.

CONCLUSION: Data indicate the possibility that oxidative damage to protein can be involved in cardiomyopathy in SMID patients. Disturbed mitochondrial functions with reduced antioxidant capacity seem to make an additional contribution to generation of cardiomyopathy, being related to selenium deficiency and HCV infection.

P-155 Abnormal white matter appearance on term FLAIR predicts neuro-developmental outcome at 6 years old consequent to preterm birth

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Purpose: Preterm infants are at significant risk of minor neuro-developmental disorders and learning disabilities at school age. Early reliable screening tools to identify high-risk infants are urgently required. The predictive value of term MRI with the minor neuro-developmental outcome at school age is still unknown. Materials and methods: 210 preterm-infants (<36 weeks) were studied to investigate clinical factors associated with white matter (WM) appearance on MRI. Results: Low-intensity signal in WM on fluid-attenuated inversion recovery (FLAIR) imaging was commonly observed (69%) at less than 2 months corrected-age. Its incidence correlated with corrected-age at scan and incidences of maternal pyrexia and cystic periventricular leukomalacia. Low-intensity signal in WM on FLAIR significantly correlated with physical and total developmental quotients, whereas diffuse high-intensity signal in WM on T2-weighted imaging correlated only with the total developmental quotient at 6 years (n=75, WISC-R). FLAIR imaging, but not T2-weighted imaging, predicted mild neuro-developmental delay at this age. Conclusion: FLAIR appeared to detect subtle WM injury related with neuro-developmental disorders at school-age, whereas T2-weighted imaging seemed to identify relatively more severe WM injury. FLAIR is a potentially sensitive screening tool for many infants that is readily available and easily interpretable.

P-156 Oxidative stress in neurodegeneration in dentatorubral-pallidoluysian atrophy

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Background: Dentatorubral-pallidoluysian atrophy (DRPLA) is one of CAG-repeat diseases, and it is classified into juvenile, showing progressive myoclonus epilepsy (PME), early adult and late adult types. The common neuropathological findings in DRPLA include degenerations of the basal ganglia and dentate nucleus. It has been discussed in Huntington’s disease that expanded polyglutamine can lead to oxidative neurodegeneration, and we examined involvement of oxidative stress in brain lesions in DRPLA.

Method: We performed immunohistochemistry for accumulation of oxidative products and expression of superoxide dismutase (SOD), a radical scavenger, in serial brain sections in autopsy cases of DRPLA.

Results: Oxidative products of nucleosides, 8-hydroxy-2’-deoxyguanosine and 8-hydroxyguanosine, were accumulated in the lenticular nucleus predominantly in DRPLA cases having PME. Mild neuronal accumulation of 4-hydroxy nonenal, a reactive lipid aldehyde, was found in the hippocampus, globus pallidus and cerebellar dentate nucleus in the adult DRPLA cases and controls. Cytoplasmic immunoreactivity for Cu/ZnSOD was reduced in the external segment of globus pallidus, dentate nucleus and cerebellar cortex in most DRPLA cases. Mitochondrial immunoreactivity for MnSOD was reduced in the lenticular nucleus and cerebellum in DRPLA cases having PME. Some DRPLA cases also showed reduced immunoreactivity for MnSOD in the cerebral cortex. Coexistence of reduced SOD expression and expanded polyglutamine was observed in the frontal cortex or lenticular nucleus in a few cases.

Conclusion: It is likely that oxidative stress can be involved also in DRPLA, although the exact relationship with expanded polyglutamine remains to be elusive.
P-157  CSF d-ROM levels in Japanese pediatric patients with CNS diseases
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[Background] Free radicals have been suggested to play a pathogenic role in a variety of central nervous system (CNS) diseases based on a growing body of evidence obtained from experimental models and the human brain.

[Methods] This study assessed the validity of using the d-ROM (Diacon-Reactive Oxygen Metabolites) test to examine the cerebrospinal fluid (CSF) oxidative status in pediatric patients with CNS diseases. The study included 75 Japanese pediatric patients with bacterial meningitis (BM; n=8), viral meningitis (VM; n=18), febrile seizure (FS; n=22), rotavirus gastroenteritis induced convulsion (RC; n=7), epilepsy (EP; n=17: cryptogenic 11, symptomatic 6), adrenoleukodystrophy (ALD; n=2) and multiple sclerosis (MS; n=1).

[Results] An analysis of the infection-associated group (BM, VM, FS, RC) showed that the CSF d-ROM levels in the BM group (average 119.4±76.2 U.CARR) were significantly higher than those in the VM (average 33±8.1 U.CARR), FS (average 9±6.1 U.CARR), RC (7±6 U.CARR) and control (average 4±4.1 U.CARR) groups. An analysis of the non-infection-associated group (EP, ALD, MS), the CSF d-ROM levels in symptomatic EP patients (27±49.5 U.CARR n=6) were higher than those in the cryptoegenic EP patients (8.0±10.0 U.CARR n=10) and controls (average 4±4.1 U.CARR) groups. A comparison of the non-infection-associated group and controls revealed the difference was not significant. As for demyelinating disease such as ALD (n=2) and MS (n=1), patients with progressive ALD or MS had higher d-ROM levels (39 and 74 U.CARR, respectively) compared to other ALD patient at early stage (2 U.CARR).[Conclusion] In patients with CNS diseases, the CSF d-ROM levels may correlate with their clinical severities or symptoms.

P-158  Maturation of proprioceptive nerve in full-term and preterm infants
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[Background] There are several studies on the maturation of proprioceptive nerves in neonates and a few in preterm infants.

[Methods] To evaluate the maturation of efferent motor nerve and afferent sensory nerve in comparison between full-term (FT) and preterm infants (PT), M waves and H-reflex were examined at a similar post-conceptional age.

[Results] Eleven FT (gestational age 38~41weeks) and PT infants (gestational age 26~34weeks) were recruited for the study. Informed consents were obtained from the parents. M-wave and H-reflex were recorded within the first week of life for the FT infants while the same parameters were measured for premature babies when they reached the expected time of birth using four channel evoked potential examination apparatus (Signal processor-7812, NEC Medical Systems). The median nerve was stimulated at the wrist and elbow and M-wave and H-reflex were recorded from the abductor pollicis brevis muscle. The motor and proprioceptive nerves conduction velocities (MCV and HCV, respectively) were determined by dividing the distance between the onset of the proximal and distal responses by that distance.

[Discussion] The MCV of PT (25.0±4.5m/s) was comparable to those of FT infants (25.5±4.5m/s). In contrast, the HCV of PT (20.1±5.6m/s) was significantly lower than those of FT infants (25.0±4.5m/s). Conclusion: These findings suggest that myelination in the afferent sensory nerves may delay in the extraterine environment for PT infants. Maturation of proprioceptive nerve of PT infants hence may be influenced by nutrition or medication after birth.

P-159  Prevalence of Developmental Delay as Detected by Routine Filipino Denver Screening on Children Ages 1-3 Years Old Seen at Barangay Minantok, Amadeo, Cavite, Philippines
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[Objective] To be able to determine the prevalence of developmental concerns in apparently well children aged 1-3 years old by using the Filipino Denver Developmental Screening Tool.

[Study Design] Cross sectional.

[Study Population] All children ages 1-3 years old (63) at Barangay Minantok, Amadeo, Cavite who fulfilled the inclusion criteria.

[Methodology] All children aged 1-3 years old were interviewed. Parents were asked to fill-out a questionnaire regarding socio-demographics. A scheduled interview regarding the socio-demographic, maternal factors, and neonatal factors was conducted. Afterwards, Filipino Denver Developmental Screening Test was administered. Background data of subjects who have been identified with developmental concern were revisited and risk factors present in their histories were determined and reported for correlation.

[Result] Almost 63 subjects screened had unremarkable demographic, maternal, and neonatal histories which may contribute to the child’s development. Two of the population screened were noted to have developmental concern, 1 as language delay and the other as fine motor delay.

[Conclusion] Four percent (4%) of the screened population had developmental delay. The earliest domain to have delay in this study is the language domain.

P-160  Neurological and immunological complications in a case of Olmsted syndrome
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[Background] Olmsted syndrome is a rare disorder which was first described by Olmsted HC in 1927, and is dermatologically characterized by sharply marginated keratoderma in the palms and soles, perioral keratoderma and alopecia. We reported a 23-year-old male patient with Olmsted syndrome showing rare neurological and immunological complications.

[Case Presentation] There was no family history of keratosis or neurological disorders. In infancy, he suffered from marginated keratoderma, and acrodermatitis enteropathica was suspected, which was temporally controlled by replacement therapy of zinc sulfate. Gradual development of periorificial and bilateral palmoplantar keratoderma with alopecia led to the diagnosis of Olmsted syndrome, and hyperkeratosis in skin biopsy specimen supported the diagnosis. He also demonstrated motor clumsiness, mental retardation, optic nerve atrophy, spastic gait, and hyporeflexia with numbness at the ends of extremities. He was suspected as having primary peripheral neuropathy because of delayed conduction velocity and reduced myelinated fibers in biopsied peroneal nerve. He also developed multiple demyelinated lesions and asymptomatic signal change in the corona radiata on magnetic resonance imaging in addition to having sepsis repetitively. At the age of 23, he was complicated with myelodysplastic syndrome (MDS), and he died of sepsis one year after.

[Conclusion] The occurrence of neurological and immunological complications itself is rare in Olmsted syndrome, but that may suggest the possible linkage between hyperkeratotic syndrome and neurological and/or immunological disturbances.
P-161 Prognosis and steroids treatment of Bell’s palsy in children

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Background: Bell’s palsy is an acute facial paralysis due to CN VII dysfunction without detectable causes. Most of patients have spontaneous recovery. Steroids treatment is widely used but its effect is still not known. Objectives: To determine the prognostic factors and outcomes of steroids treatment of Bell’s palsy in children. Methodology: Prospective study was conducted for children diagnosed Bell’s palsy for 5 years. Data collections were age, sex, prodromal symptoms, prednisolone treatment, and recovery rate. Survival analysis with Log-Rank test, Kaplan-Meier curve. Results: There were 23 children diagnosed Bell’s palsy. The mean age was 5.4 years old. Facial palsy on the right side were 56.5%. The mean duration of follow up was 53.3 days (range 8-262 days). The recovery rate was 69.6%. The mean duration of recovery was 58 days compared to 36 days of patients without recovery which was not significantly different (p value =0.36). The outcome of prednisolone treatment was not different between 2 groups. The recovery rate of prednisolone group was 61.1% compared to 100% of control group. No any prognostic factors were found in this study. Conclusion: The prognosis of Bell’s palsy in children is good. Seventy percent of patients have spontaneous recovery within 58 days. No prognostic factors were found including prednisolone treatment.

P-162 INFLUENZA-RELATED NEUROLOGIC COMPLICATIONS (INCs) IN CHILDREN HOSPITALIZED WITH LABORATORY-CONFIRMED INFLUENZA (LCI) IN HONG KONG: COMPARISON WITH USA

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Introduction & objective: In USA, the incidence of INCs in hospitalized children with LCI was 4 per 100,000 person-years reference 1. Incidence of Influenza-related hospitalization for children in Hong Kong (HK) is ~120 per 10,000 reference 2, which is 3-10-fold exceeding USA. Our objective is to examine INC in HK children.

Method: A retrospective study was performed in March 1998-February 2003 in our unit, the only public pediatric service for a population of 100,000 <16 y.o. in HK, where public sector provides ~90% medical service. Nasopharyngeal aspirate for immunoassay and culture for influenza was routinely performed in children with respiratory symptoms.

Results: There were 874 LCIs and 20% developed INCs. A comparison between HK and USA was shown in Figure 1. Majority (90%) was febrile seizure (FS) and only 5 (0.6%) were encephalopathy. Two patients died; 1 with underlying methylmalonic aciduria while the other was a previously healthy 6 y.o. girl who developed shock, DIC and died on D2 fever. CT brain showed generalized cerebral edema and hypodense lesions in thalamus, brainstem and basal ganglia. The picture is compatible with acute necrotizing encephalopathy reference 3 frequently reported in Japan.

Conclusion: Combining previous findings, incidence of INCs was ~240 per 100,000 person-years in HK. The discrepancy between HK and USA is at least partly attributable to different admission threshold for influenza-related illnesses and FSs. INC data from Japan will be of great interest if inter-ethnic difference in the neurotropic effect of influenza is to be explored.

P-163 CYP2C19 polymorphisms as a predictor of adverse effects of clobazam

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Background: Clobazam (CLB) is effective in treating intractable epilepsy, but with occasional adverse effects that often require dose decrease or termination. CLB is metabolized to N-desmethyl CLB (N-CLB) by CYP3A4, and then to an inactive metabolite by CYP2C19. We have previously shown that 1) the ratio of serum levels of N-CLB to CLB was increased in patients with two mutated CYP2C19 alleles, 2) patients co-medicated with CYP3A4 inducer showed lower CLB concentration/dose. Purpose: To examine effects on occurrence of adverse effects of CLB of the number of mutated alleles of CYP2C19 and co-medication with CYP2C19 alleles, 2) patients co-medicated with CYP3A4 inducer showed lower CLB concentration/dose. Method: A retrospective study was performed in March 1998-February 2003 in our unit, the only public pediatric service for a population of 100,000 <16 y.o. in HK, where public sector provides ~90% medical service. Nasopharyngeal aspirate for immunoassay and culture for influenza was routinely performed in children with respiratory symptoms.

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P-164 Autosomal dominant hyperkalemic periodic paralysis with biallelic mutations of the SCN4A gene

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Introduction: More than 20 missense but no truncation mutations in the skeletal muscle voltage-gated sodium channel α subunit (SCN4A) gene have been identified in various forms of skeletal muscle sodium channelopathies including hyperkalemic periodic paralysis (PP), paramyotonia congenita, potassium-aggravated myotonia, hypokalemic PP and congenital myasthenic syndrome.

Method: The proband was a Japanese 12-year-old boy, who experienced his first attack of paralysis at the age of one year. Thereafter, paralytic attacks intermittently recurred a few times per day, each lasting for several minutes to an hour. The weakness most often appeared during a rest after strenuous exercise, and repeated exercise alleviated the weakness. After informed consent was obtained, we analyzed exons 9, 13, 14, 19, 22, 23 and 24 of SCN4A, the regions of SCN4A containing mutations in hyperkalemic PP patients reported previously, using PCR and direct sequencing.

Results: We detected a missense mutation in exon 13 (c.2375T→G, V792G) of the maternal origin and a one-base deletion in exon 24 (c.4677delC, P15606X1650) of the paternal origin in the heterozygous form in the proband and his younger brother. Discussion: We have identified biallelic heterozygous novel mutations V792G and P15606X1650 in the SCN4A gene in siblings with hyperkalemic PP. Their mother and five her relatives had the same symptoms, while their father had severe stiff shoulders but no paralytic attack. The phenotype of the siblings appeared to be caused by not the P15606X1650 mutation, but the V792G mutation, located at the sixth transmembrane segment of domain 2 of SCN4A.
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13q partial monosomy presenting with Arima syndrome and bilateral retinoblastoma.

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Arima syndrome is characterized by hypoplasia of the cerebellar vermis, cystic kidney disease, and ocular abnormalities including chorioretinal coloboma, blepharoptosis, and nystagmus. The causative genes have not yet been identified. Here we present a case of Arima syndrome and bilateral retinoblastoma, who had partial monosomy 13q14.13-q32.3. <Case> The female patient was the second child of healthy parents. During gestation, there were growth retardation, oligoamnios and breech presentation. She was born by caesarean section at 37 weeks’ gestation, weighing 1665g. She showed severe psychomotor retardation, characteristic facial appearance including bilateral ptosis and nystagmus. There was neither tachypnea nor apnea. Brain magnetic resonance imaging showed hypoplasia of cerebellar vermis. Ultrasonography showed bilateral polycystic kidney. Ophthalmological examination showed partial coloboma iridis and right partial retinal dystrophy. From these symptoms, we diagnosed this case as having Arima syndrome. At 3 months of age, she was affected with bilateral retinoblastoma. Fluorescence in situ hybridization demonstrated RB1 gene (13q14.2) deletion. High resolution chromosome binding analysis of chromosome 13 showed deletion (13) (q14.13q32.3). A SNP array was used to clarify the precise region of deletion and to detect loss of heterozygosity. <Conclusion> We consider that this case had a contiguous gene syndrome resulting from partial 13q deletion. Our analysis suggests that one of the causative genes of Arima syndrome is located between 13q14.13 and q32.3.

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Single Nucleotide Polymorphisms of GABRG2 in Idiopathic Generalized Epilepsies (IGEs)

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Purpose: Mutations in γ-aminobutyric acid(GABA) A receptor γ2 subunit gene(GABRG2) were independently identified in families with generalized epilepsy with febrile seizures plus(GEFS+) and families with absence epilepsy and febrile seizures(FSs). The present study assessed the role of GABRG2 gene in idiopathic generalized epilepsies(IGEs) of Korean population. Methods: 23 IGEs and 94 healthy control subjects were selected throughout a collaborative study of Catholic Child Neurology Research Group. The SNP211037 of GABRG2 were screened by DHPLC. DNA fragments showing variant chromatograms were subsequently sequenced. Genotypes and allelic frequencies for GABRG2 gene polymorphism in three groups were compared. Results: Genotypes and allelic frequencies of the γ2 subunit of the GABA receptor gene(SNP211037) in both groups were not significantly different. The most common genotype for GABRG2 (SNP211037) gene in both groups were T/C heterozygote. The allele C and T frequencies for GABRG2 (SNP211037) in IGEs group were 45.7% and 54.3%, respectively; and in healthy control group, 42.6% and 57.4%, respectively. The number of individuals with the GABRG2 (SNP211037)-C/C genotype in IGEs group greater compared with that in healthy control group(21.7% versus 12.8%). The odds ratio for developing IGEs in individuals with the GABRG2 (SNP211037)-C/C genotype was 1.70 compare with individuals with the GABRG2 (SNP211037)-T/T genotype, but was not significantly different. Conclusion: These data suggest that genomic variations of GABRG2 might not be one of the susceptibility factors for IGEs in the Korean population.

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Optimizes Prototype for Database Collection of Child Abuse in Emergency Room Setting

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Background: Child abuse is one of the serious problems in childhood. There are only a few study in Thailand and lack of complete data collection system. Objectives: To study the epidemiologic data of child abuse case for creating an optimized prototype for data collection system at the emergency room. Methods: The medical records of child abuse cases attended in the emergency room at Ramathibodi Hospital between Jan 2001 to Dec 2004, were retrospectively reviewed. The demographic data included age, sex, type of abuse, abuser, sender, education, sibling and order, family member, parent’s career, family relationship, substance abuse in family and socioeconomic status. Then the multivariate analyses were used for determining the correlation of each variable. Results: One hundred child abuse cases (84 females, 16 males) with a mean age of 9 years, were enrolled in the study. The child abuse was defined as sexual abuse (60%) and physical abuse (40%). The prevalence of sexual abuse was gradually increased form 6 cases in the year 2001 to 9, 22 and 23 in the year 2002, 2003 and 2004 respectively. The multivariate analyses revealed that there was no statistically significant correlation between the sexual/physical abuse and all variables. This may be explained by a rather small sample size. However, the computerized data collection system for child abuse has been created. Conclusions: The prevalence of sexual abuse gradually increased. A further cohort study in a large sample size is warranted.

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Early detection of anorexia nervosa in school

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Background: In spite of the fact that anorexia nervosa is refractory disease with a high mortality rate, many patients and their parents are in strong denial about this disease and therefore early detection is considered to be difficult. We are trying to prevent and detect anorexia nervosa early by using growth curves and pulse rates in school. Methods: Since 2001, based on the physical measurement values of the girl students in the health examinations conducted twice a year in two private junior high schools, we have collected those who fall under the following conditions: (1) downward shift of weight by 1 channel and more on a growth curve and the degree of obesity ≤15%, (2) weight loss of ≥3 kg. Among these students, when bradycardia (heart rate ≤60/min) or amenorrhea is detected, we refer them to medical institutions. Results: Twenty students were referred to medical institutions, and 19 of them except one consulted a doctor. Among these 19 students, 2 were diagnosed as underweight, 17 as anorexia nervosa. In these two schools, we have performed early interventions before the level of emaciation reaches to a severe condition. Therefore, progressive anorexia nervosa has not been detected since our screening program was launched. Conclusions: When weight loss or poor weight gain on a growth curve are observed based on the physical measurement values, and bradycardia or amenorrhea is detected, the possibility of a diagnosis of anorexia nervosa should be considered, and early close examination is required.
P-169 Stop the Anorexia Nervosa: An intensive Psychophysio-educational Programme by Pediatricians-Child Psychiatrist Team in Japan

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Background: Against the backdrop of ever increasing number of anorexia nervosa (AN) among early teen-age girls in Japan, training of inpatient treatment by a full-time child psychiatrist has become an essential component of the postgraduate training programme at the Department of Pediatrics, Keio University Hospital in Tokyo. Over the past 12 years within our pediatric ward, we developed ANICU (anorexia nervosa intensive care unit), a comprehensive step-by-step program for recovery from extreme emaciation.

Methods: 70 children (64 girls, 6 boys) who underwent inpatient treatment of ANICU at Keio Hospital over the past 12 years. Results: All patients were seriously ill cases with multiple organ failures. With sincere empathic attendance and care including systematic feeding session and firm emotional containment at times of children’s distress, all patients steadily recovered physically and emotionally to their healthy weight, and endocrinological state, feeding behaviors and enhanced self-esteem. Conclusions: AN is a serious psychosomatic disease with a high risk of death, recurrence and life-long suffering. With ever increasing numbers of young teen-age AN in Japan today, combined team of child psychiatrist and pediatricians play a vital role in rescuing children with AN.

P-170 An urgent need for a 24 hour crisis center for sexually—abused young children and disabled people in Japan.

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Background: Recently, many sexual crimes are reported by mass media, which include murders, kidnap and sexual abuse by pedophiles. Although Japan approved ratification the Treaty of Children’s Right in 1994, pedophiles go unpunished in the society.

Methods: We study the present system for sexually-abused children in Japan through following case studies of young and disabled children which became court cases.

Subjects: A 3-year-old girl who was sexually abused by the male teacher in the kindergarten. A 9-year-old and a 11-year-old girls who were sexually abused by the teacher in the special education class of the elementary school. A 16-year-girl who was raped by a elder student in the high school for handicapped children. Results: Our study revealed that there are no 24 hour crisis center for sexually—abused children and disabled people in Japan. These cases revealed that the victims had no access to medical after care, making it impossible to produce any evidence. Conclusions: We should create a 24 hour crisis center to help sexually—abused children and disabled people.

Prevalence of Attention Deficit-Hyperactivity Disorder among Primary School Students in Southern Thailand

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Background: Attention deficit-hyperactivity disorder (ADHD) is a disorder in which those affected display symptoms of hyperactivity, inattention and impulsivity. Its prevalence has been reported as 3-20% in other countries but its prevalence has not been studied in our region.

Objectives: To study the prevalence and distribution of subtypes of ADHD in primary school children in Hat Yai, southern Thailand.

Method: A cross-sectional study was performed in first grade Hat Yai students from 15 primary schools using the Conners’ Abbreviated Parent/Teacher Questionnaires. Children with positive scores (> 12) and their parents were randomized and interviewed by a pediatric psychiatrist using DSM IV.

Result: 2,539 questionnaires were sent out of which 2,293 (90.3%) were returned. 1,479 (90.7%) of the students were from private schools and 814 (89.5%) from public schools. The age range was 4.0-9.9 years with a mean of 7.8±0.5 years. 949 students (34.6%) tested positive for ADHD, of whom 198 were interviewed with their parents to confirm the ADHD diagnosis. 46 were proven to have ADHD, giving a prevalence of 8.0%. The prevalences in private and public schools were not significantly different (7.6% vs. 8.1%, p=0.3). The male to female ratio was 2.5:1. Hyperactive, inattentive, and combined subtypes were found to be 2.1%, 3.1% and 2.8%, respectively. (p=0.9).

Conclusions: The prevalence of ADHD among school children in southern Thailand was 8% and males predominated. The distribution of the 3 major subtypes was similar.

Effects of prenatal visits on mood status of expectant mothers of premature infants

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Background
Expectant mothers of premature infants often have psychological problems. When pregnant women admit to the mother-fetus intensive care unit (MIFCU), they would feel to be isolated and would have mood disturbances. The purpose of this study is to evaluate the effects of prenatal visit on mood status of expectant mothers of infants.

Methods
Participants consisted of 27 women who were treated at the MIFCU in the Kansai Medical University Hospital and have delivered from December 2006 to May 2007. Prenatal visit sessions were held once a week by a neonatologist and a clinical psychologist of the neonatal intensive care unit (NICU). In the sessions, the neonatologist ask the expectant mothers about their anxieties, complaints and requests while clinical psychologists observed and helped them to open their thoughts freely. Before and after the sessions, the participants were asked to complete the Japanese version of the Profiles of Mood Status (POMS).

Results
Ages of participants ranged 24 to 42 years, average of gestational age was 31 weeks, and average length of the stay in MIFCU was 52 days. Compared the scores of POMS subscales after the prenatal visit with those of before the sessions, average score in regard to “depression” among POMS subscales was significantly decreased after the sessions. The results indicated the mood status of the participants improved after the prenatal visit sessions.

Conclusions
Prenatal visits by a neonatologist and a clinical psychologist would relieve psychological stress and improve mood status of the expectant mothers of premature infants.


P-173 Bed sharing and sleeping position in Thai neonates: the association with parental socioeconomic status

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**Background:** The American Academy of Pediatrics recommends that infants should sleep in a supine position and in a bed separate but proximate to adults to prevent Sudden Infant Death Syndrome (SIDS). Cultural differences and a lower rate of SIDS in Asian populations may affect infant sleeping arrangements.

**Objective:** To study bed sharing and sleeping position in Thai neonates and the relationship to parental and infant characteristics.

**Methods:** A cross-sectional survey based on interviews with parents of infants aged 21 days old, conducted under the Prospective Cohort study of Thai Children.

**Results:** Of the total sample, 2,236/3,692 (60.6%) shared a bed with their parents, and 39.3% shared a room but slept in a different bed. Sixty percent of the parents place their infants to sleep in a supine position, 32.2% placed on their side, and 4.9% in a prone position. Bed sharing was associated with older maternal age, higher parental education and with professional careers. Places the infants to sleep in a non-supine position was associated with older maternal age, higher parental education, higher income, professional careers, and with infant birth weight of > 2,500 gm.

**Conclusions:** Bed sharing is more common in Thai neonates than has been reported from other countries, but rates of sleeping in the non-supine positions are comparable. The main factor associated with bed sharing as well as putting infants to sleep in the non-supine positions was a higher parental socioeconomic status (SES), in contrast to previous studies in which both are associated with low maternal SES.

P-174 Preliminary study of visual reliance and target size effects on reach-to-grasp movement in children with high functioning autism

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Motor coordination problems have been reported in children with autism, however there were little studies addressing whose sensory reliance in fine motor tasks. In this study, there were four conditions of reach-to-grasp movement: large target with visual feedback (VL), small target with visual feedback (VS), large target with non-visual feedback (NL), and small target with non-visual feedback (NS). Conditions to investigate the effects of visual condition and target size. A counterbalanced repeated measure was designed. Ten children with high functioning autism (HFA) and 10 normal subjects were matched according to age and handedness. Qualisys motion analysis system was used to capture the reach-to-grasp movement. Kinematic data such as movement time (MT), peak velocity (PV), normalized jerk score (NJS), movement unit (MU), maximal grip aperture (MGA), normalized maximal grip aperture (NMGA) and so on were analyzed. The results of kinematic performance showed that children with HFA have larger MU (which represented for motor facileness) than controls in VS condition, but no differences between two groups in VL condition were found. In non-visual feedback condition, children with HFA also demonstrated significantly longer MT, larger NJS (which represented for motor smoothness) and more MU than controls, especially while the target was small. This study suggested that children with HFA have problems on motor smoothness and coordination in the process of the reach-to-grasp movement, especially in non-visual feedback and small target condition which suggested that children with HFA depend more visual cuing on performing prehension tasks and demonstrate poor coordination in high accuracy tasks.

P-175 EFFECT OF INTERNET UTILIZATION ON RISKY BEHAVIORS AND SCHOOL PERFORMANCES AMONG MIDDLE ADOLESCENTS IN BATANGAS

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**Introduction:** The advent of internet brought several advantages as well as disadvantages especially among mid adolescents. **AIM:** The study aims to determine the effect of Internet utilization among middle adolescents from Batangas province on risk taking behavior and school performance.

**Material:** A self-administered questionnaire on internet utilization, risky behavior and school performance, formulated through focused group discussion, had been accomplished Four hundred eight randomly selected high school students ages 14 - 16 year olds with no diagnosed psychiatric disorder participated in this study.

**Results:** Eighty percent of the population are internet users, 75% had been using it for more than six months. Most common place of use is at home(43.8%), internet shops (32.9%) and schools (18.3%). Frequent internet activities are using it for more than six months. Most common place of use is at home(43.8%), internet shops (32.9%) and schools (18.3%). Frequent internet activities are gaming (44.2%), research (35.7%) and chatting (14%). Adolescents who engage in gaming, downloading and chatting more are likely to smoke, Internet gamers have the highest risk of alcohol and drug use, gambling, involvement in incidents of violence and failure. Seventy percent preferred to chat with friends.

**Conclusion:** Rate of internet use among middle adolescents in Batangas is 50.4%. Those who indulge more in internet gaming and downloading entertainment materials are more likely to develop risky behavior such as smoking, alcohol drinking, illicit drug use and violent behavior. They have a higher possibility of failure in school as well. Most middle adolescent in Batangas would prefer internet interaction with people closely connected to them. Non disclosure of real identity, age and gender are common among mid adolescents internet interaction.

P-176 A Randomized Controlled-Clinical Trial Of Refrigerated Needles And Room Temperature Needles In Reducing Pain Associated With Diptheria-Pertussis-Tetanus Vaccination in 4-6 year-old Children

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**Objective:** To determine and compare the effectiveness and adverse effects of refrigerated and room temperature needles in reducing pain associated with DPT booster vaccination in 4-6 year-old children.

**Design:** Randomized, double-blind, controlled-clinical trial

**Participants:** One-hundred four pre-school children for DPT vaccination.

**Intervention:** Subjects were randomized into refrigerated and room temperature needle group prior to injection of DPT

**Outcome Measures:** The effectiveness of refrigerated needles and room temperature needles were compared in terms of pain reduction using the Wong Baker Faces Pain Scale. The heart rate, blood pressure and oxygen saturation before, during and after the vaccination were the secondary outcome measures.

**Results:** The increase in heart rate, increase in blood pressure and decrease in oxygen saturation from baseline, during and after vaccination among treatment groups were statistically insignificant (p-values 0.128, 0.209, and 1.00, respectively). The pain scores from the two groups showed marginally statistically significant result (p-value 0.055). Fifty-two percent of subjects in room temperature needle group have 0-1 pain score compared to forty-two percent with refrigerated needles. However, it is significant to note that with pain scores of 4-5, the room temperature needle group showed a higher percentage of 36.5% compared to 26.9% in refrigerated needles. Reported adverse events were redness for both needle groups. Blanching was noted with room temperature needle group.

**Conclusion:** The use of refrigerated needles does not decrease the pain associated with DPT vaccination in 4-6 year-old children as compared with room temperature needles.
P-177 A Randomized Clinical Trial on the Effectiveness of Icegel Compress versus Lidocaine-prilocaine Cream in Reducing Pain Associated with Diphtheria-Pertussis-Tetanus Vaccination

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Background: In order to determine and compare effectiveness, adverse events and cost of icegel compress and topical lidocaine-prilocaine cream in reduction of pain associated with BDPT/B vaccination in preschool children, a randomized placebo-controlled clinical trial was conducted in daycare centers in Cabiao, Nueva Ecija. Methods: One-hundred twenty-five students scheduled for BDPT/B booster were randomized into lidocaine-prilocaine, 5-minute icegel compress, 10-minute icegel compress and placebo group prior to BDPT/B injection. Effectiveness of icegel was compared with lidocaine-prilocaine and placebo in terms of pain reduction using Wong-Baker Faces and BFLACC/B (Face-Legs-Activity-Cry-Consolability) pain scales. Increase in heart rate and decrease in O2 saturation during vaccination were measured and compared with the baseline value taken before injection. Results: The mean pain scores of all treatment groups were significantly different using one-way anova test (p-value<0.00001). Bonferroni test showed that lidocaine-prilocaine was not significantly different between icegel-5 and icegel-10 (p-values=0.300). Icegel-10 has statistically significant lower pain scores compared with the icegel-5 (p-value=0.015). Placebo group has significantly higher pain scores compared to other three treatment groups (p-values<0.001). There was statistically significant difference in increase in heart rates and reduction of O2 saturation among treatment groups (p-values=0.0134 and 0.0109, respectively). Conclusion: Icegel compress is as effective as topical lidocaine-prilocaine with regards to pain reduction. Ten-minute application is more effective than 5-minute application. There is lower increase in heart rates and lower decrease in O2 saturation when icegel is applied. Icegel is more economical than lidocaine-prilocaine. No adverse events were noted on all subjects given icegel compress.

P-178 Adnexal torsion in children

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Objectives: Adnexal torsion is an acute abdominal condition often confused with other diseases in children. The objective of this study is to evaluate the diagnosis, characteristics and treatment of adnexal torsion in children to reduce morbidity.

Methods: We reviewed the medical records of all cases of children whose adnexal torsion diagnosis was proven by surgery from 1992 to 2005. Prenatal cases were excluded. Results: A total of 49 cases were enrolled; the mean age was 12.5 years. Sixteen (32.6%) cases were premenarchal girls. This group was significantly more likely to have adnexal problems missed at first clinical diagnosis compared to postmenarchal girls (P=0.032). Of patients, 32% had severe abdominal pain and 14.2% had a history of recurrent pain over 2 weeks. Of abdominal gray scale ultrasound evaluated in 43 patients, 41 were suspicious for ovarian pathology. Seventeen patients had both ultrasound (US) and abdominal computerized tomography (CT). These had relatively high infarction or necrosis compared with US alone (82.3% versus 61.5%). Fever was significantly associated with infarction or necrosis (P=0.004).

Conclusions: Adnexal torsion should be considered in pediatrics girls with abdominal mass and any degree of abdominal pain. Most pediatric adnexal torsion occurs in postmenarchal patients but should not be overlooked in premenarchal girls with abdominal pain. Ultrasound plays an important, but not definitive role in diagnosis. Multiple radiographic studies with combined CT and US did not adversely affect viability or infarction. An emergency operation should be performed, especially in suspected adnexal torsion with fever to avoid further ovarian damage.

P-179 Two adolescent-boy of influenza B virus infection complicated with abnormal behaviors.

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Introduction: In last March, the Japanese Ministry for Health, Labor and Welfare issued a warning to doctors not to prescribe oseltamivir phosphate to adolescents aged 10-19 years. This announcement was in response to unusual suicide after taking oseltamivir phosphate in Japan. We present two adolescent-boys who were noted on all subjects given icegel compress.

P-180 Effectiveness of Government-sponsored Disease Management Program in Improving Severity of Pediatric Asthma in Taiwan

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Background: Disease management for asthma obtains good effect in many countries in recent years. Bureau of National Health Insurance (BNHI) in Taiwan implemented a medical amendment (disease management) on asthma since 2001 November.

Method: This is a retrospective study by pediatric pulmonologists and asthma educators in a regional teaching hospital. The children from an outpatient pulmonology clinic were expected to receive 5 times of comprehensive evaluation visit (CEV) to classify asthma severity and receive asthma education in 1 year. We analysis the asthma severity and the severity change.

Result: 700 asthma children (0-17y/o, mean 5.7±3.4 y/o) enrolled from 2005 March to 2007 February. The severity of intermittent asthma, mild, moderate, and severe persistent asthma were 7.9%, 30.9%, 41.1%, 0.1%. 31.4% of the objects only received the first time of CEV in 1 year. Others receiving only 2.3, and completing 5 times of CEV in 1 year are 27.3%, 17.4%, 13.7%, 10.2%. We compare the asthma severity of the last time to the first time of CEV. The percentages having improved asthma in the groups receiving 2,3,4, and 5 time of CEV are 22%, 37.7%, 54.2%, 56.3%, and strongly positively relative to the times of CEV (r=0.96). Among the 72 children completing 5 times of CEV, group of 7-12y/o and moderate persistent asthma group had the largest possibility to improve asthma severity.

Conclusion: The disease management on asthma by BNHI in Taiwan improves asthma severity in majority of pediatric asthma, especially in group of 7-12y/o and group of moderate persistent asthma.
P-181 Obstructive Sleep Apnea Syndrome Presenting with Psychiatric Symptoms

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Background: Clinical symptoms of sleep apnea syndrome (SAS) may include drowsiness, inattentiveness and depressive state that mimic those of depressive disorders. Here we present two cases of SAS who were referred to our hospital because of psychiatric symptoms.

Case 1: A 12-year-old girl had daily headache for two years. She recently complained of dizziness, irritability and was often absent from school. Arialotoxics and counseling failed to relieve these symptoms. Moreover, she also had insomnia and snoring during sleep, and difficulty in waking up in the morning. On physical examination, obesity and hypertension were noted. Otorhinolaryngological examination disclosed stenosis of the upper respiratory tract due to adenoid hypertrophy. Polysomnography demonstrated severe obstructive SAS. Adenoidectomy followed by weight control markedly improved her symptoms.

Case 2: A 13-year-old girl without obesity had excessive daytime sleepiness, irritability, and difficulty in schoolwork after entering a junior high school. She was initially diagnosed as adjustment disorders and depression, but several antipsychotics had no effects. When she was referred to our hospital after a year from the onset, she had snoring and mouth breathing. Blood examination showed polycythemia. Overnight polysomnography demonstrated mild obstructive SAS. Nasal continuous positive air pressure during sleep remarkably improved her symptoms.

Conclusions: SAS should be considered in the differential diagnosis of adolescent patients presenting with psychiatric symptoms.

P-182 Efficacy and Safety of Intravenous Aminophylline Infusion in Children with Acute Exacerbation of Asthma: A Multicenter Randomized Trial

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Background: Use of aminophylline is an additional treatment for acute exacerbation of asthma. IV aminophylline is a “classical” bronchodilator but may have therapeutic advantages in its putative anti-inflammatory effect and availability to peripheral airways where inhaled drugs may inadequately reach.

Objective: To assess if the addition of aminophylline infusion to standard treatment for acute exacerbation of asthma would enhance the recovery without serious adverse events.

Methods: Children aged 2 to 15 years with acute asthma who did not respond to repeated inhalations of β2 agonists were enrolled. All subjects were treated with inhaled salbutamol and methylprednisolone/hydrocortisone infusion and were randomized to receive additional aminophylline infusion (Group A) or none (Group B). Asthma symptom score and wheezing on auscultation were compared. Results: Fifty subjects were enrolled with 26 randomly allocated to group A and 24 to group B. The groups were well matched at baseline. One in group A and 7 in B dropped out because of exacerbation or non-compliance and outcome was analyzed in 24 from A and 17 from B. Faster improvement in symptoms were seen in Group A and there was a significant difference in symptom score at 24 hours after treatment between the groups (p=0.05). The time to resolution of wheezing was significantly shorter in Group A than in B (p<0.01).

Conclusion: Our results showed that an addition of aminophylline may be a beneficial therapeutic option for children with acute asthma.

P-183 The prognosis of acquired vocal cord paralysis after open-heart surgery

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[Background] Vocal cord paralysis (VCP) after open-heart surgery subsides spontaneously in most of the childhood patients. However, it doesn’t always subside and the tracheostomy is needed in some patients. To elucidate the prognosis of VCP after open-heart surgery, we reviewed the patients with the disease.

[Methods] Between 2001 and 2006, twenty-eight babies were diagnosed as having VCP in The University of Tokyo Hospital. We can check the final condition of congenital VCP in 23 patients. In 11 patients, VCP was complicated after open-heart surgery. We examined symptoms and the mobility of vocal cord by laryngofiberscopy.

[Results] The cause of VCP was identified in 20 patients; open-heart surgery in 11 patients, extra-low-birth-weight at delivery in 4 patients, other disorders in 5 patients, and unidentified cause (idiopathic condition) in 3 patients. VCP after open-heart surgery subsided spontaneously in 8 of 11 patients (6 were fully, 2 were partially) by 6 months after the surgery. However in 3 patients, VCP did not subside by 14 to 53 months after the surgery; a case received tracheostomy at 5 months after surgery as the severity of symptoms.

[Conclusions] Our observation suggests that we can predict the prognosis of VCP after open-heart surgery at 6 months after the surgery. Tracheostomy is not recommended for the mildly symptomatic VCP patients within 6 months, as most acquired VCA who had received open-heart surgery subsided spontaneously by 6 months after the surgery. However, the VCP that did not subside by 6 months after the surgery did not subside later.